遗传资源与进化国家重点实验室
State Key Laboratory of Genetic Resources and Evolution

2021年报
ANNUAL REPORT

中国科学院昆明动物研究所
KUNMING INSTITUTE OF ZOOLOGY .CAS

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主任致辞

日月其迈，时盛岁新。2021年是中国共产党建党100周年，也是“两个一百年”奋斗目标的历史交汇点。在各级主管部门的领导与关怀下，遗传资源与进化国家重点实验室立足于我国西南和东南亚丰富的生物多样性遗传资源，面向战略生物资源的国家重大需求和世界科技前沿以及经济主战场，在任务承担、科研成果、队伍建设、开放交流等各方面工作均取得了可喜进展。

在承担科研项目方面，实验室积极发挥集群优势，组织策划国家、国际重大科技任务，成效显著。2021年，实验室新增科研项目84项，包括主持科技创新2030重大项目1项、参与1项，主持国家重点研发计划2项、参与3项，主持中科院B类先导专项培育项目1项、科技服务网络计划（STS计划）区域重点项目1项，主持云南省重大科技专项1项。本年度承担研究项目共计225项，其中包括国家级项目79项，省部级项目111项，国际合作项目4项、横向协作项目31项。新增各类研究经费12598.88万元。

在科研成果产出方面，实验室围绕三大研究方向，继续揭示生物多样性形成与演变的规律及其遗传机制，为遗传资源的保护和可持续利用提供理论依据。2021年，发表SCI论文189篇，其中以第一完成单位发表论文68篇，以论文第一单位或通讯作者（含并列）在*Science*、*Cell*、*Molecular Biology and Evolution*、*National Science Review*、*Nature Communications*等国际高水平期刊发表论文25篇；授权发明专利9项；获云南省技术发明一等奖1项、自然科学三等奖1项、科学技术进步三等奖1项。

在人才队伍建设方面，实验室继续采用“引进加培养”的方式，创新人才机制，激发队伍活力，取得明显成效。2021年，培养新增青年研究员1人，新增副高级职称6人。在固定人员中，郑萍研究员新入选国家高层次人才特殊支持计划科技创新领军人才和科技部中青年科技创新领军人才；新增中科院“西部之光”交叉团队1个（牵头人刘振研究员），董锋荣获中科院“西部之光”青年学者B类资助，尹婷婷、罗鑫、马鹏程、赵丽娜、张涛、柳延虎新入选中科院青年创新促进会会员，高云新入选中科院技术支撑人才；马鹏程、曾琳新入选云南省中青年学术和技术带头人后备人才。培养输出硕士研究生24人，博士研究生22人，出站博士后1人。此外，还成功举办2021年“进化生物学”暑期班，吸引更多有志青年加入实验室。

实验室长期遵循“交流促进合作”的原则，在2021年开展了一系列合作交流活动。定期举办“遗传资源与进化青年学者论坛”共计4期，提升了青年学者学术表达能力并充分促进了室内外交流合作。不定期举办“遗传与进化前沿交叉论坛”，邀请12名国内外知名专家来室进行学术交流。同时，实验室深度参与《生物多样性公约》缔约方大会第十五次会议（COP15），杨君兴研究员向韩正副总理现场汇报高原湖泊立体生态修复研究成果。此外，实验室还积极发挥国内相关研究领域的辐射和带动作用，对外设立开放课题14项，并将各科研平台开放共享。

2022年，为弘扬冬奥会奋勇争先精神，迎接中国共产党第二十次全国代表大会胜利召开，我们在学术委员会指导下，坚持解放思想、实事求是、与时俱进、求真务实，力争做出更大贡献。在此，我谨代表实验室向给予大力帮助的各级领导及社会各界朋友致以最诚挚的感谢，并期望能得到大家一如既往的关心和支持！

实验室主任：施鹏

实验室概况

一、实验室介绍

遗传资源与进化国家重点实验室依托于中国科学院昆明动物研究所，前身为中科院重点实验室“细胞与分子进化重点实验室”。2007 年 11 月经科技部批准筹建，2009 年 9 月通过验收。

实验室立足于我国西南和东南亚丰富的生物多样性遗传资源，面向战略生物资源的国家需求和世界科技前沿，围绕“遗传、发育与进化的统一”这一重大科学前沿问题，部署三个研究方向：遗传资源多样性的演化与保护、基因与基因组的进化、遗传发育与进化。

实验室积极发挥地域优势和资源特色，开展了大量动物和人类遗传资源收集工作，为生物多样性相关研究打下了坚实的基础。同时将资源优势与科学前沿有机结合，围绕遗传资源多样性的演变规律、自然 / 人工选择与生物适应的遗传机制等关键科学问题，在生物多样性演化的格局、过程与人工选择机制方面做出了具有影响力的代表性成果。近五年，实验室承担国家级、省部级、国际合作及横向项目共 342 项，到位研究经费共计 4.68 亿元。发表 SCI 论文共 867 篇，包括在 *Cell*、*Nature*、*Science*、*Nature Genetics*、*Cell Stem Cell*、*Cell Research*、*Molecular Biology and Evolution* 等国际高水平学术期刊上发表论文 213 篇。出版专著 9 部。授权专利 20 项。农业农村部认定水产新品种 1 项。荣获云南省自然科学一等奖 3 项、二等奖 2 项、三等奖 1 项，云南省科技进步三等奖 2 项，云南省技术发明一等奖 1 项，云南省专利二等奖、三等各 1 项。

实验室共有研究组 21 个，支撑部门 1 个。实验室固定人员 143 人，正高级职称 26 人，副高级职称 33 人。其中中国科学院院士 1 人，欧洲科学院院士 1 人，发展中国家科学院院士 1 人，人社部百千万人才工程 5 人，科技部中青年科技创新领军人才 4 人，教育部长江学者奖励计划 1 人，国家高层次人才特殊支持计划科技创新领军人才 4 人，国家高层次人才特殊支持计划青年拔尖人才 1 人，国家海外高层次人才引进计划 2 人，国家杰出青年科学基金获得者 5 人，国家优秀青年科学基金获得者 4 人。拥有博士学位的固定人员共 87 人，占比总数的 60.8%；研究队伍年轻有活力，40 岁以下的青年研究人员和技术骨干占固定人员总数的 72.1%。目前在站博士后 9 人，在读博士研究生 119 人，硕士研究生 94 人。

实验室目前建设有 7 大平台：分子实验平台、显微影像与操作平台、生物信息学平台、功能基因发掘与分析平台、生物多样性考察平台、生命条形码平台、集成家猪平台。拥有大型仪器设备共计 100 余台 / 套，设备总价值 15382 万元。这些设施除了满足实验室在后基因组时代对基因组进化与基因功能研究的需求以外，所有大型设备还依托于昆明大型仪器区域中心，并通过“仪器设备共享管理网”对实验室内外乃至研究所内外全面开放共享。

另外，实验室还拥有无量山黑长臂猿监测站、哀牢山国家级自然保护区野生动物研究基地双柏监测站等野外观察站 4 个，云南土著鱼类养殖基地 3 个，嵩明小耳猪分子育种基地 1 个，为实验室的创新发展提供了重要支撑。

实验室积极开展与国内外的交流与合作，提高实验室在国内、国际学术界的知名度和影响力，促进实验室发展。在运行管理方面，严格按照科技部及中科院对国家重点实验室的要求，进一步完善“开放、流动、联合、竞争”的运行机制，实行依托单位领导下的主任负责制，加强规范化管理，营造出团结协作、

开放自主的科研氛围。

二、研究方向及内容

1. 遗传资源多样性的演化与保护

围绕我国西南及东南亚等生物多样性热点区域，建立世界一流的遗传资源库；研究遗传资源多样性形成和演变的规律，尤其是珍稀物种的濒危机制及其保护策略、野生和家养动物遗传资源的多样性和驯化演变关系，系统发掘农业动物基因，为我国农业可持续发展提供资源、理论和技术支撑，为遗传资源的保护和合理利用提供科学依据，为阐明基因和基因组进化的模式和规律、研究遗传、发育和进化的分子机制提供素材。

2. 基因与基因组的进化

以生命进化关键节点的物种和类群为研究对象，研究基因起源方式与进化规律、基因适应性进化与形态发生和环境适应的关系、基因互作网络形成的进化模式、基因组起源与多样化形成机制；探讨基因、基因互作网络和基因组的结构、功能多样性的起源与进化，阐明生命形态与功能多样化的基因组基础。

3. 遗传发育与进化

通过对不同进化地位和近缘物种的代表类群（如昆虫、头索动物、两栖类和哺乳类等）发育调控机制的研究与比较，从而解析进化中代表性和关键性性状的进化发育规律，进而在不同进化水平分析物种演化的发育生物学机制，如新基因、新的基因表达调控机制、表观遗传元件对物种形态演化与适应性的贡献等，阐明基因和基因组进化模式和规律的分子机制，最终实现遗传、发育与进化的统一。

三、组织结构

1. 现任实验室领导

主　任

施　鹏 研究员

副主任

文建凡 研究员

毛炳宇 研究员

焦保卫 研究员

2. 第三届学术委员会

主　任

张亚平 院　士，中国科学院

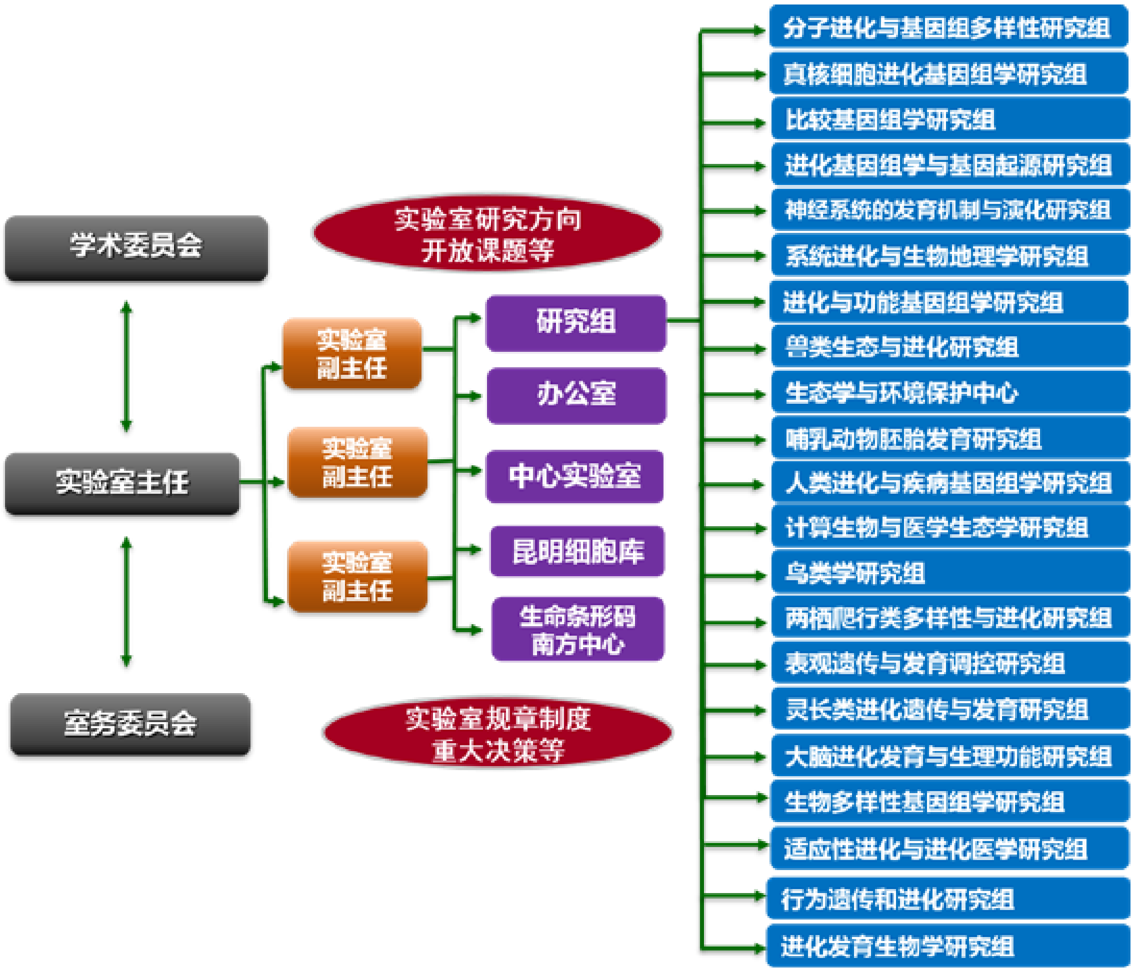
副主任

宿　兵 研究员，中国科学院昆明动物研究所

委 员

桂建芳 院 士，中国科学院水生生物学研究所
金 力 院 士，复旦大学
魏辅文 院 士，中国科学院动物研究所
吴仲义 院 士，中山大学
张克勤 院 士，云南大学
焦保卫 研究员，中国科学院昆明动物研究所
李德铢 研究员，中国科学院昆明植物研究所
施 鹏 研究员，中国科学院昆明动物研究所
汪小全 研究员，中国科学院植物研究所
王 文 研究员，中国科学院昆明动物研究所
杨 光 教 授，南京师范大学

3. 研究队伍



大事记

2021 年《生物多样性公约》缔约方大会第十五次会议（COP15）期间，杨君兴研究员向韩正副总理现场汇报“花 - 鱼 - 螺蚌 - 鸟”高原湖泊立体生态修复研究成果；鸟类研究组通过联合黑颈鹤保护的相关利益方，于 2011 年成立“中国黑颈鹤保护网络”，入选生物多样性 100+ 全球典型案例；朱建国副研究员等编著的《中国西南受威胁及特有脊椎动物》由科学出版社出版发行。

2021 年，实验室举办“青年学者论坛”（第四届论坛总决赛和第五届分论坛 3 期），为青年学者们提供展示分享科研进展的平台。每场邀请室外专家及学术带头人、研究生或青年骨干进行学术报告，嘉宾评选，激发研究生以及青年骨干的科研创新思维，促进学术交流，并吸引了研究所内外广大师生积极参与。

2021 年，实验室不定期举办“遗传与进化前沿交叉论坛”，邀请到中国海洋大学宋微波院士、多伦多大学 David Irwin 教授等国内外知名学者到室进行学术报告及课程讲授，共计 12 人次，并开展线上报告直播，追踪研究领域热点前沿，积极与国内外一流机构开展学术交流及合作研究。

科学传播与科教融合

7 月 26-31 日，实验室与研究生处联合举办了第十八届“进化生物学”暑期班，50 余名来自全国高校的优秀学员来昆参会。通过学术讲座、导师及研究生师兄师姐面对面、实验室近距离感受科研生活、研究所园区及科研平台参观等丰富的活动环节，普及前沿热点科学的同时，也吸引了优质大学生生源。

2021 年 3 月，李学燕副研究员等接受了新华网“云南青年说”栏目专访，录制了 COP15 特别策划的《地上“星星”的守护者》短片，介绍了“萤科”在全球有 2000 多种，在中国已记录的有 100 多种，云南分布有七八十种，以及萤火虫的生长环境、生活习性等科普知识。短片在新华网、中国网、新浪网等平台播出。

2021 年 9 月，由云南广播电视台邀请，实验室多位成员参与录制云南省电视台《新视野》节目。车静研究员和尹婷婷工程师以“云南：加大野生动物资源保护与研究，推动生物多样性保护与持续利用”为主题介绍了动物种质资源库；彭旻晟研究员、柳延虎副研究员以“家养动物种质资源”为主题介绍了实验室在家养动物起源与扩散方面的研究成果。这一系列节目于云南卫视播出。

第一章　科研工作进展

研究方向一：遗传资源多样性的演化与保护

代表性成果一

在生物多样性快速监测方法研究方面取得进展

Biodiversity Soup II: A bulk-sample metabarcoding pipeline emphasizing error reduction

Yang CY, Bohmann K, **Wang XY, Cai W,** Wales N, Ding ZL, Gopalakrishnan S, **Yu DW***

Abstract

Despite widespread recognition of its great promise to aid decision-making in environmental management, the applied use of metabarcoding requires improvements to reduce the multiple errors that arise during PCR amplification, sequencing and library generation. We present a co-designed wet-lab and bioinformatic workflow for metabarcoding bulk samples that removes both false-positive (tag jumps, chimeras, erroneous sequences) and false-negative ('dropout') errors. However, we find that it is not possible to recover relative-abundance information from amplicon data, due to persistent species-specific biases.

To present and validate our workflow, we created eight mock arthropod soups, all containing the same 248 arthropod morphospecies but differing in absolute and relative DNA concentrations, and we ran them under five different PCR conditions. Our pipeline includes qPCR-optimized PCR annealing temperature and cycle number, twin-tagging, multiple independent PCR replicates per sample, and negative and positive controls. In the bioinformatic portion, we introduce Begum, which is a new version of DAMe (Zepeda-Mendoza et al., 2016. BMC Res. Notes 9:255) that ignores heterogeneity spacers, allows primer mismatches when demultiplexing samples and is more efficient. Like DAMe, Begum removes tag-jumped reads and removes sequence errors by keeping only sequences that appear in more than one PCR above a minimum copy number per PCR. The filtering thresholds are user-configurable.

We report that OTU dropout frequency and taxonomic amplification bias are both reduced by using a PCR annealing temperature and cycle number on the low ends of the ranges currently used for the Leray-FolDegenRev primers. We also report that tag jumps and erroneous sequences can be nearly eliminated with Begum filtering, at the cost of only a small rise in dropouts. We replicate published findings that uneven size distribution of input biomasses leads to greater dropout frequency and that OTU size is a poor predictor of species input biomass. Finally, we find no evidence for 'tag-biased' PCR amplification.

To aid learning, reproducibility, and the design and testing of alternative metabarcoding pipelines, we provide our Illumina and input-species sequence datasets, scripts, a spreadsheet for designing primer tags and a tutorial.

Methods in Ecology and Evolution 2021, 12:1252-126

Douglas W Yu 研究团队 2012 年在国际期刊 *Methods in Ecology and Evolution*（MEE）发表了第一篇描述“生物多样性汤（Biodiversity Soup）”这一高通量条形码技术流程的文章，该文章已成为 MEE 期刊下载次数最高的文章之一。在前期研究基础上，研究团队进一步改进了高通量条形码技术流程，提高了运算速度，并能减少结果中的假阳性（如标签错配、嵌合体、错误序列）和假阴性。新流程改进了高通量条形码的实验设计和生物信息学分析，使用双胞胎标记法双向标记引物，将每个样本都进行多次独立的 PCR 扩增，并且通过 qPCR 来优化最终使用的退火温度和循环数。在生物信息学分析部分，采用的是 Begum，它在样本拆分时可以忽略为了测序中平衡碱基而添加在标签上的几个碱基，并允许引物序列的错配且提高了运算速率。Begum 能去除由于标签跳动所产生的假阳性序列，以及通过设置多个 PCR 重复和某一序列的重复出现次数来过滤 PCR 和测序等产生的错误序列。

该研究成果发表于 ***Methods in Ecology and Evolution***。为了让更多人能学习、验证并设计适合自己的高通量条形码流程，文章还提供了研究中用于构建生物多样性汤所有物种的序列、Illumina 测序数据、完整的分析命令脚本，以及用于引物标签设计的表格和指南。

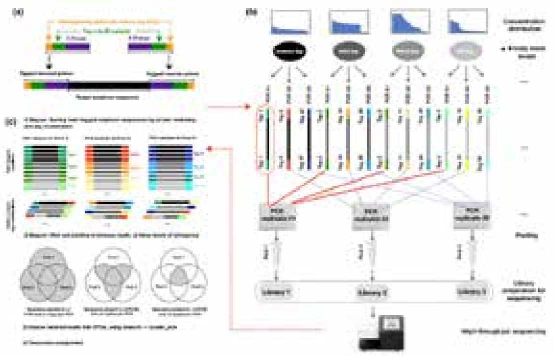


Fig. Schematic of study

Methods in Ecology and Evolution

研究方向一：遗传资源多样性的演化与保护

代表性成果二

揭示人类活动在兽类多样性格局改变中的作用

Functional diversity loss and change in nocturnal behavior of mammals under anthropogenic disturbance

Li XY, Hu WQ, Bleisch WV, **Li Q, Wang HJ,** Lu W, Sun J, Zhang FY, Ti B, **Jiang XL***

Abstract

In the Anthropocene, understanding the impacts of anthropogenic influence on biodiversity and behavior of vulnerable wildlife communities is increasingly relevant to effective conservation. However, comparative studies aimed at disentangling the concurrent effect of different types of human disturbance on multifaceted biodiversity and on activity patterns of mammals are surprisingly rare. We applied a multiregion community model to separately estimate the effects of cumulative human modification (e.g., settlement, agriculture, and transportation) and human presence (aggregated presence of dogs, people, and livestock) on species richness and functional composition of medium- and large-bodied mammals based on camera trap data collected across 45 subtropical montane forests. We divided the detected mammal species into three trophic guilds–carnivores, herbivores, and omnivores–and assessed the nocturnal shifts of each guild in response to anthropogenic activities. Overall, species richness tended to increase (β coefficient = 0.954) as human modification increased but richness decreased as human presence increased (β = –1.054). Human modification was associated with significantly lower functional diversity (mean nearest taxon distance [MNTD], β = –0.134; standardized effect sizes of MNTD, β = –0.397), community average body mass (β = –0.240), and proportion of carnivores (β = –0.580). Human presence was associated with a strongly reduced proportion of herbivores (β = –0.522), whereas proportion of omnivores significantly increased as human presence (β = 0.378) and habitat modification (β = 0.419) increased. In terms of activity patterns, omnivores (β = 12.103) and carnivores (β = 9.368) became more nocturnal in response to human modification. Our results suggest that human modification and human presence have differing effects on mammals and demonstrate that anthropogenic disturbances can lead to drastic loss of functional diversity and result in a shift to nocturnal behavior of mammals. Conservation planning should consider concurrent effects of different types of human disturbance on species richness, functional diversity, and behavior of wildlife communities.

Conservation Biology 2021, 1–13

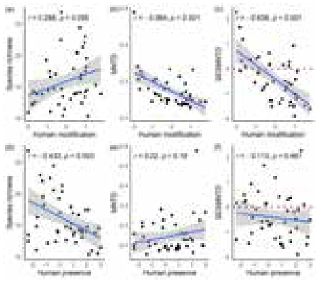


图 1. 人类改造和实时人类活动对兽类物种及功能多样性的影响

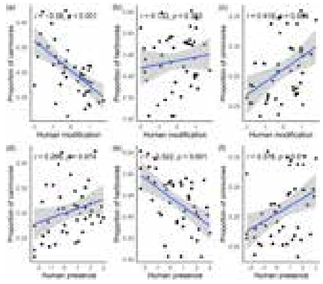


图 2. 人类改造和实时人类活动对兽类群落结构的影响

长期累积的人类改造（耕地、道路、夜间灯光等）和周期性的实时人类活动（放牧、采集、偷猎等）是野生动物面临的两大类人为干扰压力。横断山区是全球生物多样性热点地区之一，是我国生物多样性保护的关键区域。

蒋学龙研究团队长期致力于横断山区兽类多样性调查、监测与保护研究，建立了数十个长期红外相机监测样地，评估区域野生动物多样性和人为压力。本研究基于横断山区 45 个长期红外相机监测样地的数据，采用层次贝叶斯模型分析不同类型人类活动对兽类群落结构、功能及行为的影响。研究发现物种多样性随人类改造的增加而上升，但随实时人类活动的增加而下降；群落功能多样性、平均体重和食肉类占比均随人类改造的增加而显著下降；杂食类占比则随人类改造和实时人类活动的增加而显著增加；行为节律分析结果表明，人类活动致使野生动物夜行性水平显著增加，表明人类活动不仅影响野生动物群落结构和功能，还可能显著改变其行为规律。研究证实，人类改造和即时人类活动对哺乳动物群落结构及功能的影响存在差别，仅靠单一类型的人类活动指数难以真实反应区域内的人为压力；制定保护计划时应该综合考虑不同类型人类活动对野生动物物种多样性、功能多样性和行为的共同影响。

该研究成果发表于 ***Conservation Biology***。

Conservation Biology

研究方向一：遗传资源多样性的演化与保护

代表性成果三

揭示驯化下早期物种形成的基因组调控机制

Genetic Architecture Underlying Nascent Speciation—The Evolution of Eurasian Pigs under Domestication

Xie HB[1]***,** Wang LG[1], Fan CY[1], Zhang LC[1], **Adeola AC,** Yin X, Zeng ZB*, Wang LX*, **Zhang YP***

Abstract

Speciation is a process whereby the evolution of reproductive barriers leads to isolated species. Although many studies have addressed large-effect genetic footprints in the advanced stages of speciation, the genetics of reproductive isolation in nascent stage of speciation remains unclear. Here, we show that pig domestication offers an interesting model for studying the early stages of speciation in great details. Pig breeds have not evolved the large X-effect of hybrid incompatibility commonly observed between "good species." Instead, deleterious epistatic interactions among multiple autosomal loci are common. These weak Dobzhansky–Muller incompatibilities confer partial hybrid inviability with sex biases in crosses between European and East Asian domestic pigs. The genomic incompatibility is enriched in pathways for angiogenesis, androgen receptor signaling and immunity, with an observation of many highly differentiated cis-regulatory variants. Our study suggests that partial hybrid inviability caused by pervasive but weak interactions among autosomal loci may be a hallmark of nascent speciation in mammals.

Molecular Biology and Evolution 2021, 38:3556-3566.

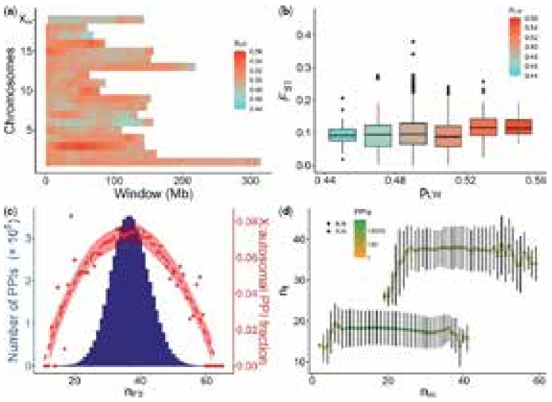


图 1. 大白与民猪 F0 始祖基因组在 F2 个体中的继承偏态及基因互作的性别拮抗作用

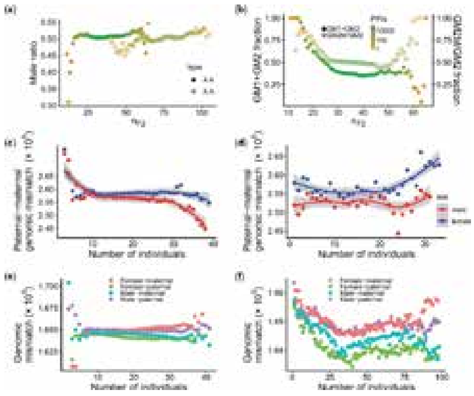


图 2. 基因互作不兼容与杂种不存活以及不兼容基因互作的性别差异分布

物种形成是进化生物学的核心问题之一，是生物种群多样性进化的重要驱动力。早在 1859 年《物种起源》一书中，达尔文便看到在人工选择下与自然选择下进化过程的相似性，并尝试利用家养动植物研究物种形成的过程。但是，家养动植物的群体遗传差异小，相关分析工作存在诸多挑战。

张亚平院士研究团队与合作者利用欧洲大白猪与东亚民猪杂交群体，构建了 F2 通过 F1 继承 F0 基因组序列的精细图谱，通过分析 F2 代个体中的大白猪与民猪来源的基因互作，研究了在驯化下早期物种形成的基因组调控机制。研究人员发现，大白猪与民猪之间已进化出非常微弱的生殖隔离作用，导致了不完全的杂种后代不存活表型；常染色体（尤其是 3 号染色体）而非 X 染色体，在大白猪与民猪生殖隔离进化中发挥了至关重要的作用。本研究对揭示物种形成萌芽阶段（尤其是哺乳动物）的生殖隔离进化具有十分重要的意义，开拓了以家养动物为对象的实验研究体系，并从连续进化的视角推动了物种形成基因组调控机制的深入探索。相关研究结果对家猪遗传改良也有重要的学术参考价值。

该研究成果发表于 ***Molecular Biology and Evolution***。

MOLECULAR BIOLOGY AND EVOLUTION

研究方向一：遗传资源多样性的演化与保护

代表性成果四

揭示东南亚土著体貌表型对热带雨林环境适应的分子机制

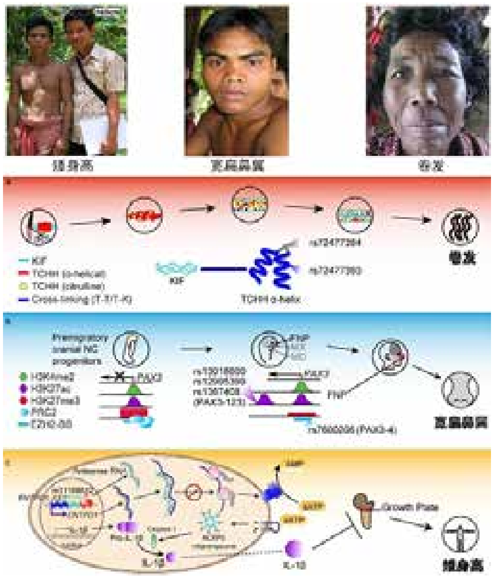
The distinct morphological phenotypes of Southeast Asian aborigines are shaped by novel mechanisms for adaptation to tropical rainforests

Zhang XM[1], Liu Q[1], **Zhang H**[1], Zhao SL[1], **Huang JH,** Sovannary T, Bunnath L, Aun HS, Samnom H, **Su B*,** Chen H*

Abstract

Southeast Asian aborigines, the hunter-gatherer populations living in tropical rainforests, exhibit distinct morphological phenotypes, including short stature, dark skin, curly hair and a wide and snub nose. The underlying genetic architecture and evolutionary mechanism of these phenotypes remain a long-term mystery. We conducted whole genome deep sequencing of 81 Cambodian aborigines from eight ethnic groups. Through a genome-wide scan of selective sweeps, we discovered key genes harboring Cambodian-enriched mutations that may contribute to their phenotypes, including two hair morphogenesis genes (*TCHH* and *TCHHL1*), one nasal morphology gene (*PAX3*) and a set of genes (such as *ENTPD1-AS1*) associated with short stature. The identified new genes and novel mutations suggest an independent origin of the distinct phenotypes in Cambodian aborigines through parallel evolution, refuting the long-standing argument on the common ancestry of these phenotypes among the worldwide rainforest hunter-gatherers. Notably, our discovery reveals that various types of molecular mechanisms, including antisense transcription and epigenetic regulation, contribute to human morphogenesis, providing novel insights into the genetics of human environmental adaptation.

National Science Review 2021, 10.1093/nsr/nwab072



东南亚分布许多古老的现生土著人群，在赤道线附近低纬度的热带雨林气候长期的自然选择下，产生了许多适应环境的体貌表型，如矮身高、深肤色、卷头发和宽扁鼻翼等。目前，对这些类似于非洲祖先的体貌表型研究较少。

宿兵研究团队与国内外团队合作，对柬埔寨土著进行了全基因组测序，并开展了系统的群体遗传学分析。研究利用全基因组数据构建的群体聚类关系表明，柬埔寨土著位于东亚人群亲缘关系树较根部的位置，与其他人群的分歧明显，印证了他们是古老人群的结论。整合非洲人群、北欧人群、南欧人群和东亚汉族的数据，分析了柬埔寨土著基因组中特有选择的信号，发现了 1,187 个受选择的基因组区域。对这些区域中基因的功能富集分析发现，与身高、头发形态和面部轮廓等体貌表型相关的基因及其受选择的突变位点，包括与卷发表型相关的基因 *TCHH* 和 *TCHHL1*，与鼻子形态相关的基因 *PAX3*，以及与身高相关的基因 *ENTPD1-AS1*。这些基因均表现为在柬埔寨土著中特有的达尔文正选择信号。*TCHH* 和 *TCHHL1* 两个基因各有一个错义突变（改变氨基酸序列）在柬埔寨土著中富集，而这两个基因均与卷发表型有关。其他两个受选择基因（*PAX3* 和 *ENTPD1-AS1*）的受选择突变均位于基因的非编码区。进一步的细胞功能验证实验证实，*PAX3* 和 *ENTPD1-AS1* 受选择突变位点影响基因的表达调控，从而可能最终影响鼻子形态和身高两个体貌表型。该研究对东南亚土著的研究为探索人类表型多样性的进化模式和遗传机制提供了范例。

该研究结果在线发表于 ***National Science Review***。

研究方向二：基因与基因组进化

代表性成果一

揭示家犬适应欧洲牛奶饮食的遗传机制

Whole-Genome Sequencing Reveals Lactase Persistence Adaptation in European Dogs

Liu YH[1]**,** Wang L[1], Zhang ZG[1], **Otecko NO, Khederzadeh S**, Dai YQ, Liang B*, **Wang GD*, Zhang YP***

Abstract

Coexistence and cooperation between dogs and humans over thousands of years have supported convergent evolutionary processes in the two species. Previous studies found that Eurasian dogs evolved into a distinct geographic cluster. In this study, we used the genomes of 242 European dogs, 38 Southeast Asian indigenous (SEAI) dogs, and 41 gray wolves to identify adaptation of European dogs . We report 86 unique positively selected genes in European dogs, among which is LCT (lactase). LCT encodes lactase, which is fundamental for the digestion of lactose. We found that an A-to-G mutation (chr19:38,609,592) is almost fixed in Middle Eastern and European dogs. The results of two-dimensional site frequency spectrum (2D SFS) support that the mutation is under soft sweep . We inferred that the onset of positive selection of the mutation is shorter than 6,535 years and behind the well-developed dairy economy in central Europe. It increases the expression of LCT by reducing its binding with ZEB1, which would enhance dog's ability to digest milk-based diets. Our study uncovers the genetic basis of convergent evolution between humans and dogs with respect to diet, emphasizing the import of the dog as a biomedical model for studying mechanisms of the digestive system.

Molecular Biology and Evolution 2021, 38:4884-4890.

家犬大约在 1 万五千年前到 4 万年前从欧亚大陆的灰狼驯化而来，现在已遍布世界大部分有人类居住的地方。家犬与人类生活在相同的环境，在很多方面存在趋同进化。

张亚平院士及王国栋研究团队，与云南大学梁斌研究团队合作，开展深入研究，利用 242 只欧洲品种犬、38 只东南亚家犬和 41 只灰狼的基因组数据，全基因组选择信号扫描揭示编码乳糖酶基因 *LCT*（lactase）在欧洲家犬中受到强烈的正选择，该基因与人群中乳糖酶耐受和牛奶饮食习惯相关。进一步分析显示位于家犬 19 染色体 38,609,592 位置的 A-to-G 突变在欧洲家犬和中东家犬中频率接近固定，分别为 91.7% 和 92.2%。2D SFS 分析结果表明该突变在欧洲家犬中受到 soft sweep，突变受到正选择的时间为 ~6,500 年内，而此时欧洲人群的牛奶饮食习惯已普遍存在。利用已发表的 737 只犬科动物基因组数据，解析该突变在亚欧非大陆家犬中的分布。结果显示其在不同地区的分布趋势与人类乳糖酶耐受表型相似，暗示了家犬与人类在牛奶饮食的趋同进化。基于 JASPAR 数据库，我们预测到该突变可能影响到与转录因子 ZEB1 的结合效率。细胞学功能实验证明该突变降低了 *LCT* 与 ZEB1 的结合，从而显著地提高了 *LCT* 表达量。该研究首次揭示家犬适应欧洲牛奶饮食习惯的遗传机制。

该研究成果发表于 ***Molecular Biology and Evolution***。

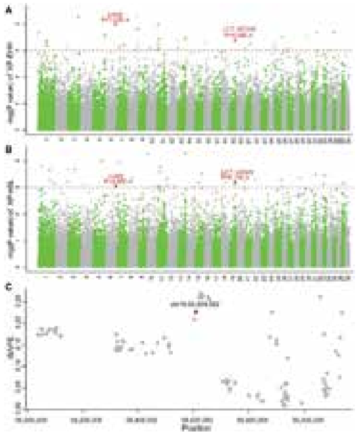


图 1. 乳糖酶 *LCT* 在欧洲家犬中受到强烈的正选择作用

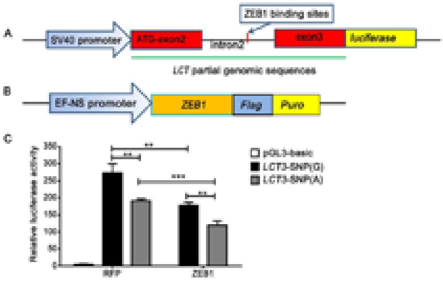


图 2. A-to-G 突变影响与 ZEB1 的结合进而提高 *LCT* 的表达量

研究方向二：基因与基因组进化

代表性成果二

解析灵长类苦味受体分子的功能演化及分子机制

A New World Monkey Resembles Human in Bitter Taste Receptor Evolution and Function via a Single Parallel Amino Acid Substitution

Yang H[1]*, Yang SL[1], Fan F, Li Y, Dai SX, Zhou X, Steiner CC, Coppedge B, Roos C, Cai XH, Irwin DM, **Shi P***

Abstract

Bitter taste receptors serve as a vital component in the defense system against toxin intake by animals, and the family of genes encoding these receptors has been demonstrated, usually by family size variance, to correlate with dietary preference. However, few systematic studies of specific Tas2R to unveil their functional evolution have been conducted. Here, we surveyed *Tas2R16* across all major clades of primates and reported a rare case of a convergent change to increase sensitivity to β-glucopyranosides in human and a New World monkey, the white-faced saki. Combining analyses at multiple levels, we demonstrate that a parallel amino acid substitution (K172N) shared by these two species is responsible for this functional convergence of Tas2R16. Considering the specialized feeding preference of the white-faced saki, the K172N change likely played an important adaptive role in its early evolution to avoid potentially toxic cyanogenic glycosides, as suggested for the human *TAS2R16* gene.

Molecular Biology and Evolution 2021, 38:5472-5479

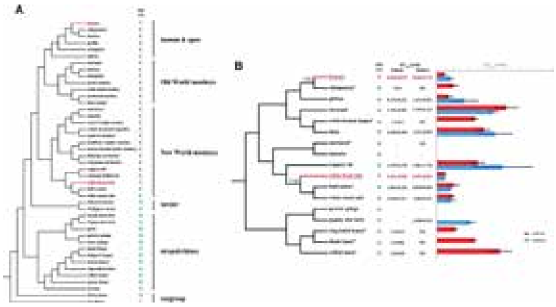


Fig 1. Amino acid states at site 172 of Tas2R16 in primate species involved in this study and their in vitro function in representative species

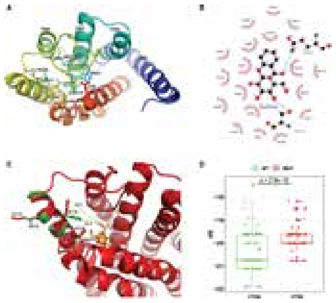


Fig 2. Binding mode and energy change for salicin to the white-faced saki Tas2R16

自然界中很多苦味物质都具有毒性，因此，苦味受体（Tas2R）作为毒物防御机制的重要一环在动物生存适应中发挥作用，对苦味受体功能演化及其分子机制的探索也成为进化生物学的一项重要研究内容。以往虽然对苦味受体家族基因数目与动物食性的关系进行了广泛探讨，但对于特定基因的功能进化仍然缺乏系统性的研究。

施鹏研究团队联合国内外多家研究机构，广泛收集样品，以食性丰富多样的灵长类物种为对象，系统研究了苦味受体 Tas2R16 的功能演化并对其分子基础进行解析，系统揭示了灵长类不同类群物种 Tas2R16 识别相应苦味物质的能力差异，反映出 Tas2R16 在不同食性物种中的功能变化。更重要的是，研究发现了一个少见的趋同演化例子：一种新大陆猴（白面僧面猴）与人类 Tas2R16 均对有毒的 β- 吡喃葡萄糖苷特别敏感。通过分子进化、3D 建模、功能验证等多个层次的分析，证明了这两个物种中通过平行进化发生的 K172N 突变是造成功能趋同的关键位点。考虑到白面僧面猴极其特殊的食性，该突变可能在其早期进化历程中发挥着重要作用。该研究从多方面多层次证明了该突变对于物种适应环境的有利作用，为适应性趋同演化增加了一个经典案例。

该研究成果发表于 ***Molecular Biology and Evolution***。

MOLECULAR BIOLOGY AND EVOLUTION

研究方向二：基因与基因组进化

代表性成果三

实验室多团队合作研究证实新的回声定位动物——猪尾鼠

Echolocation in soft-furred tree mice

He K, Liu Q, Xu DM, Qi FY, Bai J, He SW, Chen P, Zhou X, Cai WZ, Chen ZZ, **Liu Z*, Jiang XL*, Shi P***

New echolocator

Echolocation is a well demonstrated convergent sensory mode in bats and toothed whales. These lineages are not closely related, and this sense might be more broadly distributed than we recognize. Using a suite of approaches, He *et al.* show that the lineage of soft-furred tree mice (genus *Typhlomys*) includes multiple echolocators. Clear evidence of the behavioral use of echolocation under fully dark conditions was supported by the convergence of ear bone morphology and hearing-related genes with other echolocating mammals.

Abstract

Echolocation is the use of reflected sound to sense features of the environment. Here, we show that soft-furred tree mice (*Typhlomys*) echolocate based on multiple independent lines of evidence. Behavioral experiments show that these mice can locate and avoid obstacles in darkness using hearing and ultrasonic pulses. The proximal portion of their stylohyal bone fuses with the tympanic bone, a form previously only seen in laryngeally echolocating bats. Further, we found convergence of hearing-related genes across the genome and of the echolocation-related gene *prestin* between soft-furred tree mice and echolocating mammals. Together, our findings suggest that soft-furred tree mice are capable of echolocation, and thus are a new lineage of echolocating mammals.

Science 2021, 372:1305-+.

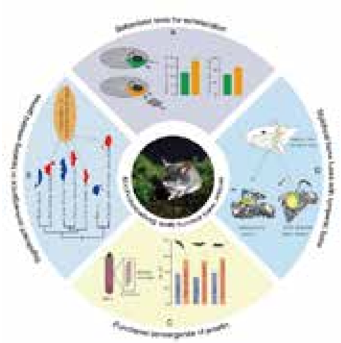


图 1. 多个实验证据证实猪尾鼠具有回声定位的能力

图 2. 中华猪尾鼠（*Typhlomys cinereus*），供图：刘奇，马晓峰

Science

回声定位（Echolocation）是指动物通过比较发出声波和接收回声的信息差别，进行导航、觅食等活动的一种定向行为。人们所熟知的回声定位动物主要包括食虫蝙蝠和齿鲸等。

施鹏研究团队、刘振研究团队、蒋学龙研究团队通过整合行为学、解剖学、基因组学以及基因功能实验多个独立的证据，证实了啮齿目猪尾鼠属（*Typhlomys*）的物种具有的回声定位能力。这一类新的回声定位的哺乳动物类群的发现，使得适应性复杂性状回声定位独立起源和演化的次数提高到了至少 6 次，成为自然界中性状趋同演化的典型案例。

施鹏研究团队和刘振研究团队长期从事回声定位的趋同演化和分子遗传机制等方面的研究工作，已发表了一系列的研究论文，包括 *Current Biology* (2010), *Molecular Biology and Evolution* (2014), *Science Advances* (2018) 等。蒋学龙研究团队长期从事猪尾鼠的行为生态和系统发育与分类的研究工作，并在 2017 年报道了猪尾鼠属的一个新种（*Journal of Mammalogy*, 2017）。在此基础上，三个团队综合利用行为学实验、解剖特征分析、比较基因组分析、基因功能实验等交叉研究手段，证实了猪尾鼠是一个全新的、独立演化出回声定位适应性性状的哺乳动物类群，提示着学界可能在很大程度上低估了适应性复杂表型的生物多样性。

该研究成果以 Research Article 的形式发表于 ***Science***。同时，第一作者刘奇在中科院之声微信公众号发表科普文章：《神奇动物在哪里？》。

研究方向二：基因与基因组进化

代表性成果四

揭示差异表达的长链非编码 RNA(lncRNA) 对百岁老人的潜在保护作用

Decoding the role of long noncoding RNAs in the healthy aging of centenarians

Jiang JJ, Cheng LH, Yan L, **Ge MX, Yang LQ,** Ying HQ, **Kong QP***

Abstract

Aging is the largest risk factor of major human diseases. Long noncoding RNAs (lncRNAs) as the key regulatory elements have shown a strong impact on multiple biological processes as well as human disease mechanisms. However, the roles of lncRNAs in aging/healthy aging processes remain largely unknown. Centenarians are good models for healthy aging studies due to avoiding major chronic diseases and disabilities. To illustrate their ubiquitous nature in the genome and the ‘secrets’ of healthy aging regulation from the perspective of lncRNAs, peripheral blood samples from two regions consisting 76 centenarians (CENs), 54 centenarian-children (F1) and 41 spouses of centenarian-children (F1SP) were collected for deep RNA-seq. We identified 11 CEN-specific lncRNAs that is particularly expressed in longevous individuals. By kmers clustering, hundreds of human lncRNAs show similarities with CEN-specific lncRNAs, especially with *ENST00000521663* and *ENST00000444998*. Using F1SP as normal elder controls (age: 59.9±6.6 years), eight lncRNAs that are differentially expressed in longevous elders (CEN group, age: 102.2±2.4 years) were identified as candidate aging/health aging–related lncRNAs (car-lncs). We found that the expression of eight car-lncs in human diploid fibroblasts displayed dynamic changes during cell passage and/or H2O2/rapamycin treatment; of which, overexpression either of *THBS1-IT1* and *THBS1-AS1*, two lncRNAs that highly expressed in CENs, can remarkably decrease p16, p21 and the activity of senescent related β-galactosidase, suggesting that *THBS1-IT1* and *THBS1-AS1* can inhibit cellular senescence. We provided the first comprehensive analysis of lncRNA expression in longevous populations, and our results hinted that dysregulated lncRNAs in CENs are potential protective factors in healthy aging process.

Briefings in Bioinformatics 2021, 22:14.

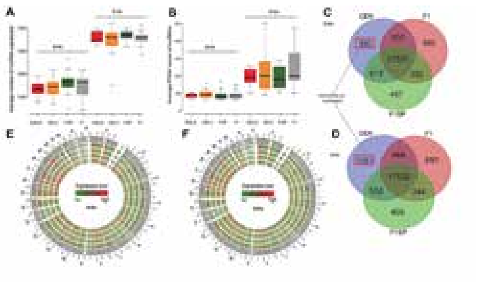


图 1. 中国长寿人群 lncRNA 分布规律及特征

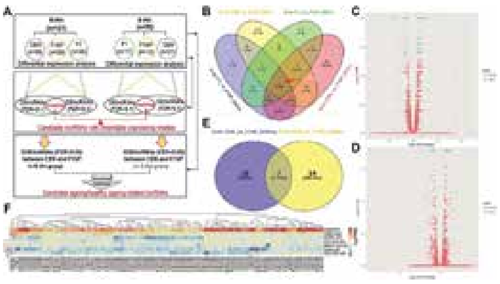


Fig 2. Identification of candidate aging/heathy aging-related lncRNAs (car-lncs)

衰老是人类疾病的最大危险因子之一，随着世界人口老龄化情况的日趋严重，如何在衰老的同时保持健康的状态成为了一大亟需探索和解决的难题。长链非编码 RNA（long noncoding RNA, lncRNA）是一类广泛参与人类疾病发生机制的调控元件，且在过去的研究中发现，lncRNA 与衰老有着密切的关系。

为了深入了解人群寿命延长的分子机制，孔庆鹏研究团队以百岁老人及其家庭成员为研究对象，对百岁老人家系 171 例样本（包括百岁老人，百岁 F1 后代和 F1 后代配偶，F1 后代配偶作为一般对照）的外周血白细胞进行转录组测序，以 lncRNA 为出发点，挖掘 lncRNA 在衰老及抗衰老过程中的作用。我们分析鉴定出了 8 个 lncRNA 可能与衰老 / 健康衰老相关，其中两个 lncRNA（*THBS1-AS1* 和 *THBS1-IT1*）在百岁老人中呈显著高表达。在复制衰老型细胞系中对这两个 lncNRA 进行过表达实验，证明其不仅显著降低了 p16 和 p21 的蛋白表达，且显著降低了衰老相关的 β- 半乳糖苷酶的活性，表明它们的高表达延缓细胞衰老相关表型。该研究首次报道了 lncRNA 在健康长寿老人中的表达规律，并发现一些差异表达的 lncRNA 具有潜在的抗衰老作用。

该研究成果发表于 ***Briefings in Bioinformatics***。

研究方向三：遗传发育与进化

代表性成果一

揭示人类大脑进化的基因组调控机制

3D Genome of macaque fetal brain reveals evolutionary innovations during primate corticogenesis

Luo X, Liu YT, Dang DC, **Hu T,** Hou YP, **Meng XY, Zhang FY,** Li TT, Wang C, **Li M, Wu HX, Shen QS, Hu Y, Zeng XR,** He XC, Yan LZ, Zhang SH*, Li C*, **Su B***

Summary

Elucidating the regulatory mechanisms of human brain evolution is essential to understanding human cognition and mental disorders. We generated multi-omics profiles and constructed a high-resolution map of 3D genome architecture of rhesus macaque during corticogenesis. By comparing the 3D genomes of human, macaque, and mouse brains, we identified many human-specific chromatin structure changes, including 499 topologically associating domains (TADs) and 1,266 chromatin loops. The human-specific loops are significantly enriched in enhancer-enhancer interactions, and the regulated genes show human-specific expression changes in the subplate, a transient zone of the developing brain critical for neural circuit formation and plasticity. Notably, many human-specific sequence changes are located in the human-specific TAD boundaries and loop anchors, which may generate new transcription factor binding sites and chromatin structures in human. Collectively, the presented data highlight the value of comparative 3D genome analyses in dissecting the regulatory mechanisms of brain development and evolution.

Cell 2021, 184:723-+

人类大脑起源于漫长的进化过程，其最显著的改变是大脑的认知功能，反映在脑容量的显著扩增和脑结构的高度精细化。人类进化过程中，哪些遗传改变造就了人类大脑，是国际科学界长期力图回答的重要科学问题。

宿兵研究团队联合国内研究人员，开展了跨物种大脑发育三维基因组的研究。首先，构建了中国猕猴胎脑的高分辨三维基因组图谱，并综合猕猴胎脑的转录组图谱、染色质开放区图谱以及染色质锚定蛋白 CTCF 的分布图谱，首次构建了猕猴胎脑发育过程中的染色质精细空间构象，鉴定了包括染色质区室、染色质拓扑结构域（简称 TAD）以及染色质环 (简称 Loop) 等不同尺度的染色质结构，以及基因组在大脑发育中发挥重要作用的调控元件（如增强子等）。其次通过与已发表的公共数据整合，利用跨物种三维基因组的比较（人类、猕猴和小鼠），发现了多个具有人类特异染色质结构的基因组位点，包括 499 个人类特异 TADs 和 1266 个人类特异 Loops。这些人类特异 Loops 显著富集增强子 - 增强子互作的调控模式，提示大脑发育在人类祖先中进化出更为精细的转录调控网络。这一研究成果首次产生了非人灵长类动物的高精度三维基因组学图谱资源，并利用大脑三维基因组的跨物种多组学分析，发现了人类特异的染色质结构和脑发育调控元件，为阐明人类大脑发育的进化机制提供了新思路和证据。

该研究成果发表于 ***Cell***。该成果入选 2021 年度中国生物信息学十大进展。

图 1. 研究课题的意象图，图中正在冥想的猴子表征灵长类大脑和智力的进化

图 2. 研究项目设计与研究结果图解

研究方向三：遗传发育与进化

代表性成果二

在家猪胸腰椎发育转换基因表达调控研究中取得进展

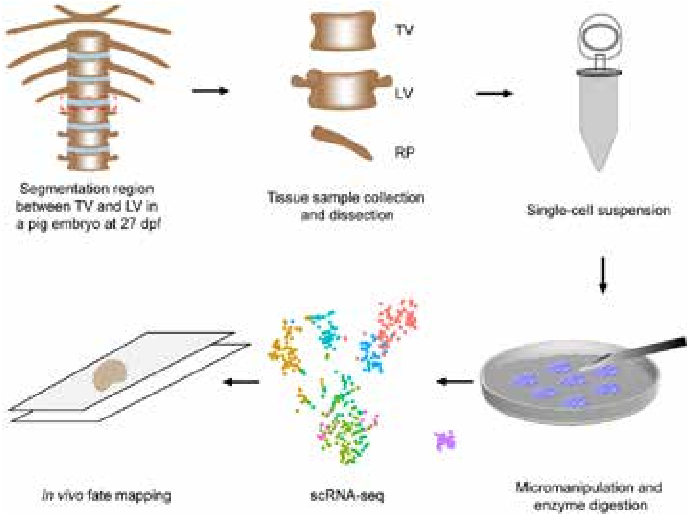
Single-cell RNA Sequencing Reveals Thoracolumbar Vertebra Heterogeneity and Rib-genesis in Pigs

Li JB, Wang LG, Yu DW, Hao JF, Zhang LC, **Adeola AC, Mao BY, Gao Y, Wu SF, Zhu CL,** Zhang YQ, Ren JL, **Mu CG, Irwin DM,** Wang LX*, Hai T*, **Xie HB*, Zhang YP***

Abstract

Development of thoracolumbar vertebra (TLV) and rib primordium (RP) is a common evolutionary feature across vertebrates, although whole-organism analysis of the expression dynamics of TLV- and RP-related genes has been lacking. Here, we investigated the single-cell transcriptome landscape of thoracic vertebra (TV), lumbar vertebra (LV), and RP cells from a pig embryo at 27 days post-fertilization (dpf) and identified six cell types with distinct gene expression signatures. In-depth dissection of the gene expression dynamics and RNA velocity revealed a coupled process of **osteogenesis** and **angiogenesis** during TLV and RP development. Further analysis of cell type-specific and strand-specific expression uncovered the extremely high level of *HOXA10* 3′-UTR sequence specific to osteoblasts of LV cells, which may function as anti-*HOXA10*-antisense by counteracting the *HOXA10*-antisense effect to determine TLV transition. Thus, this work provides a valuable resource for understanding embryonic osteogenesis and angiogenesis underlying vertebrate TLV and RP development at the cell type-specific resolution, which serves as a comprehensive view on the transcriptional profile of animal embryo development.

Genomics Proteomics & Bioinformatics 2021, 19:423-436



不同的家猪品种在胸椎和腰椎数量上高度可变，胸椎与腰椎数量与猪的体长密切相关，是重要的经济性状。长期以来，猪体节数量性状是猪遗传育种的重要研究方向之一，但胸腰椎数量的变异与发育转换机制目前仍不清楚。由于胸腰椎的体节发生过程对应于早期胚胎发育阶段，对相应的收集与研究存在众多困难，导致这一过程中的基因表达调控机制研究存在诸多挑战。

张亚平院士研究团队与合作者通过单细胞测序解析了猪胸腰椎发育和肋骨发生过程中的细胞类群鉴定与发育阶段胸腰椎的基因差异表达分析。研究通过显微操作获取受精后 27 天家猪胚胎胸腰椎连接处的脊椎和肋骨原基单细胞，分析发现胸椎和腰椎在细胞组成上没有显著差异，均由 6 种类群细胞：成骨细胞，成纤维细胞，软骨，基质细胞，造血内皮细胞，间充质干细胞。胸腰椎虽然在单细胞类群组成上并无差异，但在子类群的细胞数量上存在差异。发育拟时间和 RNA 速率分析发现胸腰椎发育和肋骨形成主要有两个发育过程，为成骨作用和血管生成。进一步分析发现，*Hoxa10* 在胸腰椎存在差异表达，其在胸椎细胞中几乎不表达，在腰椎细胞中高表达且主要在成骨细胞中表达。发现腰椎成骨细胞 *Hoxa10* 的高表达主要集中在 3’UTR 区域 (包含 *Hoxa10*-antisense 基因)，通过链特异的表达分析发现 *Hoxa10* 的高表达主要来自正链表达，推测在胸腰椎转换过程中存在 anti-*Hoxa10*-antisense 的作用。

该研究成果发表于 ***Genomics, Proteomics & Bioinformatics***。

Genomics, Proteomics & Bioinformatics

研究方向三：遗传发育与进化

代表性成果三

多能干细胞中 lncRNA 介导的基因组稳态调控新机制

A novel lncRNA Discn fine-tunes replication protein A (RPA) availability to promote genomic stability

Wang L, Li JZ, Zhou H, **Zhang WD,** Gao J, **Zheng P***

Abstract

RPA is a master regulator of DNA metabolism and RPA availability acts as a rate-limiting factor. While numerous studies focused on the post-translational regulations of RPA for its functions, little is known regarding how RPA availability is controlled. Here we identify a novel lncRNA *Discn* as the guardian of RPA availability in stem cells. *Discn* is induced upon genotoxic stress and binds to neucleolin (NCL) in the nucleolus. This prevents NCL from translocation into nucleoplasm and avoids undesirable NCL-mediated RPA sequestration. Thus, *Discn*-NCL-RPA pathway preserves a sufficient RPA pool for DNA replication stress response and repair. *Discn* loss causes massive genome instability in mouse embryonic stem cells and neural stem/progenigor cells. Mice depleted of *Discn* display newborn death and brain dysfunctions due to DNA damage accumulation and associated inflammatory reactions. Our findings uncover a key regulator of DNA metabolism and provide new clue to understand the chemoresistance in cancer treatment.

Nature Communications 2021, 12:15

多能干细胞是个体发育的基础，也是再生医学的重要种子细胞之一。由于发育地位特殊，多能干细胞基因组具高度稳态（如小鼠胚胎干细胞的基因组变异率仅为胚胎成纤维细胞的 1/100）。

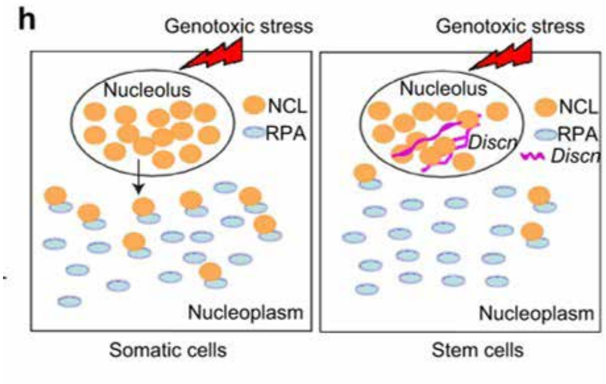


图 1. *Discn* 通过调节自由 RPA 含量高效调控基因组稳态

郑萍研究团队长期研究多能干细胞基因组稳态特征和独特调控机制。长链非编码 RNA（long noncoding RNA, lncRNA）能通过相变，和蛋白因子形成 condensates, 有效增强蛋白因子浓度，从而显著提高工作效率。研究团队对小鼠胚胎干细胞进行不同种类的 DNA 损伤处理，结合 RNA-seq 分析，筛选到了 10 多个表达响应损伤处理的干细胞特异 lncRNA。并针对其中 1 个尚未注释、且表达变化最为显著、也具物种保守性的 lncRNA（命名为 *Discn*，DNA damage-induced stem cell specific noncoding RNA）进行了深入的功能和机制分析。发现 *Discn* 对维持多能干细胞基因组稳定性至关重要，并揭示了其作用机制。*Discn* 定位于核仁，和核仁蛋白 NCL 结合，阻止 NCL 在 DNA 损伤情况下迁移到核质和 RPA 形成蛋白复合体，从而增强自由 RPA 含量。自由存在的 RPA 是 DNA 代谢（DNA 复制、修复和重组）的关键调控因子。因此，*Discn*-NCL-RPA 轴能高效调控 DNA 复制和修复。 *Discn* 也广泛表达于神经干细胞、精原干细胞等成体干细胞中，提示其有重要生理功能。同时也构建了 *Discn* 基因敲除小鼠，发现 *Discn* 基因敲除可导致新生致死及神经发育异常，这些表型主要是由体内 DNA 损伤产生的严重炎症反应引起。该研究揭示了多能干细胞中 lncRNA 介导的基因组稳态调控新机制。

该研究结果发表于 ***Nature Communication***。

研究方向三：遗传发育与进化

代表性成果四

揭示实体肿瘤在空间异质性选择下的生长与进化

Evolution under Spatially Heterogeneous Selection in Solid Tumors

Li GH[1]**,** Yang ZY[1], Wu DF, Liu SX, Li XN, Li T, Li YW, Liang LJ, Zou WL, Wu CI, Wang HY*, **Lu XM***

Abstract

Spatial genetic and phenotypic diversity within solid tumors has been well documented. Nevertheless, how this heterogeneity affects temporal dynamics of tumorigenesis has not been rigorously examined because solid tumors do not evolve as the standard population genetic model due to the spatial constraint. We therefore, propose a neutral spatial (NS) model whereby the mutation accumulation increases toward the periphery; the genealogical relationship is spatially determined and the selection efficacy is blunted (due to kin competition). In this model, neutral mutations are accrued and spatially distributed in manners different from those of advantageous mutations. Importantly, the distinctions could be blurred in the conventional model. To test the NS model, we performed a three-dimensional multiple microsampling of two hepatocellular carcinomas. Whole-genome sequencing (WGS) revealed a 2-fold increase in mutations going from the center to the periphery. The operation of natural selection can then be tested by examining the spatially determined clonal relationships and the clonal sizes. Due to limited migration, only the expansion of highly advantageous clones can sweep through a large part of the tumor to reveal the selective advantages. Hence, even multiregional sampling can only reveal a fraction of fitness differences in solid tumors. Our results suggest that the NS patterns are crucial for testing the influence of natural selection during tumorigenesis, especially for small solid tumors.

Molecular Biology and Evolution 2021, 39(1)

实体肿瘤空间上的遗传和表型异质性已被充分报道。然而，这种异质性如何影响肿瘤发生时的动态变化还没有得到解析，其原因是实体肿瘤受到较强的空间约束，其进化过程不遵循传统的群体遗传学模型。

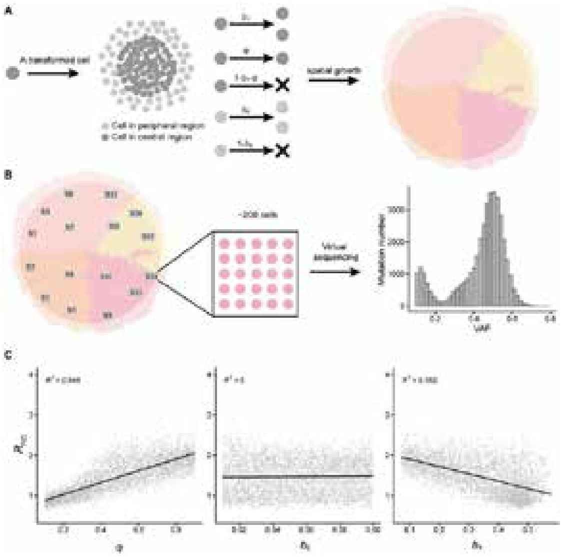


Fig 1. Spatial tumor growth model

吕雪梅研究团队与台湾大学王弘毅教授合作对肿瘤在空间上的生长和进化做了深入研究，提出了一个中性空间 (NS) 模型，在该模型中，突变积累随着肿瘤的向外生长而增加，谱系关系是由空间位置决定的，自然选择的效能微弱 (由于亲缘竞争)。中性突变的累积和空间分布的方式与优势突变不同，而在传统模型中，这些区别可能会被掩盖。为了验证NS模型，对两个肝细胞肿瘤（T1和 T2）进行了三维多点微采样和全基因组测序。结果显示，肿瘤外围样本检测到的突变是内部样本的 2 倍，肿瘤外部细胞具有更高的分裂速度，从而积累更多的突变，通过刻画肿瘤内克隆的大小和分布，在两个肿瘤中都检测到了自然选择。由于肿瘤细胞迁移能力有限，优势克隆快速生长从而占据肿瘤的大部分空间，早期出现的小克隆由于优势克隆的扩张而灭绝。因而，即使是多区域采样也只能揭示实体肿瘤适应性差异的一部分。研究模型展现了中性条件性下环境限制驱动了肿瘤内遗传结构、克隆多样性的形成以及自然选择下肿瘤的克隆扩张。肿瘤这种外围细胞比内部细胞分裂速度快的现象可能对肿瘤的治疗有一定的影响，提示需要使用针对不同表型和肿瘤微环境的联合治疗方法。

该研究成果发表于 ***Molecular Biology and Evolution***。

MOLECULAR BIOLOGY AND EVOLUTION

系统进化与生物地理学

杨君兴，博士，研究员，博士生导师。现任农业部濒危水生野生动植物物种科学委员会委员、世界自然保护联盟（IUCN/WI）淡水鱼类专家组（FFSG）中国区主席、中国动物学会第十八届理事会理事、云南省动物学会理事长、云南省水产学会顾问、第五届云南省省级自然保护区评审委员会委员、云南省中青年学术和技术带头人、蓝色粮仓科技创新咨询专家等。研究方向包括：生物多样性的考察监测及评价、系统分类、系统发育与生物地理学；珍稀特有物种的生态学研究和保育；湿地生态系统的恢复研究。至今已主持项目 40 余项，2021 年发表论文 20 余篇，其中 SCI 论文 10 余篇，获得国家授权专利 3 项，受理专利 3 项。2021 年获得云南“最美科技工作者”荣誉称号。

重要成果及产出：

1. **Zhang YW[1], Pan XF,Yin YH, Yang JX, Wang XA*.**Fertilization and growth pereformance in reciprocal hybrida of Dianchi golden-line barbel (*Sinocyclocheilus grahami*) and domestic common carp(Cyprinus carpio)and crucian carp (Carassius auratus).2021. ***Aquaculture Reports*** 21:100893.IF 3.216.
2. **Yin YH[1]** , Zhang XH[1], **Wang XA[1]** ,Li RH[1], **Zhang YW,** Shan XX, You XX , **Huan XD** , **Wu AL,** Mo Wang , **Pan XF,** Chao Bian, Jiang WS* , Shi Q* , **Yang JX*.**Construction of a chromosome-level genome assembly for genome-wide identification of growth-related quantitative trait loci in *Sinocyclocheilus grahami*.2021. ***Zoological Research*** 42(3):262-266. IF 4.56.
3. Du LN*, Yang J, Min R, Chen XY, **Yang JX*.**A review of the Cypriniform tribe Yunnanilini Prokofiev, 2010 from China, with an emphasis on five genera based on morphologies and complete mitochondrial genomes of some species.2021.***Zoological Research*** 42(3):310-334. IF 4.56.
4. Li B, **Zhang YW** , Liu X, Ma L*, **Yang JX*.** Molecular mechanisms of intermuscular bone development in fish: a review.2021. ***Zoological Research*** 42(3):362-376. IF 4.56.
5. 和友*，**王晓爱，潘晓赋，杨君兴*.** 滇池金线鲃视顶盖组织学观察. 2021. 复旦学报（自然科学版）60(1):120-125. IF 0.49.
6. **张源伟，王晓爱，潘晓赋，杨君兴**. 一种滇池金线鲃和鲫鱼杂交方法. 专利号：202110154107.1（2021.02.06 受理）
7. **Yuanwei Zhang,Xiaoai Wang,Xiaofu Pan,Junxing**. HYBRIDIZATION METHOD OF SINOCYCLOCHEILUS GRAHAMI AND CARP. Application Number:17204302（2021.03.17 受理）
8. **Yuanwei Zhang,Xiaoai Wang,Xiaofu Pan,Junxing Yang**. Artificial Propagation Method of *Sinocyclocheilus Rhinocerous*. Application Number:17164743（2021.02.01 受理）

1. 滇池金线鲃和鲤、鲫远缘杂交

远缘杂交是将不同物种的基因组组合在后代中实现杂种优势的有效途径，且杂交种在水产养殖业具有重要的经济价值。本课题组突破了国审新品种“鲃优 1 号”和鲤属鱼类间的远缘杂交，但关于“鲃优 1 号”和其他鲤属鱼类以及鲫属鱼类的杂交亲和性尚不清楚。结合之前的研究发现，当母本的染色体数目较低但接近于父本，且双亲的遗传关系较近时，虽然受精率和孵化率通常低于其父母本，但仍有可能获得存活后代，且杂交品种结合双亲优良品质。而部分杂交（滇池金线鲃♀×鲫♂）不能获得存活后代，因此，怀疑遗传分化可能是杂交失败的原因，但还需要进一步的基因组水平分析。

【Zhang YW et al. 2021 ***Aquaculture Reports***，IF=3.216】

2. 高原湖泊生态系统修复

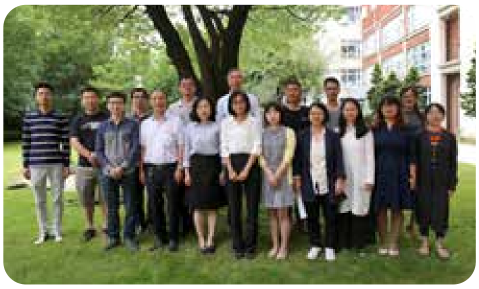
习总书记强调，要坚持绿水青山就是金山银山的理念，坚定不移走生态优先、绿色发展之路，并对云南高原湖泊保护十分重视。本课题组 2021 年围绕 COP15 大会，全程参与设计和布展 COP15 主场馆——宝丰湿地和植物园扶荔宫，并作为科学顾问，参与 COP15 大型纪录片《生命之歌》的制作。会议期间，杨君兴研究员向韩正副总理汇报了高原湖泊生态修复成果。该成果得到韩正副总理和 COP15 执行秘书长的充分肯定。

3. 云南珍稀特有鱼类品种创制和人工繁殖、养殖推广和野外种群复壮

目前，完成软鳍新光唇鱼水产新品种“墨龙 1 号”选育工作，申报材料已提交国家农业部，正在评审中。保存土著鱼类活体 102 种，60 余万尾，无重大鱼病出现。单位养殖水体的养殖密度逐年提高。对西畴、曲靖、会泽、通海、芒市、保山、丽江、大理等养殖基地定期进行技术指导。

2021 年度累计生产土著鱼类 200 余万尾，在滇池、牛栏江流域、李仙江流域放流滇池金线鲃 12 万余尾，短须裂腹鱼 2.6 万尾，昆明裂腹鱼 0.6 万尾，金沙鲈鲤 0.5 万尾，云南光唇鱼 0.6 万尾，软鳍新光唇鱼 1 万尾。

Phylogenetics and Biogeography



Dr. Junxing Yang, Professor. Current agriculture endangered aquatic wildlife species science committee, the world conservation union (IUCN/WI) freshwater fish expert group (FFSG), chairman of China, China institute of zoology, the 18th session of board of directors, yunnan province, chairman of the institute of zoology, aquatic consultant in yunnan province, the fifth in yunnan province, yunnan provincial nature reserve review committee members Provincial young and middle-aged academic and technical leaders, blue Granary science and technology innovation consulting experts, etc. The research team is mainly interested in biodiversity monitoring survey and evaluation, fauna taxonomic, phylogenetic and biogeographic; ecology and conservation research to rare and native species; especially focuses on the restoration of wetland ecosystem and application. Till now, presided over more than 40 projects, in 2021,published more than 10 SCI papers.3 national invention patent and accepted 3 patents. 2021 "Ultima Science and Technology Workers" in Yunnan (10 people in total).

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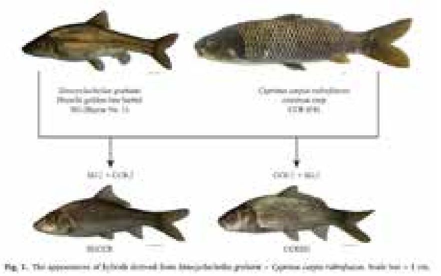
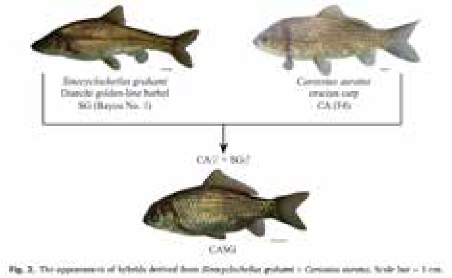
1.Fertilization and growth pereformance in reciprocal hybrida of Dianchi golden-line barbel (Sinocyclocheilus grahami) and domestic common carp(Cyprinus carpio)and crucian carp (Carassius auratus)

We used *S. grahami* hybrids with *C. carpio* rubrofuscus and *C. auratus* to explore the fertilization and growth performance of reciprocal hybrids. Here, the growth rates of the hybrid fish fell between their parental species. We found that when growth performance differed significantly between the parent species, their offspring obtained a medium growth rate. Thus, the SGCCR, CCRSG, and CASG hybrids resolved the disadvantages of slow growth rate and small body size in SG.These three hybrids exhibit considerable commercial and aquacultural application potential.

【Zhang YW et al. 2021 ***Aquaculture Reports***, IF=3.216】





2. Restoration of plateau lake ecosystem

General Secretary Xi stressed that we should adhere to the concept that clear waters and lush mountains are invaluable assets, unswervingly take the road of ecological priority and green development, and attach great importance to the protection of yunnan plateau lakes. In 2021, the plateau Lake Ecological Restoration Pavilion will be set up to participate in COP15 conference, focusing on the restoration of dianchi lake water ecosystem and ecological restoration plan by adopting dianchi Lake indigenous aquatic creatures “flower (cauliflower), fish (native fish), snail mussel and bird”. Han said the protection and restoration work should be carried out from the perspective of ecosystem integrity, and wetlands should play an important role in restoring and protecting lakeside biodiversity. The results were also highly appraised by the Executive Secretary-General of COP15.

3. The variety creation , artificial breeding, production and releasing in the wild of endangered fishes

In this year, we completion of the creation of a new species of *Neolissochilus benasi*, cultivated and produced more than 2 million fish fry of these fishes, including *Sinocyclocheilus grahami*, *Sinocyclocheilus tingi*, *Neolissochilus benasi*, *Percocypris retrodorslis*, *Schizothorax taliensis*, *Anabarilius liui chenghaiensis*, *Zacco platypus*, *Anabarilius grahami*, *Torqiaojiensis* and *Distoechodon macrophthalmus*. More than 0.16million individuals were released in wild to rebuilt and restore the wild population of these fishes.

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车星锦 Xingjing Che 2020

兽类生态与进化

蒋学龙，博士，研究员。立足于东喜马拉雅 - 横断山地区开展哺乳动物生态与进化研究，主要研究内容包括哺乳动物分类、系统演化与生物地理，灵长类动物的生态行为，兽类资源考察、监测与保护，以揭示横断山地区哺乳动物多样性的形成机制及在特殊生态条件下的适应性进化与保护。近年来，主要以东喜马拉雅 - 横断山地区特有与常见小型哺乳动物、灵长类及地栖大中型兽类为研究对象，重点研究横断山区哺乳动物分布格局及其演化机制、西黑冠长臂猿的生态行为与适应性，并全面布局横断山区兽类资源监测网络与数据库建设，开展亚洲象生态学研究，为人象冲突防范与亚洲象保护提供科学对策。

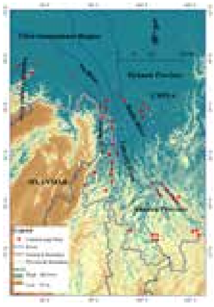
重要成果及产出：

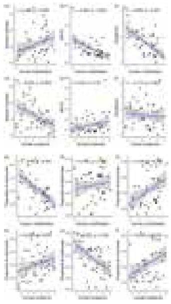
1. **He K**[1], **Liu Q**[1], **Xu DM**[1], **Qi FY**, **Bai J**, **He SW**, **Chen P**, **Zhou X**, **Cai WZ**,Chen ZZ, **Liu Z***, **Jiang XL***, **Shi P***.2021. Echolocation in soft-furred tree mice. ***Science***, 372 (6548).IF51.4332.
2. **Li XY**, **Hu WQ**, Bleisch WV, **Li Q**, **Wang HJ**, Lu W, Sun J, Zhang FY, Ti B, **Jiang XL***.2021. Functional diversity loss and change in nocturnal behavior of mammals under anthropogenic disturbance. ***Conservation Biology***. IF7.8379.
3. **Li Q**[1], **Cheng F**[1], Jackson SM[1], Helgen KM, Song WY, Liu SY, Sanamxay D, Li S, Li F, Xiong Y, Sun J, **Wang HJ**, **Jiang XL***.2021. Phylogenetic and morphological significance of an overlooked flying squirrel (Pteromyini, Rodentia) from the eastern Himalayas with the description of a new genus. ***Zoological Research***, 42(4): 389-400. IF4.5603.
4. Khanal L*, Chalise MK, Fan PF, Kyes RC, **Jiang XL***.2021. Multilocus phylogeny suggests a distinct species status for the Nepal population of Assam macaques (Macaca assamensis): implications for evolution and conservation. ***Zoological Research***, 42(1): 3−13. IF4.5603.
5. **Onditi KO**, **Li XY**, **Song WY**, **Li Q**, Musila S, Mathenge J, Kioko E, **Jiang XL***.2021.The management efectiveness of protected areas in Kenya. ***Biodiversity and Conservation***, 30:3813-3836. IF3.9189.
6. **Onditi KO**, **Song WY**, **Li XY**, **Chen ZZ**, **Li Q**, **He SW**, Musila S, Kioko E, **Jiang XL***.2021. Patterns and predictors of small mammal phylogenetic and functional diversity in contrasting elevational gradients in Kenya. ***Frontiers in Ecology and Evolution***, 2021.742524.IF3.9070.
7. Jackson SM[1], **Li Q**[1], Wan T, **Li XY**, Yu FH, Gao G, He LK, Helgen KM*, **Jiang XL***.2021. Across the great divide: revision of the genus Eupetaurus (Sciuridae: Pteromyini), the woolly flying squirrels of the Himalayan region, with the description of two new species. ***Zoological Journal of the Linnean Society***, XX, 1–25.IF3.3213.
8. **Chen ZZ**, **He SW**, **Hu WH**, **Song WY**, **Onditi KO**, **Li XY**, **Jiang XL***.2021. Morphology and phylogeny of scalopine moles (Eulipotyphla: Talpidae: Scalopini) from the eastern Himalayas, with descriptions of a new genus and species. ***Zoological Journal of the Linnean Society***, 193：432–444. IF3.3213.

1. 人类活动在兽类多样性格局改变中的作用

基于横断山区 45 个长期红外相机监测样地的数据，采用层次贝叶斯模型分析不同类型人类活动对兽类群落结构、功能及行为的影响。研究发现物种多样性随人类改造的增加而上升，但随实时人类活动的增加而下降；群落功能多样性、平均体重和食肉类占比均随人类改造的增加而显著下降；杂食类占比则随人类改造和实时人类活动的增加而显著增加；行为节律分析结果表明，人类活动致使野生动物夜行性水平显著增加，表明人类活动不仅影响野生动物群落结构和功能，还可能显著改变其行为规律；研究证实，人类改造和即时人类活动对哺乳动物群落结构及功能的影响存在差别，仅靠单一类型的人类活动指数难以真实反应区域内的人为压力；制定保护计划时应该综合考虑不同类型人类活动对野生动物物种多样性、功能多样性和行为的共同影响。

【Li XY et al. 2021 ***Conservation Biology***，IF=7.8379 】

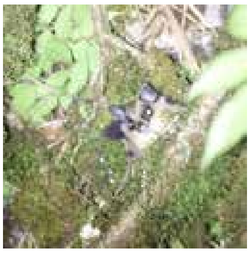


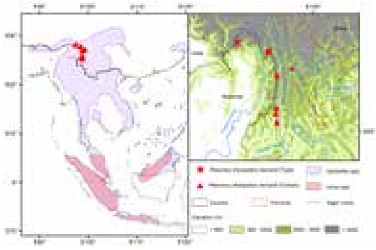


2. 发现鼯鼠族新属 —— 喜山大耳飞鼠属

研究发现李氏小飞鼠在遗传上和巽它群岛特有的大耳飞鼠属（*Iomys*）最为接近，而非黑白飞鼠。但李氏小飞鼠在形态和分布上却与大耳飞鼠有很多不同，如：李氏小飞鼠的牙齿结构显示其更偏向于杂食性，而大耳飞鼠的牙齿结构显示它更偏向于植食性；李氏小飞鼠仅分布于东喜马拉雅地区的亚热带、温带森林中，而大耳飞鼠则分布在克拉地峡以南的热带森林中，两者分布区之间隔着广阔的中南半岛。根据生物学建立新属的三原则——“单系性”、“合理紧凑性”和“生态 / 形态 / 生物地理足够差异性”，研究团队认为李氏小飞鼠不仅是一个有效种而且还应作为一个新属。新属喜山大耳飞鼠属的发现对研究鼯鼠的牙齿进化、性选择、同域成种和中南半岛晚新生代的海侵事件、气候变化和动植物保护具有重要意义。

【Li Q et al. 2021 ***Zoological Research***，IF=4.5603】





Mammal Ecology and Evolution

Prof. Xuelong Jiang, Professor, The laboratory is mainly interested in specimen-based investigations of biodiversity inventory, taxonomy and systematics, phylogenetics and phylogeography of small mammals with a special focus in the Henduanshan Region, and also in spatial ecology of rare and cryptic mammal faunas, behavior and conservation of black crested gibbon, as well as conservation biology of Asian elephant and other large mammals.

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1. The management effectiveness of protected areas in Kenya

Merely designating new and/or expanding existing protected areas (PAs) does not guarantee the protection of critical ecosystems and species. The management of PAs must be effective to sustain meaningful conservational outcomes. We inferred the management effectiveness of PAs in Kenya based on the representation of ranges and distribution of multiple diversity dimensions of terrestrial mammals and their association with governance and designation types. We hypothesized that different governance types underlie variable management efficacies, such that stricter-managed PAs have better habitats that attract more wildlife, translating to higher species diversity compared to less strictly-managed PAs, especially for focal species groups (large carnivores, large herbivores, and endangered species). The results showed nearly all terrestrial mammals in Kenya represented in at least one PA. However, the relative proportion of represented ranges were low, and analysis of spatial conservation prioritization showed significant expansion beyond current PAs needed to achieve a one third coverage of focal species' ranges in a best-solution reserve system. Differences in PA governance and designation types were not systematically associated with diversity variances, and while there were more unique species in state-managed PAs than in privately-managed ones, averaged diversity coefficients were comparable between categories. Diversity variances explained by PA size and status year were low in a combined species pool but increased in focal species groups. These findings suggest that success in terrestrial mammal conservation in PAs in Kenya require clearly and formally streamlined definition, performance feedback, and collaboration terms between state-managed and privately-managed PAs.

【Onditi KO et al. 2021 ***Biodiversity and Conservation***，IF=3.9189】

2. Morphology and phylogeny of scalopine moles (Eulipotyphla: Talpidae: Scalopini) from the eastern Himalayas, with descriptions of a new genus and species

All scalopine moles are found in North America, except the Gansu mole (*Scapanulus oweni*), which is endemic to central-west China. In 2019, we collected two specimens of Scalopini on Mt Namjagbarwa in the eastern Himalayas, Tibet, China. We sequenced two mitochondrial (*CYT B* and 12S) and three nuclear (*APOB*, *BRCA1* and *RAG2*) genes to estimate the phylogenetic relationships of the two moles, and also compared their morphology with other genera and species within the Scalopini. Both morphological and molecular analyses strongly suggest that the specimens represent a new monotypic genus and species, which are formally described here as ***Alpiscaptulus medogensisgen*. et sp. nov**. The dental formula of the new mole (44 teeth) is distinct from the Chinese *Scapanulus oweni* (36 teeth) and its hairy and pale brown tail is unique among species of the Scalopini. The Kimura-2-parameter (K2P).
distances of *CYT B* between A. *medogensis* and the four recognized Scalopini genera range from 14.5% to 18.9%. A sister relationship between A. *medogensis* and *Scapanulus oweni* was strongly supported in the phylogenetic trees. The divergence between A. *medogensis* and *Scapanulus oweni* occurred in the mid-Miocene (c. 11.56 Mya), which corresponds with the rapid uplift of the Himalayan-Tibetan Plateau.

【Chen ZZ et al. 2021 ***Zoological Journal of the Linnean Society***，IF=3.3213】

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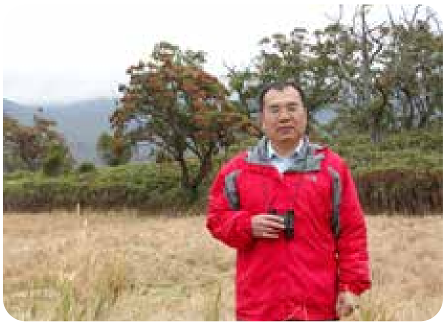
汪思远 Siyuan Wang	硕士生 2021 级
Sambaya Brian Anoto	硕士生 2021 级



鸟类学

杨晓君，研究员，主要从事西南地区鸟类分类区系、系统演化、生物地理、群落生态学及珍惜鸟类的行为生态学和保护生物学研究。近年来更关注青藏高原旗舰物种——黑颈鹤的保护及鸟类系统演化研究。目前已出版执行主编和副主编专著 9 部，发表论文 100 余篇。

重要成果及产出：

1. Nestedness theory suggests wetland fragments with large areas and macrophyte diversity benefit waterbirdsWang, R., **Yang, XJ**.Ecology and Evolution, 2021, 11(18), pp. 12651–12664.
2. Population genomic, climatic and anthropogenic evidence suggest the role of human forces in endangerment of green peafowl (Pavo muticus)**Dong, F.**, Kuo, HC., Chen, GL., Liu, Y., **Yang, XJ**.Proceedings of the Royal Society B: Biological Sciences, 2021, 288(1948), 0073.
3. Waterbird Composition and Changes with Wetland Park Construction at Lake Dianchi, Yunnan-Guizhou PlateauWang, RX., **Yang, XJ**.Mountain Research and Development, 2021, 41(1), pp. R29–R37.
4. Habitat use, preference and utilization distribution of two crane species (Genus: Grus) in Huize National Nature Reserve, Yunnan-Guizhou Plateau, ChinaKong, D., Luo, W., Huan, G., Li, Z., **Yang, XJ**.PeerJ, 2021, 6, e5105.
5. Potential Himalayan community turnover through the Late Pleistocene**Dong, F.**, Hung, CM., Li, SH., **Yang, XJ**.Climatic Change, 2021, 164(1-2), 6.
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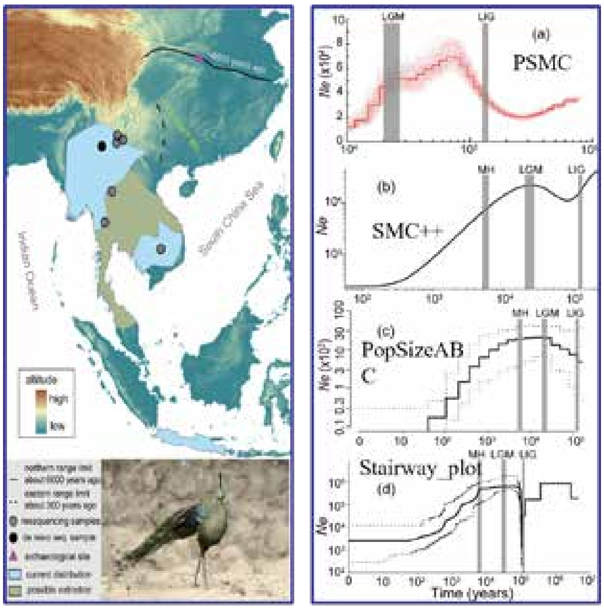
种群基因组、气候和人为证据表明，人类活动威胁绿孔雀

根据考古和历史记载，绿孔雀曾广泛分布于中国南方和东南亚，后来经历了剧烈的种群收缩，目前仅片段化分布于云南及东南亚的局部区域。但目前尚不清楚绿孔雀种群衰退过程中的主要致危因素，尤其是气候变化和人类活动在其中的相对作用。



Dong et al., 2021. *Proc. R. Soc. B.*

基于种群基因组数据和四种溯祖模拟分析（PSMC、SMC++、PopSizeABC 和 Stairway_ plot）揭示绿孔雀经历了中全新世（MH，～ 6000 年以来）种群数量的快速下降过程。

与上述基因组数据分析结果形成鲜明对照，历史气候预测绿孔雀自中全新世以来潜在适宜分布面积整体稳定（图中深蓝色代表分布不变，浅蓝代表分布扩张，紫色代表分布收缩），暗示气候变化不是绿孔雀种群衰退的主要因素。

相关性统计分析显示，绿孔雀的种群数量下降过程与人类干扰强度（如人口数量，popc；建筑面积，uopp；农地面积；cropland 和牧场面积，grazing）存在显著负相关性，暗示人类干扰是绿孔雀走向濒危的主要驱动因素。

Ornithology

Prof. Yang Xiaojun, Principle Investigator, Kunming Institute of Zoology, Chinese Academy of Sciences. My research interest lies at bird taxonomy and fauna, phylogeny, biogeography, community ecology, as well as behaviour ecology and conservation biology of endangered bird species. Till now, 8 books and more than 100 papers have been published.

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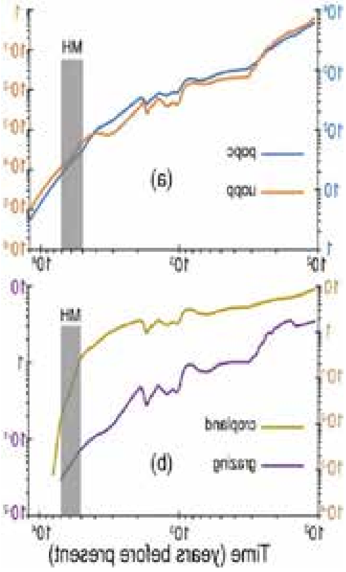
1. Population genomic, climatic and anthropogenic evidence suggest the role of human forces in endangerment of green peafowl (Pavo muticus)

Both anthropogenic impacts and historical climate change could contribute to population decline and species extinction, but their relative importance is still unclear. Emerging approaches based on genomic, climatic and anthro_x0002_ pogenic data provide a promising analytical framework to address this question. This study applied such an integrative approach to examine poten_x0002_tial drivers for the endangerment of the green peafowl (Pavo muticus). Several demographic reconstructions based on population genomes congru_x0002_ently retrieved a drastic population declination since the mid-Holocene. Furthermore, a comparison between historical and modern genomes suggested genetic diversity decrease during the last 50 years. However, climate-based ecological niche models predicted stationary general range during these periods and imply the little impact of climate change. Further analyses suggested that human disturbance intensities were negatively cor_x0002_related with the green peafowl's effective population sizes and significantly associated with its survival status (extirpation or persistence). Archaeological and historical records corroborate the critical role of humans, leaving the footprint of low genomic diversity and high inbreeding in the survival populations. This study sheds light on the potential deep-time effects of human disturbance on species endangerment and offers a multi-evidential approach in examining underlying forces for population declines.



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生态学与环境保护中心

Douglas W. Yu, 博士，研究员。生态学与环境保护中心负责人，首批云南省高端人才项目引进人才。主要关注两个方面的研究内容：生物多样性快速评估方法和互利共生研究。目前已发表超过 90 篇论文于国际期刊 *Nature, Science, PNAS, PLoS Biology, Ecology Letters, Ecological Monographs, Ecology, American Naturalist, Evolution* 等上。

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重要成果及产出：

1. **Chunyan Yang**[1], Kristine Bohmann, **Xiaoyang Wang, Wang Cai**, Nathan Wales, **Zhaoli Ding**, Shyam Gopalakrishnan, **Douglas W. Yu***. (2021) Biodiversity Soup II: A bulk-sample metabarcoding pipeline emphasizing error reduction. *Methods in Ecology and Evolution.* 2021;00:1–13.
2. Nerea Abrego[1], Tomas Roslin, Tea Huotari, **Yinqiu Ji**, Niels Martin Schmidt, Jiaxin Wang, **Douglas W. Yu*** and Otso Ovaskainen*. (2021) Accounting for species interactions is necessary for predicting how arctic arthropod communities respond to climate change. *Ecography*. 44: 1–12, 2021.
3. **Wang Cai**[1], **Chunyan Yang, Xiaoyang Wang, Chunying Wu**, Laurent Larrieu, Carlos Lopez-Vaamonde, Qingzhong Wen, **Douglas W. Yu*.** The ecological impact of pest-induced tree dieback on insect biodiversity in Yunnan pine plantations, China. *Forest Ecology and Management.* 491 (2021) 119173.
4. **Ji, Y.Q.**[1], Baker, C.C.M., **Li, Y.H.**, Popescu, V.D., **Wang, J.X.**, **Wang, L.**, Wen, Q.Z., **Yang, C.Y.**, Xu, C.C.Y., Pierce, N.E., **Yu, D.W*.** Measuring Protected-area Vertebrate Biodiversity Using Leech iDNA. bioRiv. doi:10.1101/2020.02.10.941336 https://www.scmp.com/lifestyle/health-wellness/article/3050703/how-leeches-could-help-prevent-future-coronavirus (in review)

1. “ 生物多样性汤 ” 二代技术：生物多样性快速监测方法

课题组在前期研究的基础上，进一步改进了高通量条形码技术流程，提高了运算速度，并能减少结果中的假阳性（如标签错配、嵌合体、错误序列）和假阴性。新流程改进了高通量条形码的实验设计和生物信息学分析，使用双胞胎标记法双向标记引物，将每个样本都进行多次独立的 PCR 扩增，并且通过 qPCR 来优化最终使用的退火温度和循环数。在生物信息学分析部分，采用的是 Begum，它在样本拆分时可以忽略为了测序中平衡碱基而添加在标签上的几个碱基，并允许引物序列的错配且提高了运算速率。Begum 能去除由于标签跳动所产生的假阳性序列，以及通过设置多个 PCR 重复和某一序列的重复出现次数来过滤 PCR 和测序等产生的错误序列。为了让更多人能学习、验证并设计适合自己的高通量条形码流程，文章还提供了研究中用于构建生物多样性汤所有物种的序列、Illumina 测序数据、完整的分析命令脚本，以及用于引物标签设计的表格和指南。

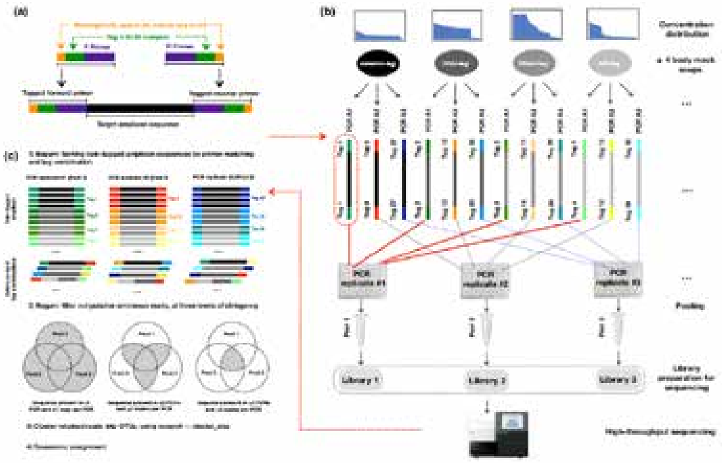

图 1. 高通量条形码技术流程及原理

2、云南松林病虫害致树木枯死对昆虫多样性的生态影响

中国最近宣布了一项林业政策改革，其主要目标是从单一的人工林向异质林转变，这种异质林具有更高的病虫害抗性和更多的生物多样性。本研究以具有枯梢病的云南松 (Pinus yunnanensis) 为研究对象，采用马氏网诱捕方法对此类云南松高空的节肢动物 (主要为昆虫) 的多样性进行了采样，并采用 meta_x0002_barcoding 方法对昆虫群落特征进行了分析。我们的研究结果表明，云南松的枯死现象模拟了天然林中自然形成的树木空缺，与小蠹虫作为欧洲针叶林的危害物种的解释一致。在欧洲，有人提出包括小蠹虫为害在内的自然干扰，有效地创造了森林异质性，因此无需人工清除枯木或重新种植新的树木。考虑到本地云南小蠹虫枯梢病的严重程度和发生频率的增加，应辅以枯枝筛除和多树种种植等人为处理，加快人工林向异质林的演替。

Ecology, Conservation, & Environment Center(ECEC)

Dr. Douglas W. Yu. Yu's research covers two fields, (1) game-theoretical models of symbiosis, and (2) rapid biodiversity assessment using genomics. In the first area, we have developed new genomics methods for biodiversity rapid assessment. In the second, we have been elucidating the mechanisms stabilizing cooperation among species, using in fig-wasp and ant-plant mutualisms as experimental models. Yu has 90 publications, including in Nature, Science, PNAS, PLoS Biology, Ecology Letters, Ecological Monographs, Ecology.

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1. Biodiversity Soup II: A bulk-sample metabarcoding pipeline emphasizing error reduction

Despite widespread recognition of its great promise to aid decision-making in environmental management, the applied use of metabarcoding requires improvements to reduce the multiple errors that arise during PCR amplification, sequencing and library generation. This paper presents a co-designed wet-lab and bioinformatic workflow for metabarcoding bulk samples that removes both false-positive (tag jumps, chimeras, erroneous sequences) and false-negative ('dropout') errors. To aid learning, reproducibility, and the design and testing of alternative metabarcoding pipelines, the authors provide the Illumina and input-species sequence datasets, scripts, a spreadsheet for designing primer tags and a tutorial.

2. The ecological impact of pest-induced tree dieback on insect biodiversity in Yunnan pine plantations, China

China has recently announced a reform of forestry policy, with a major goal being to transform from plantation to heterogeneous forests, which have higher resistance to pests and disease and house more biodiversity. We sampled aerial arthropods (mostly insect) biodiversity along gradients of Pinus yunnanensis dieback severity using Malaise traps and used meta_x0002_barcoding to characterise the insect community. Our results thus suggest that bark-beetle dieback mimics natural forest-gap dynamics, consistent with the interpretation of bark beetles as a keystone species in European conifer forests, where it has been proposed that forest heterogeneity can be created efficiently by allowing natural disturbances, including bark-beetle outbreaks, to proceed naturally, without being mitigated by deadwood removal and dense replanting. In Yunnan's situation, and given predicted increases in bark-beetle dieback severity and frequency, this strategy should probably be supplemented with anthropogenic treatments, such as deadwood enhancement and planting of multiple tree species, to accelerate the succession of plantations into heterogeneous forests.

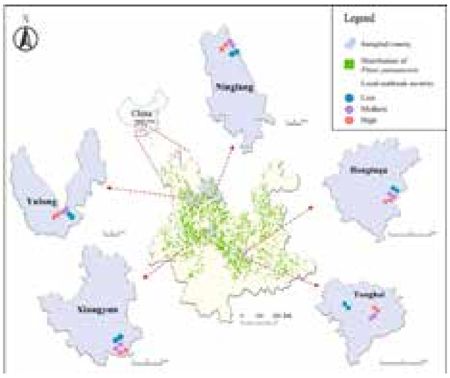

figure 2. Map of study area, Yunnan province, southwest China.

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两栖爬行类多样性与进化

车　静，研究员，博士生导师。世界两栖爬行动物学大会执委；中国动物学会两栖爬行动物学分会副理事长；中华人民共和国濒危物种科学委员会委员；中国人与生物圈（MAB）国家委员会专家咨询委员会委员。2019 年度当选美国鱼类和两栖爬行动物联合学会（ASIH）终身外籍荣誉会员；入选国家高层次人才特殊支持计划科技创新领军人才（2019 年度）；2017 年获国家基金委优秀青年基金。

学科组长期立足中国及东南亚丰富的多样性资源，从宏观生物学问题出发，坚持多学科交叉，以整合的方法和进化的视角，瞄准两栖爬行动物多样性形成、演化、适应的前沿科学问题及濒危物种保护的重大需求开展工作。牵头出版专著 1 部《西藏两栖爬行动物——多样性与进化》；作为通讯（第一）作者在 *Science*、*PNAS*、*Syst Biol*、*Nati Sci Rev* 等一系列国际学术期刊发表 107 篇 SCI 论文。

重要成果及产出：

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2. Shao-Bing Hou, Yuan ZY, Wei PF, Zhao GG, Liu GH, Wu Y-H, Shen WJ, Chen JM, Guo P*, **Che J***. 2021. Molecular phylogeny and morphological comparisons of the genus Hebius Thompson, 1913 (Reptilia: Squamata: Colubridae) uncover a new taxon from Yunnan Province, China, and support revalidation of Hebius septemlineatus (Schmidt, 1925). ***Zoological Research***. 42(5): 620−625.
3. Chatmongkon Suwannapoom*, Jiang K, Wu YH, Pawangkhanant P, Lorphengsy S, Nguyen TV, Poyarkov NA, **Che J***. 2021. First records of the fanged frogs Limnonectes bannaensis Ye, Fei & Jiang, 2007 and L. utara Matsui, Belabut & Ahmad, 2014 (Amphibia: Anura: Dicroglossidae) in Thailand. ***Biodiversity Data Journal***. 9: e67253.
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8. Shao-Bing Hou, Wang K, Guo P, Chen JM, Yuan ZY*, **Che J***. 2021. Two new species and a new country record of the genus Achalinus (Reptilia:Squamata: Xenodermidae) from China. ***Zootaxa***. 4950 (3): 528–546.

1. 中国西南山地及东南亚地区生物多样性研究新进展

围绕生物多样性保护、生态文明建设的国家战略需求，积极推进第二次青藏高原综合科学考察研究及高黎贡山生物多样性保护等系列项目开展。2021 年度在中国西南地区增加两栖、爬行动物新种共 8 个，新纪录种 2 个，恢复有效性物种 2 个。其中在横断山脉发现的杨氏脊蛇 *Achalinus yangdatongi* 种本名 “yangdatongi” 源于中科院昆明动物研究所杨大同研究员。以杨先生名字命名该物种，以致敬他长期推动中国西南、尤其是云南省两栖爬行动物学研究做出的卓越贡献。此外，基于长期的国际合作研究，为泰国两栖动物多样性新增 7 个物种：新种 1 个，泰国新纪录种 6 个。泰国新种 *Leptobrachella murphyi* 种名 “murphyi” 源于 Robert W. Murphy 教授（加拿大皇家安大略博物馆），国际两栖爬行动物 DNA 条形码计划（ColdCode）发起人之一，以致敬他推动 ColdCode 计划的努力，并感谢他对昆明动物研究所在东南亚开展跨境研究的支持。

Leptobrachella murphyi（chen et al. 2021. ***Zootaxa***）

杨氏脊蛇 *Achalinus yangdatongi*（Hou et al. 2021. ***Zootaxa***）

Diploderma bowoense（Wang et al. 2021. ***Zootaxa***）

Achalinus panzhihuaensis（Hou et al. 2021. ***Zootaxa***）

2. 践行使命，科学助力《生物多样性公约》第十五次缔约方大会（COP15）

2021 年 10 月，COP15 第一阶段会议在云南昆明举行。车静研究员代表国家濒科委参加了 COP15 平行论坛之一的非政府组织平行论坛——“基金会助力生物多样性保护”主题论坛。做了题为“中国的生物多样性危机与努力”的报告，并与基金会和政府代表人员就未来十年基金会在生物多样性保护中的作用与角色开展对话与研讨，为生物多样性保护提供科学的建议。

车静研究员参加 COP15 非政府组织平行论坛

同期车静研究员作为中国西南野生生物种质资源库动物分库执行主任参与云南电视台《新视野》节目录制，重点介绍中国西南野生生物种质资源库动物种质资源库的建设，推进生物多样性保护的宣传工作。

Herpetological Diversity and Evolution

Dr. Jing Che, Principal Investigator. Using amphibians and reptiles as model, we explore biodiversity and evolutionary questions within a phylogenetic framework. We are interested in how historical and ongoing processes have shaped the patterns of biodiversity of amphibians and reptiles that exist today, and how the species have adapted to and evolved.

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1. New progress in biodiversity research in southwest China and Southeast Asia

To meet the national strategic needs of biodiversity conservation and ecological civilization development, we have actively promoted the Second Tibetan Plateau Scientific Expedition and Research Program and the biodiversity conservation projects in Gaoligong Mountain. In 2021, a total of 8 new species of amphibians and reptiles , 2 new record species and 2 revalidation species in southwest China have been published. For the new species *Achalinus Yangdatongi*, the species name, yangdatongi, is a patronym honoring the Chinese herpetologist, Dr. Da-Tong Yang. We name the new species after Dr. Yang in recognition of his great contributions to the herpetological research in Southwestern China, particularly in Yunnan Province where the new species is found. In addition, based on long-term international cooperation, 1 new species and 6 new record species in Thailand have been published. This has enriched the biodiversity of herpetofauna of Thailand. The new specie *Leptobrachella murphyi*, epithet “murphyi” is derived from the name of Prof. Robert W. Murphy from the Royal Ontario Museum, Canada, the co-founder of ColdCode, the international effort to DNA barcode species of amphibians and reptiles. To salute his contribution to support of our study across the country border from China to Southeast Asia.

Field research photos

2. Support of COP15 with Science Strength

In October 2021, Fifteenth conference of the parties to the United Nations Framework Convention on climate change was held in Kunming. Prof. Che, on behalf of the Endangered Species Scientific Commission, P. R. China, participated in the theme forum of “Foundations for Biodiversity Conservation”, one of the parallel forums of COP15 for Non-Governmental organizations. Professor Che gave a report entitled “A crisis for biodiversity and efforts in China”, and had a discussion with representatives of foundations and governments on the role of foundations in biodiversity conservation.

Prof. Che on televised talk show

Prof. Che was invited to appear on a televised talk show of Yunnan TV named Horizon, where she introduced the exploration and achievements of biodiversity conservation in Yunnan Province, especially the construction of the Animal Branch of the Germplasm Bank of Wild Species, and also promoted the popularization of biodiversity conservation.

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余传鑫 Chuanxin Yu
易木荣 Murong Yi
董文捷 Wenjie Dong
曹如君 Rujun Cao
冯小刚 Xiaogang Feng
于中斌 Zhongbin Yu
卢宸祺 Chenqi Lu
尹浩萍 Haoping Yin
万 涵 Wang Han
荀 皓 Xun Hao

分子进化与基因组多样性研究

张亚平，博士，研究员，中国科学院院士，发展中国家科学院院士，欧洲科学院院士。中国科学院副院长，遗传资源与进化国家重点实验室学术委员会主任，*Hum Mol Genet* 编委。近年来重点围绕家养动物起源与驯化历史、动物环境适应的基因组进化机制以及动物复杂性状形成的遗传基础开展研究工作。在 2021 年联合多家研究机构，组织开展合作研究揭示驯化下欧亚家猪早期物种形成的基因组调控机制，运用单细胞转录组测序技术解析家猪胸腰椎异质性和肋骨形成机制，家犬适应欧洲牛奶饮食的遗传机制，运用多种基因组学手段深入解析了珍珠鸡的驯化历史。在国际 SCI 刊物上发表了论文 11 篇，其中 IF>10 的 4 篇，包括 ***Mol Biol Evol* (2)**，***Genom Proteom Bioinf*(1)**，***Nat Sci Rev* (1)**。带领团队获得云南省自然科学一等奖 “ 家养动物的起源与进化 ”。

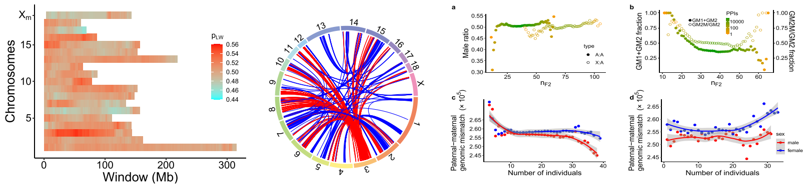
重要成果及产出：

1. **云南省自然科学奖一等奖：家养动物的起源与进化　张亚平，吴东东，王明山，彭旻晟，**刘益平，陈善元，苗永旺 .
2. **Xie HB**[1*], Wang LG[1], Fan CY[1], Zhang LC[1], **Adeola AC**, Yin X, Zeng ZB*,Wang LX*, **Zhang YP***. Genetic architecture underlying nascent speciation of Eurasian domestic pigs. 2021. ***Molecular Biology and Evolution*** 38(9);3556-3566. IF18.67.
3. **Li JB**[1], Wang LG[1], Yu DW[1], Hao JF[1], Zhang LC[1], **Adeola AC**, Mao BY, Gao Y, Wu SF, Zhu CL, Zhang YQ, Ren JL, **Mu CG, Irwin DM,** Wang LX*,Hai T*, **Xie HB*, Zhang YP***.Single-cell RNA-sequencing Reveals Thoracolumbar Vertebra Heterogeneity and Rib-genesis in Pigs. 2021. ***Genomics Proteomics & Bioinformatics.*** IF11.12.
4. **Liu YH**[1], Wang L[1], Zhang ZG[1], **Otecko O.N**, **Khederzadeh S**, Dai YQ, Liang B*, **Wang GD*, Zhang YP***. Whole-genome sequencing reveals a lactase persistence adaption in European dogs. 2021. ***Molecular Biology and Evolution*** 38(11);4884-4890. IF18.67.
5. **Wang MS**[1], **Zhang JJ**[1], Guo X[1], Li M, Rache Meyer[1], Hidayat Ashari1, Zheng ZQ, **Wang S, Peng MS**, Jiang Y, **Thakur M**, Suwannapoom C, **Esmailizadeh A**, Hirimuthugoda NY, Zein M, Kusza, S, Kharrati-Koopaee H, **Zeng L**, Wang YM, **Yin TT, Yang MM, Li ML, Lu XM**, Lasagna E, Ceccobelli S, Gunwardana H, Senasig TM, **Feng SH**, Zhang H, Bhuiyan A, Khan MS, Silva G, Thuy LT, Mwai OA, Ibrahim M. N. M, Zhang G, Qu K. X, Hanotte OS, Ibrohim M*, **Zhang GJ,** Qu KX, Hanotte O, Shapiro B, Bosse M, **Wu DD***, Han JL*, **Zhang YP***. Large-scale genomic analysis reveals the genetic cost of chicken domestication. 2021. ***BMC Biology.*** 19(1);118. IF8.182.
6. **Shen QK**[1], **Peng MS**[1], **Adeola AC** [1],Kui L[1],Duan SC, Miao YW, Eltayeb NM, Lichoti JK, **Otecko NO**, Strillacci MG, Gorla E, Bagnato A, Olaogun SC, Sanke OJ, Dawuda PM, Okeyoyin AO, Musina J, Njoroge P, Agwanda B, Kusza S, Nanaei HA, Pedar R, **Xu MM**, Du Y, **Nneji LM**, Murphy RW, Wang MS, Esmailizadeh A*, Dong Y*, Ommeh SC*, **Zhang YP***. Genomic analyses unveil helmeted guinea fowl (Numida meleagris) domestication in West Africa. 2021. ***Genome Biology and Evolution***. 13(6);evab090. IF4.079.

1. 驯化下欧亚家猪早期物种形成的基因组调控机制

为探讨欧亚家猪基因组间的互作不兼容，本课题组联合国内外研究人员，选取了欧洲的商品猪种大白猪和中国的地方猪种民猪作为研究对象，在 589 头 F2 资源家系中研究大白与民猪基因组互作对杂交后代存活率的影响。通过追踪 F0 代基因组在 F2 后代中的分布，从群体水平推断特定基因型组合的互作基因对个体存活率的影响。结果显示，大白猪与民猪基因组间已形成生殖隔离，微弱的基因组不兼容性导致 F2 存在明显的继承偏态；特定基因型组合的互作基因上，雄性后代分布仅为 30% 左右，提示存在霍尔丹效应；3 号染色体与其它常染色体之间的互作是导致大白猪与民猪基因组互作的重要原因。这项工作对研究猪杂交育种下品种基因组互作和早期物种形成机制具有重要意义。

【Xie HB et al. 2021 ***Molecular Biology and Evolution***，IF= 18.670】



2. 单细胞转录组解析家猪胸腰椎异质性和肋骨形成

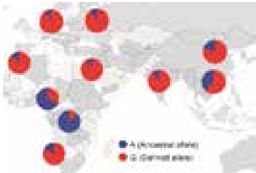
不同的家猪品种在胸椎和腰椎数量上高度可变，胸椎与腰椎数量与猪的体长密切相关，是重要的经济性状。长期以来，猪脊椎数量性状是猪遗传育种的重要研究方向之一，但胸腰椎数量变异与发育转换的分子机制目前仍不清楚。本课题联合国内多个课题组，利用 Smart-seq2 技术获取家猪 27 天胚胎的胸椎、腰椎和肋骨原基的单细胞转录组数据，分析发现早期胸腰椎和肋骨发育的主要进程为血管生成和成骨作用，在胸腰椎转换过程中可能存在 anti-*HOXA10*-antisense 的关键作用。

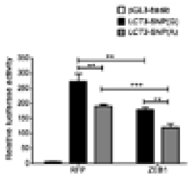
【Li JB et al. 2021 ***Genomics, Proteomics & Bioinformatics***，IF= 11.120】

3. 家犬适应欧洲牛奶饮食的遗传机制

本课题组联合多个课题组组成攻关团队，从全基因组揭示编码乳糖酶基因 *LCT* 在欧洲家犬中受到强烈的正选择，该基因与人群中乳糖酶耐受和牛奶饮食习惯相关。位于 19:38,609,592 的 A-to-G 突变在欧洲家犬和中东家犬中频率接近固定，该突变受到正选择的时间为 ~6,500 年内，而此时欧洲人群的牛奶饮食习惯已普遍存在。该突变在亚欧非大陆的分布趋势与人类乳糖酶耐受表型相似。基于 JASPAR 数据库，我们预测到该突变可能影响到与转录因子 ZEB1 的结合效率。细胞学功能实验证明该突变降低了 *LCT* 与 ZEB1 的结合，从而显著地提高了 *LCT* 表达量。本研究揭示了家犬与人类在牛奶饮食的趋同进化。

【Liu YH et al. 2021 ***Molecular Biology and Evolution***，IF= 18.670】





Molecular Evolution and Genome Diversity

Prof. Ya-Ping Zhang, Academician of Chinese Academy of Sciences (CAS), The World Academy of Sciences, and Academia Europaea. He serves as Vice President of CAS and the editorial board of ***Hum Mol Genet***. He focuses on the origin, domestication and artificial selection of domestic animals, the local adaptation of animals, and the evolution of complex traits of animals. In 2021, Prof. Zhang organized joint team to conduct series of evolutionary genomic researches on domestic animals, including the evolution of reproductive barriers in domestic pigs,gene expressional pattern in developing thoracolumbar vertebra, convergent evolution between humans and dogs with respect to diet, domestication history of guinea fowl. Prof. Zhang's group published 11 SCI-indexed papers, including ***Mol Biol Evol (2)***, ***Genom Proteom Bioinf (1)***, ***Nat Sci Rev (1)***. They also won the Natural Science Prizes of Yunnan Province, First Grade.

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1. Genetic architecture of nascent speciation of Eurasian pigs under domestication

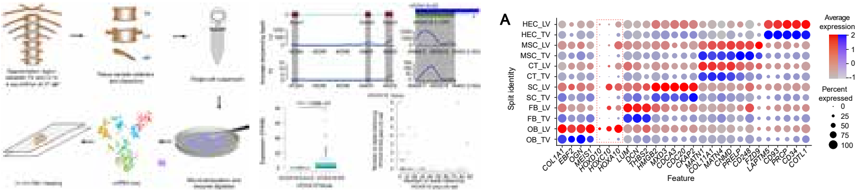
To explore the genomic incompatibility evolved between European and Chinese domestic pigs, we selected the Large White and Min pigs as a model to explore the genetic interactions associated with hybrid inviability. We explored the genetic incompatibility by screening the genetic interactions in 589 F2 individuals by conducting an analysis of the genome inheritance in the whole family. We found that weak reproductive barriers have evolved between Large White and Min pigs. In the F2 individuals, the lowest male ratio was observed as about 0.3 on some autosomal interactions, indicating a presence of hybrid male inviability conforming to the Haldane's rule. We found that epistatic interactions between chromosome 3 and other autosomes caused hybrid male inviability. The results is important in exploring the genomic interactions in pig breeding and in exploring the mechanism of nascent speciation.

【Xie HB et al. 2021 ***Molecular Biology and Evolution***, IF= 18.670】

2. Single-cell RNA-sequencing Reveals Thoracolumbar Vertebra Heterogeneity and Rib-genesis in Pigs

The number of thoracic vertebrae and lumbar vertebrae are highly variable between different domestic pigs, while the molecular mechanism of underlying vertebrae number variation among domestic pigs remains limited. Here, we investigated the single-cell transcriptome landscape of thoracic vertebra (TV), lumbar vertebra (LV), and RP cells from a pig embryo at 27 days post-fertilization. Further analysis of cell type-specific and strand-specific expression uncovered the extremely high level of HOXA10 3′-UTR sequence specific to osteoblasts of LV cells, which may function as anti-*HOXA10*-antisense by counteracting the *HOXA10*-antisense effect to determine TLV transition.

【Li JB et al. 2021 ***Genomics, Proteomics & Bioinformatics,*** IF= 11.120】



3. Convergent evolution between humans and dogs with respect to diet

A research consortium led by Prof. Yaping Zhang revealed *LCT* (lactase) is under strong positively selection in European dogs. Mutations of *LCT* may be related with lactase persistence (LP) in European, Middle Eastern and African humans. One SNP (chr19:38,609,592, A-to-G) show high allele frequency in European dogs (91.7%) and Middle Eastern dogs (92.2%). Its time to the most recent common ancestor is 6,535±180 years ago at which dairy economy has been well-developed in central Europe. Transcription factor *ZEB1* potentially binds to the SNP position. It increases the expression of *LCT* by reducing its binding with *ZEB1*, which would enhance dog's ability to digest milk-based diets. Our study uncovers the genetic basis of convergent evolution between humans and dogs with respect to diet.

【Liu YH et al. 2021 ***Molecular Biology and Evolution***, IF= 18.670】

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陶 林 Tao L
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母昌概 Mu CK
吴然燃 Wu RR
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进化基因组学与基因起源

王　文，中国科学院昆明动物研究所，研究员、博士生导师，进化基因组学与基因起源学科组负责人。长期以来一直致力于进化基因组学的研究。目前已经在 *Science*、*Nature Biotechnology*、*Nature Communications*、*Nature ecology & evolution*、*Molecular plant* 等重要学术杂志上发表论文 220 余篇，2021 年在国际权威杂志上发表了论文 11 篇，其中 IF>10 的有 6 篇，包括 *Cell* (2), *Nature genetics* (1), *Nature Communications* (1), *Science Advance* (1), *Molecular plant* (1)。两项 973 项目首席科学家，国家基金委创新群体项目负责人，中科院战略性先导专项 (B) 两个首席科学家之一，　2012 年获得“国家自然科学二等奖”(第一完成人)，2017 年获得两项“云南省自然科学二等奖”(分别为第一完成人和第二完成人)，2019 年获得“云南省自然科学奖一等奖”(第三完成人)。

实验室主页：http://internal.kiz.ac.cn/wangw2013/WenWang_Labweb/page0002.htm

重要成果及产出：

1. Bi XP[1], Wang K[1], Yang LD[1], Pan HL[1], Jiang HF[1], Wei QW[1], Fang MQ, Yu H, ……**Wang W***, Zhu M*, He SP*, Zhang GJ*. 2021. Tracing the genetic footprints of vertebrate landing in non-teleost ray-finned fishes. ***Cell***. 184(5): 1377–1391.
2. Wang K[1], Wang J[1], Zhu CL[1], Yang LD[1], Ren YD[1], Ruan J[1], Fan GY[1], Hu J[1], Xu WJ, Bi XP, Zhu YA, Song Y, Chen HT, Ma TT, **Zhao RP**, ……Zhao WM*, Qiu Q*, He SP*, **Wang W***. 2021. African lungfish genome sheds light on the vertebrate water-to-land transition. ***Cell***. 184(5): 1362–1376.
3. Lü ZM[1], Gong L[1], Ren YD[1], Chen YJ[1], Wang ZK[1], Liu LQ[1], Li HR[1], Chen XQ, Li ZZ , ……**Wan WT**, Qin YL, Zhang JZ, Zhu L, Shi W, He SP, Mao BY, **Wang W***, Kong XY*, Li YX*. 2021. Large-scale sequencing of flatfish genomes provides insights into the polyphyletic origin of their specialized body plan. ***Nature genetics***. 53(5): 742–751.
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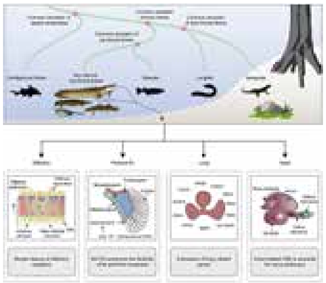
5. Liu C[1], Gao JB[1], Cui XX[1], Li ZP[1], Chen L[1], Yuan Y[1], Zhang YL[1], Mei LW, Zhao L, Cai D, Hu ML, Zhu BT, Li ZH, Qin T, ……Heller R*, **Wang W***, Huang JH*, Qiu Q*. 2021. A towering genome: Experimentally validated adaptations to high blood pressure and extreme stature in the giraffe. ***Science Advance***. 7(12): eabe9459.
6. Chen J[1], Wang X[1], Liu XN[1], Zhu XX[1], Li ZH[1], Chu HY, …… Liu YW, Lu L, Liu H, Yang T, Ge QJ, Shi CC, **Liu GC**, **Dong ZW**, Xu X*, **Wang W***, Jiang HF*, Ma YH*. 2021. Chromosome-level genome of Himalayan yew provides insights into the origin and evolution of the paclitaxel biosynthetic pathway. ***Molecular plant***. 14(7): 1199–1209.
7. **Wan WT**[1], **Dong ZW,** Ren YD, Yang J, Pan XY, **He JW**, **Chang Z**, Liu W, **Liu GC**, **Zhao RP**, **Hu P**, **Mao CY**, **Li J**, **Wang W***, **Li XY*.** 2021. Chromatin accessibility profiling provides insights into larval cuticle color and adult longevity in butterflies. ***Zoological Research***. 42(5): 614–619.
8. **Liu GC**[1], Liu W[1], **Zhao RP**[1], **He JW**[1], **Dong ZW**, Chen L, **Wan WT**, **Chang Z**, **Wang W***, **Li XY***. 2021. Genome-wide identification and gene-editing of pigment transporter genes in the swallowtail butterfly *Papilio xuthus*. ***BMC Genomics.*** 22(1):120.
9. **He JW**[1], **Liu GC**[1], Dong PX[1], **Dong ZW**, **Zhao RP**, **Wang W***, **Li XY***. 2021. Molecular cloning, characterization, and evolution analysis of the luciferase genes from three sympatric sibling fireflies (Lampyridae: Lampyrinae, *Diaphanes*). ***Photochemical &Photobiological Sciences***. 20(8): 1053–1067.
10. Zhang R, **Li J**, **Mao CY**, **Dong ZW**, **He JW**, **Liu GC**, **Zhao RP**, **Wang W***, **Li XY***. 2021. The mitochondrial genome of one “twisted-wing parasite” *Xenos* cf. *moutoni* (Insecta, Strepsiptera, Xenidae) from Gaoligong Mountains, Southwest of China. ***Mitochondrial DNA Part B: Resources***. 6(2): 512–514.
11. Hu JH[1], Huang LY[1], Chen GL[1], Liu H[1], Zhang YS, Zhang R, Zhang SL, Liu JT, Hu QY, Hu FY, W**ang W***, Ding Y*. 2021. The elite alleles of *OsSPL4* regulate grain size and increase grain yield in rice. ***Rice.*** 14(1): 90.

1. 脊椎动物水生到陆生演化之谜



为了更好的适应地球生态环境的改变，一些脊椎动物进行着从水生到陆生的进化过程，这是脊椎动物演化中最重要的科学问题之一。第一项研究不仅在分子水平揭示了许多脊椎动物重要器官的同源关系，还揭示了调控这些器官和相关功能的分子遗传机制。基于物种演化过程的比较分析还首次提出与四足动物陆生适应相关器官和生理功能的遗传调控机制在其硬骨鱼祖先中即已经开始出现雏形；特别是调控空气呼吸功能、骨骼运动灵活性以及心肺系统发育相关的古老基因和调控元件为后续肉鳍鱼登陆演化出四足动物这一飞跃提供了重要的遗传创新基础。

第二项关于脊椎动物水生到陆生演化的工作报道了迄今解析的首个完整且高质量的超大基因组——即非洲肺鱼基因组，其大小高达 400 多亿对碱基 (40 Gb) 是人类基因组大小 (3 Gb) 的 10 多倍；为高质量解析这一高复杂度巨大基因组，该项目催生了两个三代测序组装软件 NextDenovo 和 wtdbg.2.0，最终肺鱼基因组组装结果与预测大小吻合，该基因组包含了 95% 以上的脊椎动物完整基因；我们还确定了与肺表面活性物质、抗焦虑能力、五指肢和咽重构等陆地适应特性相关的潜在基因和调控元件。这些研究结果为理解从鱼类到人类的演化过程提供了新思路和重要资源。

【Bi *et al*., 2021, ***Cell***; Wang *et al*., 2021, ***Cell***.】

2. 昆虫重要表型特征 (形态、行为等) 适应性进化的遗传基础研究

昆虫具有多样的表型特征适应环境。我们以蝴蝶和萤火虫等具有重要表型特征的昆虫为研究对象，通过整合形态学、生物化学、多组学数据和基因功能验证等方法，揭示了昆虫重要表型特征 (形态、行为等) 适应性进化的遗传基础。以三种凤蝶科和一种蛱蝶科蝴蝶为例，在全基因组层面对幼虫和蛹的染色质开放峰在调控元件上进行了注释，结果表明不同发育时期染色质开放区域是高度动态变化的；此外，我们还发现了与黑色素合成途径的相关基因在柑橘凤蝶，以及与寿命相关的基因在枯叶蛱蝶中有重要表达调控变化，可能分别与幼虫表皮色彩和成虫滞育越冬有关；这些结果为蝴蝶调控元件的注释提供了重要的数据资源。以柑橘凤蝶为例，鉴定了 56 个 ABC 转运蛋白家族基因拷贝及 58 个 Rab 家族基因拷贝；利用 CRISPR/Cas9 基因编辑技术对其中 5 个基因 (ABC: *white, scarlet, brown, ok*; Rab: *lightoid*) 进行功能验证，结果表明，每个基因的敲除都会在 G0 个体的幼虫 (表皮、精巢) 和 / 或成虫眼睛的颜色中产生色素沉着异常的表型。本研究结果表明转运蛋白在柑橘凤蝶色彩形成中起了非常重要的作用，并为了解转运蛋白和小 G- 蛋白在蝴蝶形态发育中的作用提供了新的思路。

为了更好地了解同地域萤火虫的荧光素酶在识别配偶中的作用，我们克隆了三种同地域林间短角窗萤属萤火虫 (*Diaphanes nubilus, Diaphanes pectinealis* 和 *Diaphanes* sp2) 的荧光素酶基因，并对它们的酶特性进行了评价。结果表明，三种荧光素酶的氨基酸序列高度保守，包括相似度和蛋白结构。三个体外重组的荧光素酶在 pH 7.8 时均具有显著的发光活性和相似且最大的发光光谱。综上，同地域短角窗萤属具有相似的荧光素酶特征，提示它们可能采用其他策略 (如信息素、活动时间等) 来识别配偶；这些结果为短角窗萤属荧光素酶及其进化提供了新见解。

【Wan *et al*., 2021, ***Zoological Research***; Liu *et al*., 2021, ***BMC Genomics***; He *et al*., 2021, ***Photochemical &Photobiological Sciences***.】

Evolutionary Genomics and Origin of New Genes

Prof. Wen Wang, Professor, Head of Evolutionary Genomics and Origin of New Genes Research Group, KIZ, CAS. Prof. Wang has been focusing on evolutionary genomics. So far, he published more than 220 papers in such scientific journals as *Science*, *Nature Biotechnology*, *Nature Communications* etc., He is Chief Scientist of both 973 project (Scientific and technology Ministry) and Strategic Priority Research Program B (CAS), and also the leader of Innovative research group (NSFC). He received one second prize in China's National Natural Science Award in 2012, two second prize in Yunnan Natural Science Award in 2017 and one first prize in Yunnan Natural Science Award in 2019.

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1. The evolution mystery of vertebrates from aquatic to terrestrial

In order to better adapt to the changes of the earth's ecological environment, some vertebrates evolved from aquatic to terrestrial, which is one of the most important scientific issues in the evolution of vertebrates. The first study revealed not only the relation of vital organs homology in many vertebrates at the molecular level, but also the molecular genetic mechanisms that regulate these organs and related functions. Based on the comparative analysis of species evolution, it is proposed for the first time that the genetic regulation mechanism of organs and physiological functions related to terrestrial adaptation of tetrapods has begun to take shape in the ancestors of teleosts. In particular, the ancient genes and regulatory elements related to the regulation of air respiratory function, skeletal motor flexibility, and the development of the cardiopulmonary system provided an important genetic innovation basis for the subsequent landing of lobe-finned fish and the evolution of tetrapods. In particular, the ancient genes and regulatory elements related to the regulation of air respiratory function, skeletal motor flexibility, and the development of the cardiopulmonary system provided an important genetic innovation basis for the subsequent adaptive evolution from aquatic lobe-finned fishes to Terrestrial tetrapods.

The second study on aquatic to terrestrial evolution of vertebrates reported the complete and high-quality superlarge largest African lungfish (*Protopterus annectens*) genome so far, which has a size of more than 40 billion base pairs (40 Gb), more than 10 times the size of the human genome (3 Gb). Two third-generation sequencing assembly software, NextDenovo and WTDBG.2.0, were developed for the high-quality analysis of this large and highly complex genome. The lungfish final genome assembly results were consistent with the predicted size, which contained more than 95% of complete vertebrate genes. We also identified potential genes and regulatory elements related to such terrestrial adaptation traits as pulmonary surfactant, anxiolytic ability, pentadactyl limbs, and pharyngeal remodeling. These results provide insights and key resources for understanding the evolutionary from fish to humans.

2. Genomic basis of adaptive evolution of important phenotypic traits in insects

Insects are the most diverse group of animals on earth, and the adaptive evolution of their phenotypic traits is an important topic in biology. Due to their enigmatic phenotypic traits such as morphological diversity and behavior, butterflies and luminous beetles have been one of the important groups for studying the adaptive evolution of species since the Darwin era. Using three species of Papilionidae and one species of Nymphalidae as case, we annotated chromatin open peaks on regulatory elements within genome-wide at larval and pupal stages. The results showed that the chromatin openness was highly dynamic at different developmental stages. Furthermore, some regulatory regions located in promoter regions of melanogenesis- and longevity-related genes may be closely related to larval cuticle color and diapause in butterflies, respectively. Our results provide important data resource for annotation study of butterfly regulatory elements. Here, we have successfully identified 56 ABC transporters and 58 Rab members in the genome of swallowtail butterfly *Papilio xuthus*. Aiming to investigate the contribution of the five genes which are orthologous to well-studied pigment transporters (ABCG: *white*, *scarlet*, *brown* and *ok*; Rab: *lightoid*) of fruit fly or silkworm during the development of swallowtail butterflies, we performed CRISPR/Cas9 gene-editing of these genes using *P. xuthus* as a model and sequenced the transcriptomes of their morphological mutants. Our results indicate that the disruption of each gene produced mutated phenotypes in the colors of larvae (cuticle, testis) and/or adult eyes in G0 individuals but have no effect on wing color. Our data indicated these transporter proteins play an important role in body color of *P. xuthus* and provides new insights into the function of ABC transporters and small G-proteins in the morphological development of butterflies.

To better understand the role of the luciferases of sympatric fireflies in recognizing mates, we cloned the luciferase genes of three sympatric forest dwelling fireflies (*Diaphanes nubilus*, *Diaphanes pectinealis* and *Diaphanes* sp2) and evaluated their enzyme characteristics. Our data show that the amino acid (AA) sequences of all three luciferases are highly conserved, including the identities and the protein structures. Three recombinant luciferases produced in vitro all possess significant luminescence activity at pH 7.8, and similar maximum emission spectrum. Phylogenetic analyses support that *D. nubilus* is sister to *D. pectinealis* with *Diaphanes* sp2 at their base. All combined data indicate that sympatric *Diaphanes* species have similar luciferase characteristics, suggesting that other strategies (e.g., pheromone, active time, etc.) may be adopted to recognize mates. Our data provide new insights into *Diaphanes* luciferases and their evolution.

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比较基因组学

宿　兵，博士，研究员，中国科学院“百人计划”项目引进人才，国家自然科学基金杰出青年科学基金获得者，“新世纪百千万人才工程”国家级人选，国务院政府特殊津贴获得者，云南省有突出贡献优秀专业技术人才，中科院知识创新工程学科带头人，云南省万人计划“云岭学者”、“兴滇人才”与“科技领军人才”。主要研究方向为“动物与人类大脑演化的遗传与进化调控机制”、“东亚人群的起源、迁徙与适应性进化的遗传学机制”。主持 973 计划、NSFC 杰出青年科学基金、重点项目、创新群体项目、重大研究计划重点项目、云南省 NSFC 联合重点项目、中国科学院战略性先导科技专项 B 类项目、云南省万人计划科技领军人才项目等国家和部门科研项目 20 余项，在 *Cell*、*Science*、*Nature*、*PNAS*、*Nature Reviews Genetics*、*Nature Communications*、*National Science Review*、*Genome Research*、*Molecular Biology and Evolution* 等国际核心学术刊物上发表各类研究论文 200 多篇。获国家自然科学奖二等奖 1 项，谈家桢生命科学创新奖一项，云南省自然科学奖一等奖 5 项 。

实验室主页：http://159.226.149.45/compgenegroup/compgenegroup.htm

重要成果及产出：

1. Luo X. #, Liu Y. #, Dang D.#, Hu T., Hou Y., Meng X., Zhang F., Li T.,Wang C., Li M., Wu H., Shen Q., Hu Y., Zeng X., He X., Yan L., Zhang S. *, Li C. * & **Su B.** * 3D Genome of macaque fetal brain reveals evolutionary innovations during primate corticogenesis. ***Cell*** 184, 723-740.e21 (2021).
2. Zhang X.#, Liu Q.#, Zhang H.#, Zhao S.#, Huang J., Sovannary T., Bunnath L., Seang A., Samnom H., **Su B.***, Chen H.*. The distinct morphological phenotypes of Southeast Asian aborigines are shaped by novel mechanisms for adaptation to tropical rainforests. ***National Science Review*** (2021).
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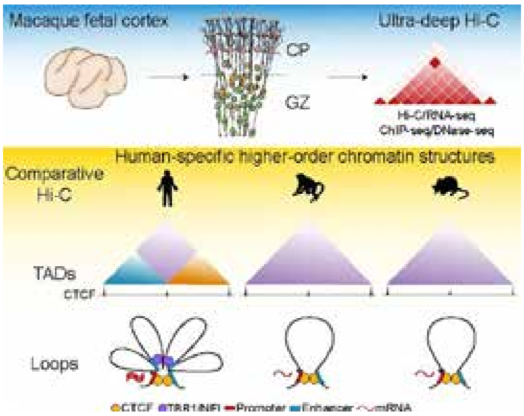
1、跨物种多组学分析揭示了三维基因组参与人类大脑发育的进化机制

人类大脑起源于漫长的进化过程，其最显著的改变是大脑的认知功能，反映在脑容量的显著扩增和脑结构的高度精细化。人类进化过程中，哪些遗传改变造就了人类大脑，是国际科学界长期力图回答的重要科学问题。本课题组联合国内研究人员，开展了跨物种大脑发育三维基因组的研究。首先，构建了中国猕猴胎脑的高分辨三维基因组图谱，并综合猕猴胎脑的转录组图谱、染色质开放区图谱以及染色质锚定蛋白 CTCF 的分布图谱，首次构建了猕猴胎脑发育过程中的染色质精细空间构象，鉴定了包括染色质区室、染色质拓扑结构域（简称 TAD）以及染色质环 (简称 Loop) 等不同尺度的染色质结构，以及基因组在大脑发育中发挥重要作用的调控元件（如增强子等）。其次通过与已发表的公共数据整合，利用跨物种三维基因组的比较（人类、猕猴和小鼠），发现了多个具有人类特异染色质结构的基因组位点，包括 499 个人类特异 TADs 和 1266 个人类特异 Loops。这些人类特异 Loops 显著富集增强子 - 增强子互作的调控模式，提示大脑发育在人类祖先中进化出更为精细的转录调控网络。该工作于 2021 年 1 月 27 日在线发表在国际顶尖学术期刊 *Cell* 上。



2、全基因组测序揭示了东南亚土著体貌表型对热带雨林环境适应的分子机制

东南亚分布许多古老的现生土著人群，在赤道线附近低纬度的热带雨林气候长期的自然选择下，产生了许多适应环境的体貌表型，如矮身高、深肤色、卷头发和宽扁鼻翼等。目前，对这些类似于非洲祖先的体貌表型研究较少。本课题组与国内外研究团队合作，对柬埔寨土著进行了全基因组测序，并开展了系统的群体遗传学分析。研究利用全基因组数据构建的群体聚类关系表明，柬埔寨土著位于东亚人群亲缘关系树较根部的位置，与其他人群的分歧明显，印证了他们是古老人群的结论。整合非洲人群、北欧人群、南欧人群和东亚汉族的数据，分析了柬埔寨土著基因组中特有选择的信号，发现了 1,187 个受选择的基因组区域。对这些区域中基因的功能富集分析发现，与身高、头发形态和面部轮廓等体貌表型相关的基因及其受选择的突变位点，包括与卷发表型相关的基因 TCHH 和 TCHHL1，与鼻子形态相关的基因 PAX3，以及与身高相关的基因 ENTPD1-AS1。这些基因均表现为在柬埔寨土著中特有的达尔文正选择信号。TCHH 和 TCHHL1 两个基因各有一个错义突变（改变氨基酸序列）在柬埔寨土著中富集，而这两个基因均与卷发表型有关。其他两个受选择基因（PAX3 和 ENTPD1-AS1）的受选择突变均位于基因的非编码区。进一步的细胞功能验证实验证实，PAX3 和 ENTPD1-AS1 受选择突变位点影响基因的表达调控，从而可能最终影响鼻子形态和身高两个体貌表型。该研究对东南亚土著的研究为探索人类表型多样性的进化模式和遗传机制提供了范例，研究结果在线发表在 *National Science Review* 上。

Comparative Genomics

Dr. Bing Su, principal investigator, The enlarged brain and highly developed cognitive skills are the most significant characteristics that set us apart from our relatives, the non-human primates. This evolutionary expansion is believed to be crucial to the highly developed cognitive abilities in humans, yet its genetic basis remains unsolved. our laboratory focuses on (1) the genetic mechanism underlying the dramatic enlargement of human brain and its highly developed cognitive skills during human evolution; (2) Origins and migration of modern human populations in East Asia and its adaptation to environmental stress.

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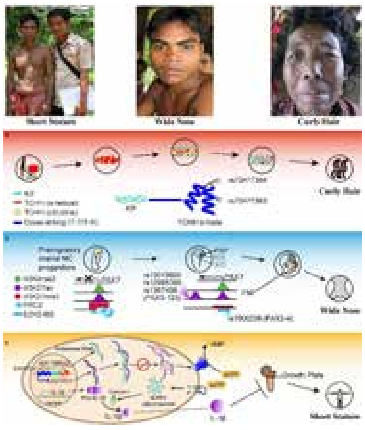
1. 3D Genome of macaque fetal brain reveals evolutionary innovations during primate corticogenesis

Elucidating the regulatory mechanisms of human brain evolution is essential to understanding human cognition and mental disorders. We generated multi-omics profiles and constructed a high-resolution map of 3D genome architecture of rhesus macaque during corticogenesis. By comparing the 3D genomes of human, macaque, and mouse brains, we identified many human-specific chromatin structure changes, including 499 topologically associating domains (TADs) and 1,266 chromatin loops. The human-specific loops are significantly enriched in enhancer-enhancer interactions, and the regulated genes show human-specific expression changes in the subplate, a transient zone of the developing brain critical for neural circuit formation and plasticity. Notably, many human-specific sequence changes are located in the human-specific TAD boundaries and loop anchors, which may generate new transcription factor binding sites and chromatin structures in human. Collectively, the presented data highlight the value of comparative 3D genome analyses in dissecting the regulatory mechanisms of brain development and evolution.

2. The distinct morphological phenotypes of Southeast Asian aborigines are shaped by novel mechanisms for adaptation to tropical rainforests

Southeast Asian aborigines, the hunter-gatherer populations living in the tropical rainforests, exhibit distinct morphological phenotypes including short stature, dark skin, curly hair and wide and snub nose. The underlying genetic architecture and evolutionary mechanism of these phenotypes remain a long-term mystery. Here we conducted whole genome deep sequencing of 81 Cambodian aborigines from 8 ethnic groups. Through genome-wide scan of selective sweeps, we discovered key genes harboring Cambodian-enriched mutations that may contribute to their phenotypes, including two hair morphogenesis genes (TCHH and TCHHL1), one nasal morphology gene (PAX3) and a set of genes (such as ENTPD1-AS1) associated with short stature. The identified new genes and novel mutations suggest an independent origin of the distinct phenotypes in Cambodian aborigines through parallel evolution, refuting the long-standing argument on the common ancestry of these phenotypes among the world-wide rainforest hunter-gatherers. Notably, our discovery reveals that various types of molecular mechanisms, including antisense transcription and epigenetic regulation, contribute to human morphogenesis, providing novel insights into the genetics of human environmental adaptation.



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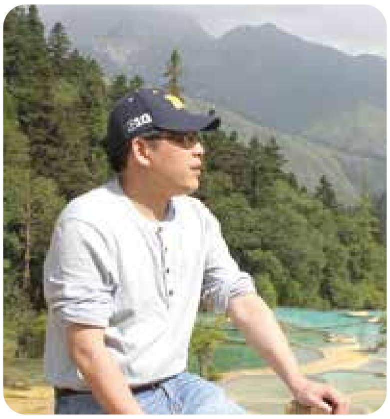
进化与功能基因组学



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2. **Xu DM[1]**, Yang CP[1], Shen QS[1], Pan SK[1], Liu Z[1], Zhang TZ[1], **Zhou X**, **Lei ML**, **Chen P**, **Yang H**, **Zhang T**, **Guo YT**, Zhan XJ*, Chen YB*, **Shi P***. 2021. A single mutation underlying phenotypic convergence for hypoxia adaptation on the Qinghai-Tibetan Plateau. ***Cell Res*** 31:1032-1035. IF$_{5\text{-year}}$=25.924
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5. Liu Z[1], **Chen P[1]**, **Li YY[1]**, **Li MW**, **Liu Q**, Pan WL, **Xu DM**, **Bai J**, Zhang LB*, Tang J*, **Shi P***. 2021. Cochlear hair cells of echolocating bats are immune to intense noise. ***J Genet Genomics*** 48:984-993. IF$_{5\text{-year}}$=5.223
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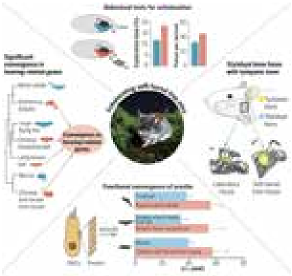
7. Jiang XL[1], He YM[1], Shen QS, Duan LC, Yuan YX, Tang L, Shi YL, Liu BY, Zhai HQ, **Shi P***, Yang CP*, Chen YB*. 2021. RETSAT Mutation Selected for Hypoxia Adaptation Inhibits Tumor Growth. ***Front Cell Dev Biol*** 9:744992. IF$_{5\text{-year}}$=7.219

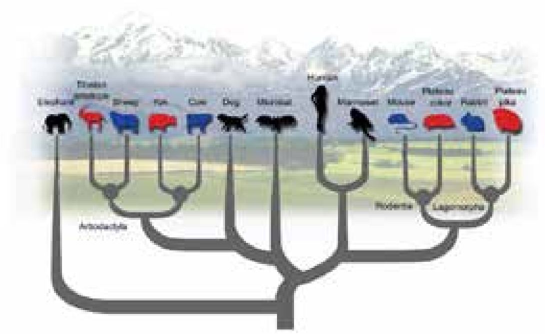
1. 证实新的具有回声定位能力的哺乳动物 —— 猪尾鼠



通过整合行为学、解剖学、基因组学以及基因功能实验等多个独立的证据，证实了啮齿目猪尾鼠属的物种具有回声定位能力。这一类新的回声定位的哺乳动物类群的发现，将动物回声定位行为扩展到了啮齿目，使得适应性复杂性状回声定位独立起源和演化的次数提高到了至少 6 次，成为自然界中性状趋同演化的典型案例。该工作发表后，受到学界的广泛关注，国内外主流媒体也对其进行了专题报道。（He K et al., *Science*）

2. 单个突变可以引起青藏高原哺乳动物低氧适应相关表型的趋同

通过比较基因组学研究发现四个高原哺乳动物牦牛、藏羚羊、高原鼢鼠和高原鼠兔同时在 *Retsat* 基因上发生了一个平行突变（Q247R）。该平行突变位点显著地增强了 RETSAT 酶的催化活性。并且，带有该平行突变位点的小鼠具有更高的心脏体重比，更强的心脏输出能力，更低的肺动脉压等有利于动物适应高原低氧环境的表型。更主要的是，该突变小鼠能在急性低氧环境下生存更久，提示这一突变在哺乳动物低氧适应中的重要意义。(Xu DM et al., ***Cell Research***)



3. 灵长类苦味受体 Tas2R16 的功能演化及分子机制

苦味受体作为毒物防御机制的重要一环在动物生存适应中发挥作用。我们以 *Tas2R16* 基因为例，对其在灵长类中的功能演化和分子基础进行了解析，系统揭示了其在灵长类中的功能变化，并发现了一个少见的趋同演化例子：一种新大陆猴（白面僧面猴）与人类 Tas2R16 均对有毒的 β- 吡喃葡萄糖苷特别敏感。通过分子进化、3D 建模、功能验证等多个层次的分析，证明了这两个物种中通过平行进化发生的 K172N 突变是造成功能趋同的关键位点。考虑到白面僧面猴极其特殊的食性，该突变可能在其早期进化历程中发挥着重要作用。（Yang H et al., ***Molecular Biology and Evolution***）

Evolutionary and Functional Genomics

Prof. Peng Shi, Principal Investigator, has long been engaged to the researches on evolutionary and functional genomics. The work in Shi's laboratory covers two fields:

(1) molecular mechanism of adaptation to various environments in animals. We study the genotype-phenotype relationship at the genomic level under the guidance of natural selection theory, while combining multiple advanced techniques including NGS, bioinformatics and functional assays, etc.

(2) novel disease-related gene identification and the etiopathogenesis study. Through genomic analyses using non model organisms, we try to aid the comprehensive understanding of the etiopathogenesis in human longevity, cardiovascular diseases and tumors from a different angle.

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1.Echolocation in soft-furred tree mice

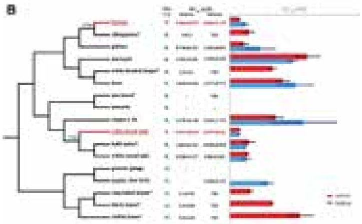
Echolocation is the use of reflected sound to sense features of the environment. Here, we show that soft-furred tree mice (Typhlomys) echolocate based on multiple independent lines of evidence. Behavioral experiments show that these mice can locate and avoid obstacles in darkness using hearing and ultrasonic pulses. The proximal portion of their stylohyal bone fuses with the tympanic bone, a form previously only seen in laryngeally echolocating bats. Further, we found convergence of hearing-related genes across the genome and of the echolocation-related gene *Prestin* between soft-furred tree mice and echolocating mammals. Together, our findings suggest that soft-furred tree mice are capable of echolocation, and thus are a new lineage of echolocating mammals.

2.A single mutation underlying phenotypic convergence for hypoxia adaptation

Applying comparative genomics analysis, we identified a parallel amino acid substitution (Q247R) in the *Retsat* gene shared by four indigenous mammals living on the Qinghai-Tibetan Plateau. The catalytic activity of the Retsat enzyme could be significantly enhanced *in vitro* through this mutation. The Q247R knock-in mice exhibit phenotypic characteristics that are adaptive to the hypoxic environment of the plateau, such as higher ratio of heart mass to body mass, stronger cardiac output capacity and lower pulmonary artery pressure. Notably, the mutant mice survive longer under acute hypoxia, hinting the important role this substitution may play during mammal adaptation to the plateau.

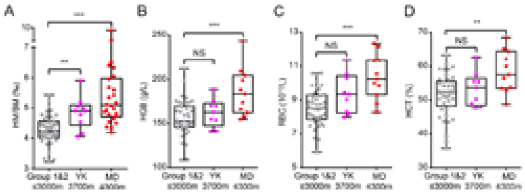
3.Functional evolution of primate bitter taste receptor Tas2R16

Bitter taste receptors play a critical role in preventing toxin intake by animals, however, few systematic studies of specific Tas2R to unveil their functional evolution have been conducted. Here, we surveyed *Tas2R16* across all major clades of primates and reported a rare case of a convergent change to increase sensitivity to β-glucopyranosides in human and a New World monkey, the white-faced saki. Combining analyses at multiple levels, we demonstrate that a parallel amino acid substitution (K172N) shared by these two species is responsible for this functional convergence of Tas2R16. Considering the specialized feeding preference of the white-faced saki, the K172N change likely played an important adaptive role in its early evolution to avoid potentially toxic cyanogenic glycosides, as suggested for the human *TAS2R16* gene.



4.Phenotypic and genomic adaptations to the extremely high elevation in plateau zokor

To explore whether endemic animals adopt uniform mechanism during their adaptation to different elevational environments, we investigated the phenotypic and genomic data of seven populations of plateau zokor along elevations ranging from 2,700 to 4,300 m. The results show that populations at above 3,700 m diverged from others nearly 10,000 years ago, and have elevated ratios of heart mass to body mass. Genomic analysis of selective sweeps indicates that positive selection might contribute to the observed phenotypic alterations, with the adaptive cardiovascular phenotypes possibly evolving under the functional constrains of their common ancestral population. Taken together, we show that heterogeneous stressors may impact mammal adaptation to extreme elevations, providing new insights into plateau adaptation.



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真核细胞进化基因组学

文建凡，博士，研究员，遗传资源与进化国家重点实验室副主任。研究方向为“ 真核细胞进化基因组学 ”。以处在真核生物进化的关键地位的单细胞生物 (如贾第虫、衣藻、眼虫、领鞭毛虫等) 为主要研究对象，向下追溯到原核生物，向上扩展到多细胞生物，开展真核细胞的结构和功能，特别是基因、基因家族、功能途径基因群和基因组的多样性形成与进化研究，以及从适应性进化角度开展有害生物 (如寄生虫）防治靶标的发掘利用，有益生物 (如藻类) 的高效、特异代谢途径的进化形成机制及其应用的基础研究。

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重要成果及产出:

1. **Cheng J-N#, Lyu Z-X#, Wen J-F***. Duplication and functional differentiation of important energy metabolism genes and adaptive radiation. (submitted)
2. **Xue M#, Li Y-J, Deng Q, Wen J-F***. Intron gain of prokaryotic FBPase in chlorophyta after its horizontal transfer from prokaryotes. (submitted)
3. **Shen J#, Lyu Z-X#, Bai H-X, Wen J-F***. Inhibitory effect and molecular mechanism of several Traditional Chinese Medicines against *Giardia intestinalis* in vitro. (submitted)

1. 原核型 FBPase 基因水平转移至真核绿藻后其内含子获得的研究

我们在莱茵衣藻这一真核生物的基因组中发现存在一个原核型的 FBPase 基因，经扩大调查，发现此基因竟在真核生物的绿藻门中普遍存在而不存在于其它真核生物中。经分子系统分析，发现绿藻中的 FBPase 先聚为一支再与放线菌的 FBPase 形成姐妹支（图 1）。这表明该酶的基因是在绿藻门的共同祖先时期从放线菌水平转移而获得的。那么，从原核基因的无内含子状态如何真核化获得内含子的呢？这是一个有趣且对揭示从原核生物进化成真核生物的过程中内含子如何起源的具有重要意义的问题。对绿藻中的此基因进行内含子的鉴定和系统的比较分析，发现：该基因内含子的产生存在着相位和序列方面的偏好性 —— 绝大多数的内含子都是产生在即使发生错误剪接和内含子滑动也不易产生不利影响的 0 相位，且明显地倾向于产生在 “G|G” 这种 proto-splice sites 中（图 2）；且此基因中的内含子密度与其所在绿藻的全基因组的内含子密度基本是一致的。以上结果对内含子的起源的提示：内含子在最初起源时，对相位和插入位点方面是存在偏好性的。而且进入到真核生物的原核基因中内含子产生的多寡与其所在的具体物种的整体基因组环境密切相关。

图 1. FBPase 的系统发生分析结果
Fig1. Maximum likelihood phylogenetic tree for FBPase sequence

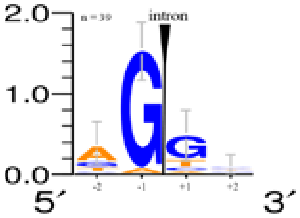

图 2. 内含子位点上下游各两碱基序列的偏好性分析结果
Fig2. Conservative analysis of the upstream and downstream two nucleotide sequences around introns

2. 重要能量代谢基因的复制和功能分化与适应性辐射

本实验室首次发现一种重要的糖代谢酶 ONTIM 在罗非鱼中发生了复制，并且我们对序列和结构分析表明虽然复制后产生的新酶在许多方面与原来的酶相似，但一些关键的氨基酸位点已经发生了重大变化，酶活实验也证实了新酶极大可能已经不行使原功能。随后根据该酶的组织性特异分布猜测新酶的功能跟免疫有关（图 3），并通过免疫刺激实验进一步证实了这一猜测（图 4）。有趣的是，我们随后对整个硬骨鱼类展开调查发现，该新酶普遍且只存在于慈鲷科的鱼类中，并且新酶在慈鲷科内非常保守，这一发现表明新酶一定是通过相对古老的复制出现在慈鲷科的共同祖先中。慈鲷科鱼类作为脊椎动物中迄今发现的成种最快、最多的适应性辐射的典型代表而一直是进化生物学研究的热点，目前发现它们可能通过增加各种耐受性（pH、温度、盐度等）来适应各种不同的生态环境，我们的研究提示该能量代谢基因发生了复制和功能分化，能够显著增强慈鲷科鱼类的免疫功能，可能为该科鱼类能发生这种惊人的适应性辐射提供了重要潜能。

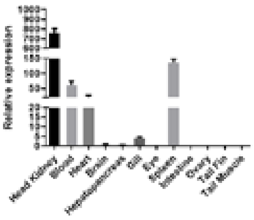

图 3. 新酶在罗非鱼中的组织特异性表达
Fig3.Tissue-specific expression of the novel enzyme in *Oreochromis niloticus*

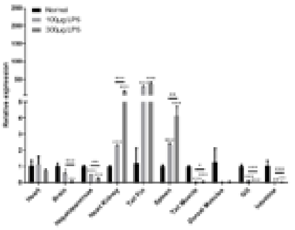

图 4. LPS 刺激罗非鱼免疫反应后各个组织新酶的表达量变化
Fig4. Expression of the novel enzyme in different tissues of *Oreochromis niloticus* after LPS stimulated immune response

Evolutionary Genomics of Eukaryotic Cells

Prof. Jian-Fan Wen, Principal Investigator, Vice Director ofthe State Key Laboratory of Genetic Resources and Evolution.His group is mainly interested in the origin and evolution of theeukaryotic cell. Taking the protists, which occupy key positions inthe eukaryotic cell evolution, as models, and combining with thedata of prokaryotes and multicellular organisms, they study thebiodiversity and origin and evolution of the structures and functions, especially of genes, gene families, gene groups offunctional pathways and genomes, of the eukaryotic cells. Based on these basic studies, they also explore the new waysfor the control and treatment of some harmful organisms (e.g. parasitic protozoa and schistosomes) and the applications of the effective and specifc metabolic pathways.

1. Intron gain of prokaryotic FBPase in chlorophyta after its horizontal transfer from prokaryotes

We found that the prokaryotic gene FBPase in the genome of the eukaryote *Chlamydomonas reinhardtii* , after extensive investigation, it was found that this gene is ubiquitous in the Chlorophyta of eukaryotes but not in other eukaryotes. By molecular phylogenetics, it was found that the FBPase of Chlorophyta are clustered together then formed a sister clade with FBPase of Actinomycetes in the phylogenetic tree (figure 1) , so the FBPase in green alga is arise from Actinobacteria during the common ancestor of Chlorophyta. Then, how to obtain introns from the intron-free state of prokaryotic genes? This is an interesting and important question for reveal the origin of intron during the evolution from prokaryotes to eukaryotes.We collected and identified the FBPase genes of several species of green algae, and then identified and conducted a systematic analysis about their introns. The analysis results show that prokaryotic genes show phase-biased and sequence-biased when inserting new introns—the vast majority of introns are phase 0 that are less prone to adverse effects when mis-splicing and intron sliding occur; these introns tend to be inserted into the proto-splice sites of G|G (figure 2) ; And the the intron density in each FBPase is approximately same as the intron density of the genome in which it is located. This may indicate that: when introns are originally produced in eukaryotic genes, there is a preference for phase and insertion sites. Moreover, the amount of introns produced in prokaryotic genes entering eukaryotes is closely related to the overall genomic environment of the particular species in which they are located.

2. Duplication and functional differentiation of important energy metabolism genes and adaptive radiation

The duplication of an important glucose metabolism enzyme ONTIM in *Oreochromis niloticus* was found for the first time in our laboratory. Our sequence and structure analysis indicated that although the novel enzyme is similar to the original enzyme in many respects, but some key amino acid sites have undergone significant changes. The enzyme activity experiment also confirmed that the novel enzyme may not perform its original function. Subsequently, according to the tissue specific distribution of the novel enzyme (Figure 3), we guessed that the function of the novel enzyme was related to immunity, which was further confirmed by immune stimulation experiments (Figure 4). It is interesting to note that we then investigate the teleost fishes found that novel enzyme exists ubiquitously and exclusively in the fishes of the family Cichlidae, and the novel enzyme is very conservative in the cichlid family, suggesting the novel enzyme must have emerged in the common ancestor of cichlids through a relatively ancient duplication of the original enzyme. Cichlid is a typical model of the fastest and largest adaptive radiation found in vertebrates, and have always been a hotspot in evolutionary biology research. It has been found that they may adapt to various ecological environments by increasing various tolerances (pH, temperature, salinity, etc.). Our research suggests that the duplication and functional differentiation of this key energy metabolism gene can significantly enhance the immune function of cichlid, which may provide important potential for this striking adaptive radiation in cichlid.

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马占山，研究员，博导，计算生物与医学生态学学科负责人。 2010 年 11 月中科院“百人计划(引进杰出技术人才)”引进。2011 年入选“云南省高端科技人才”和“百名海外高层次人才”计划；2015 年入选“云岭产业技术领军人才”。美国 Idaho 大学计算机科学 (2008 年) 和昆虫学 (1997 年) 双博士、计算机科学和计算生物学研究科学家。并具有在硅谷等地长达八年多的涵盖电子、网络、软件、信息安全领域的计算机高级工程师经历。曾是美国“人类微生物菌群宏基因组研究计划 (HMP) 主要研发科学家之一 (2008-2010)，总部设在英国伦敦的 “Faculty 1000 of Biology & Medicine” 成员 (2008-2016)，并担任 I. J. Network Science 主编 (2015-2017)。以第一或责任作者在计算机科学、工程数学、计算智能、昆虫学、生态学、医学微生物学等领域发表 100 余篇论文。

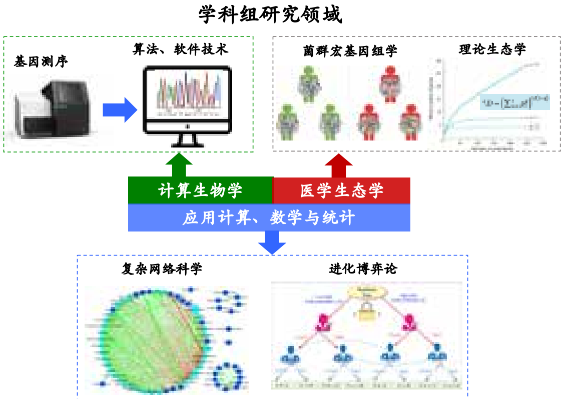
重要成果及产出:

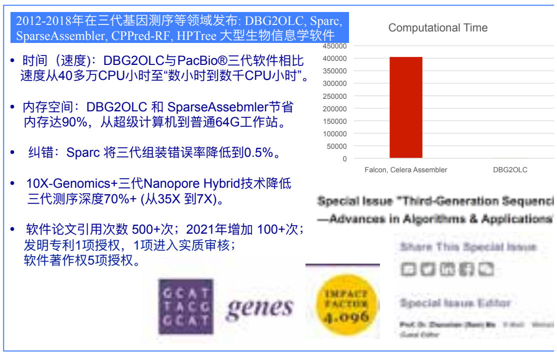
1. Ma ZS. (2021) Cross-scale analyses of animal and human gut microbiome assemblies from metacommunity to global landscape. *mSystems*. 6:e00633-21.
2. Ma ZS. (2021). Philosophical Skepticism Concerning the Neutral Theory or Randomness: Misplaced or Misconceived? A Reply to Madison, “Stochasticity and Randomness in Community Assembly: Real or As-If?” *mSystems*. 6:5.
3. Ma ZS. (2021) Spatial Heterogeneity Analysis of the Human Virome with Taylor’s Power Law. *Computational and Structural Biotechnology Journal*. 19:2921-2927.
4. Ma ZS. (2021) A unified survival-analysis approach to insect population development and survival times. *Scientific Reports*. 11, 8223.
5. Ma ZS. (2021) Evaluating the Assembly Dynamics in the Human Vaginal Microbiomes With Niche-Neutral Hybrid Modeling. *Frontiers in Microbiology*. 12:699939
6. Ma ZS (2021) Microbiome transmission during sexual intercourse seems stochastic. *Frontiers in Microbiology. doi: 10.3389/fmicb.2021.789983.*
7. Ma ZS (2021) Coupling Power Laws Offers a Powerful Method for Problems such as Microbiome diversity and COVID-19 Fatality Predictions. *Frontiers in Applied Mathematics and Statistics, doi: 10.3389/fams.2022.801830.*
8. Li WD & Ma ZS. (2021) Population-level diversity-disease relationship (DDR) in the human microbiome associated diseases. *Computational and Structural Biotechnology Journal*.19:2297-2306.
9. Li WD, *et al.* (2021) Ecological and network analyses identify four microbial species with potential significance for the diagnosis/treatment of ulcerative colitis (UC). *BMC Microbiology.* 4;21(1):138.
10. Li LW, et al (2021). Structure and Dynamics of the Breast Tissue Microbiomes Under Tumor Influences: An Approach With Neutral, Near-Neutral, and Niche-Neutral Hybrid Models. *Frontiers in Microbiology*, 12:614967.
11. Xiao WM, *et al.* (2021) Diversity Scaling Analysis of Chinese Gut Microbiomes Across Ethnicities and Lifestyles. *Frontiers in Microbiology*. 12:736393.
12. Xiao WM & Ma ZS. (2021) Inter-Individual Diversity Scaling Analysis of the Human Virome With Classic Diversity-Area Relationship (DAR) Modeling. *Frontiers in Genetics*. 2:627128.
13. Chen HJ, *et al.* (2021) Diversity Scaling of Human Digestive Tract (DT) Microbiomes The Intra-DT and Inter-individual Patterns. *Frontiers in Genetics*, 12:724661.
14. Qiao YT, *et al.* (2021) Integrated diversity and shared species analysis of human viromes. *Archives of Virology*, 166(10):2743-2749.
15. Ma ZS, et al (2021). Microbiome-host phylogeny relationship in animal gastrointestinal tract microbiomes. *FEMS Microbiology Ecology* (minor revisions)
16. Ma ZS, Ellison AM. (2021) In silico trio-biomarkers for bacterial vaginosis revealed by species dominance network analysis. *Computational and Structural Biotechnology Journal*. 19:2979-2989.
17. Ma ZS, Ellison AM. (2021) Toward a unified diversity–area relationship (DAR) of species and gene diversity illustrated with the human gut metagenome. *Ecosphere*, 12(11):e03807.

发明专利 (2021 年授权 6 项)

ZL 201710949841.0	ZL 201711223008.4
ZL 201611126939.8	ZL 201711289534.0
ZL 201611127036.1	ZL 201611126940.0

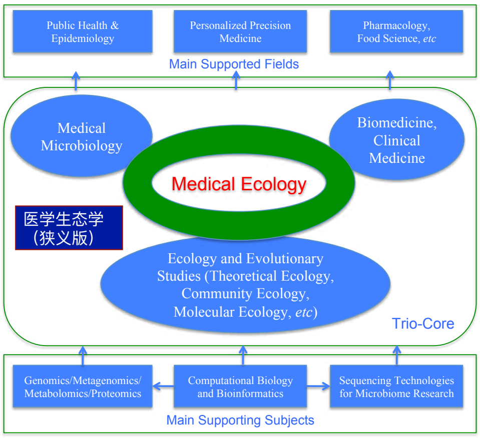
学科介绍 (Research Interests)





2012-2018年在三代基因测序等领域发布: DBG2OLC, Sparc, SparseAssembler, CPPred-RF, HPTree 大型生物信息学软件

- 时间（速度）：DBG2OLC与PacBio®三代软件相比速度从40多万CPU小时至“数小时到数千CPU小时”。
- 内存空间：DBG2OLC 和 SparseAssebmler节省内存达90%，从超级计算机到普通64G工作站。
- 纠错：Sparc 将三代组装错误率降低到0.5%。
- 10X-Genomics+三代Nanopore Hybrid技术降低三代测序深度70%+ (从35X 到7X)。
- 软件论文引用次数 500+次；2021年增加 100+次；发明专利1项授权，1项进入实质审核；软件著作权5项授权。



Computational Biology and Medical Ecology Lab

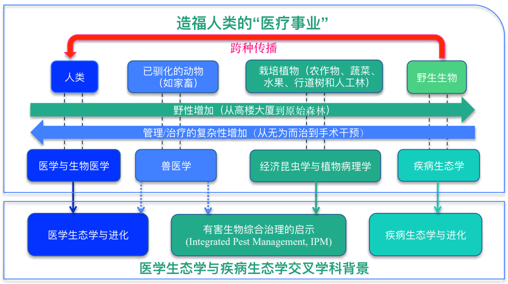
Bio-sketch of the lab Principal Investigator (PI): **Zhanshan (Sam) Ma** received his double PhDs in Computer Science, and Entomology in 2008, and 1997, respectively, both from the University of Idaho (UI), USA. In November 2010, he was retained as a Professor and Principal Investigator by Kunming Institute of Zoology (KIZ), the Chinese Academy of Sciences (CAS) through "The 100 Talents PI Program" of the CAS. Prior to joining in KIZ, he was a Research Scientist (in Computational Biology & Computer Science) at UI. He was a senior network and software engineer from 1998 to 2006 in the computer industry in Silicon Valley, USA. Dr. Ma has been keeping dual track publishing in both Computer Science and Biology with more than 100 peer-refereed papers in premier platforms such as *IEEE Transactions on Reliability*, *Science Translational Medicine*, *The ISME Journal, Ecological Monographs,* and *Advanced Science*. He was a member of London-based "*Faculty 1000 of Biology and Medicine*".

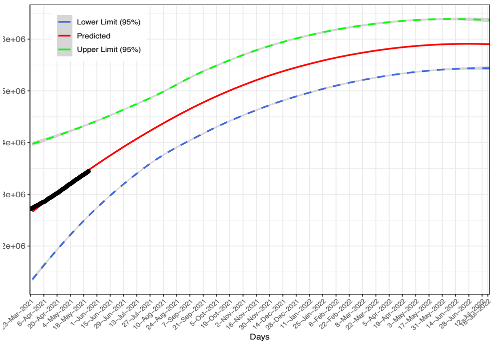
研究团队及研究方向

姓　名（学位；早期背景；目前研究方向）

李连伟（特别研究助理；生物科学；生物信息学 ）
陈红菊（博士生；数学；进化博弈论）
肖琬蒙（博士生：林学；生物信息学）
杨　旭（硕士生：昆虫学；生物信息学）

李文迪（博士生；生物医学；医学生态学）
MD Motiur Rahman (博士生；概率统计；深度学习)
邹　权（博士；计算机科学、人工智能；客座）
乔玉亭（博士生：生物信息学；生物信息学）

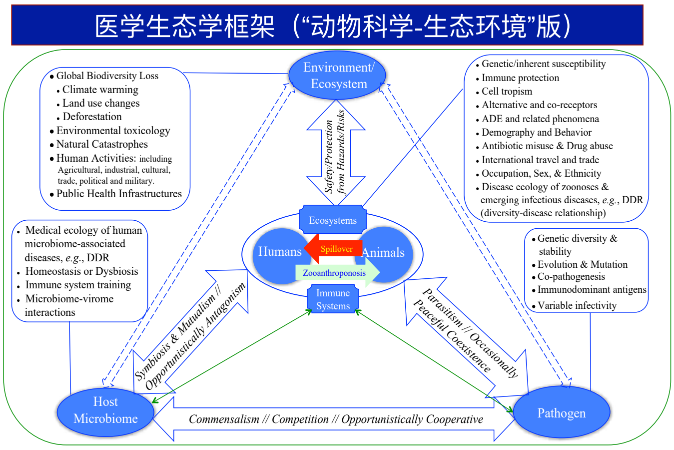




[1] Murray, CJL (2022) COVID-19 will continue but the end of the pandemic is near. The *Lancet*, January 19th, 2022.

[2] Ma ZS (2022) Coupling Power Laws Offers a Powerful Modeling Approach to Certain Prediction/Estimation Problems with Quantified Uncertainty. *Frontiers in Applied Mathematics and Statistics*. [Jan 24th, 2022], DOI: 10.3389/fams.2022.801830.

[3] Ma ZS (2021) Coupling Power Laws Offers a Powerful Method for Problems such as Biodiversity and COVID-19 Fatality Predictions. ArXiv Preprint [May 23, 2021]: https://arxiv.org/abs/2105.11002.



"耦合幂定律"预测新冠大流行不大可能在三月底结束："柳叶刀"期刊发文预测或许"不靠谱"

2022 年 1 月 19 日美国华盛顿大学 IHME 建模团队负责人 Murray 教授在柳叶刀 (The Lancet) 发文预测新冠大流行或将于 2022 年 3 月结束"。自大流行以来，该团队和英国帝国理工学院建模团队的预测一直为美国和英国政府所关注；该文发表后，各大媒体对其做出了广泛报道和分析（包括白宫医疗专家介绍讨论）。

2021 年 5 月学科组在 arXiv 预印本平台"立此存照"：发布基于耦合幂定律的新冠死亡预测模型。与 2022 年 1 月 24 日 (该研究正式发表于 Applied Mathematics and Statistics 之日) 全世界公布的新冠死亡人数相比，其预测误差仅为 7%(精度 93%)（左图）。该研究预计死亡高峰（拐点）应该在 2022 年 7 月之后。当然，这仅仅是预测死亡高峰的到达，而到达高峰后大流行是否结束是另一问题。换句话说，疫情在到达死亡高峰前（七月）当然不能算是过去了，而高峰之后也不一定能算过去了。这一结果与华盛顿大学预测显然不同。

科技日報
SCIENCE AND TECHNOLOGY DAILY
人类病毒组异质性评估报告发表

人类进化与疾病基因组学

孔庆鹏，中科院昆明动物所，研究员、博导。迄今在 *Am J Hum Genet*、*Genome Res*、*Mol Biol Evol*、*Natil Sci Rev*、*PNAS*、*Theranostics* 及 *Hum Mol Genet* 等国际重要 SCI 期刊上发表论文 100 余篇，论文被各类 SCI 刊物累计引用 4900 余次，H 指数 33。主持有国家重点研发计划专项（任首席科学家）、国家基金委重点国际合作、重大研究计划等项目；2013 年入选科技部科技创新中青年领军人才计划；2016 年入选“国家高层次人才特殊支持计划”领军人才；2020 年先后入选昆明市“春城科技领军人才”、云南省万人计划“云岭学者”。研究组目前的主要研究方向：人群起源演化及健康长寿分子机制。

重要成果及产出：

1. **Jiang JJ**, Cheng LH, Yan L, **Ge MX**, **Yang LQ**, Ying HQ, **Kong QP***. Decoding the role of long noncoding RNAs in the healthy aging of centenarians. *Briefings in Bioinformatics*,2021,22(5): bbaa439. (IF=11.622)
2. Shen T, **Xia WX**, Min SN, Yang ZX, **Cheng LH**, Wang W, Zhan QX, Shao FH, Zhang XH, Wang ZY, Zhang Y, Shen GD, Zhang HF, Wu LL, Yu GY, **Kong QP***, Wang XT*. A pair of long intergenic non-coding RNA LINC00887 variants act antagonistically to control Carbonic Anhydrase IX transcription upon hypoxia in tongue squamous carcinoma progression. *BMC Biology*,2021,19(1):192. (IF=7.431)
3. **Ge MX**, Hu LA, Hong S, Zi MT, **Kong QP*,** He YH*. Senolytic targets and new strategies for clearing senescent cells. *Mechanisms of Ageing and Development*, 2021, 4(195):111468. (IF=5.432)
4. **Rahman ZU, Tian JY, Gao Z L, Wang HT, Xia WX, Yang B Y, Yang L Q, Li YC*, Kong QP***. Complete mitogenomes document substantial genetic contribution from the Eurasian Steppe into northern Pakistani Indo-Iranian speakers. *European Journal of Human Genetics*, 2021, 29(6): 1008-1018. (IF=4.246)

1. 揭示差异表达的长链非编码 RNA(lncRNA) 对百岁老人的潜在保护作用

对百岁老人家系 171 例样本（包括百岁老人，百岁 F1 后代和 F1 后代配偶，F1 后代配偶作为一般对照）的外周血白细胞进行转录组测序，以 lncRNA 为出发点，挖掘 lncRNA 在衰老及抗衰老过程中的作用。我们分析鉴定出了 8 个 lncRNA 可能与衰老 / 健康衰老相关，其中两个 lncRNA（THBS1-AS1 和 THBS1-IT1）在百岁老人中呈显著高表达。在复制衰老型细胞系中对这两个 lncNRA 进行过表达实验，证明其不仅显著降低了 p16 和 p21 的蛋白表达，且显著降低了衰老相关的 β- 半乳糖苷酶的活性，表明它们的高表达延缓细胞衰老相关表型。该研究首次报道了 lncRNA 在健康长寿老人中的表达规律，并发现一些差异表达的 lncRNA 具有潜在的抗衰老作用（Jiang et al.2021, ***Briefings in Bioinformatics***）。

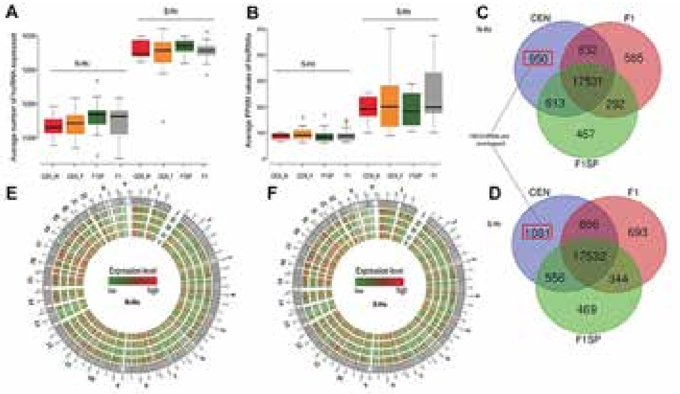


图 1. 中国长寿人群 lncRNA 分布规律及特征。

【Jiang et al.2021, ***Briefings in Bioinformatics***】

2. 揭示印欧语系向巴基斯坦北部的扩散伴随着人群迁徙

基于巴基斯坦北部的印欧语系人群共 213 个个体的线粒体基因组测序数据，结合已发表的巴基斯坦及其周边的现代及古代样本的线粒体 DNA（mtDNA）数据，系统研究了印欧语系向巴基斯坦的扩散模式。结果表明，巴基斯坦北部的印欧语系人群的主要母系遗传组分来源于欧亚西部。其中，单倍群 W3a1a 和 J1b1a1 等类群的起源和扩散与印欧语系的传播十分相似，因而可能与印欧语系人群的迁徙有关。这说明，印欧语系向南亚的扩散可能不仅仅是简单的文化扩张，也伴随着一部分的人群迁徙。研究结果还表明，巴基斯坦北部可能在印欧语系向南亚的扩散中起着重要的通道作用（Rahman et al. 2021, ***European Journal of Human Genetics***）。

Human Evolution and Disease Genomics

Dr. Qing-Peng Kong, Principal Investigator, Kunming Institute of Zoology, Chinese Academy of Sciences.

The main research interests of my laboratory are: (1) tracing the origin and evolutionary history of modern humans and (2) disclosing the molecular mechanism of healthy aging by studying longevity individuals. Our research group has already published over 100 papers on the international peer-reviewed journals such as *Am J Hum Genet, PNAS, Genome Res, Mol Biol Evol*, *Natil Sci Rev*, *Theranostics* with total citations over 4,000 times.

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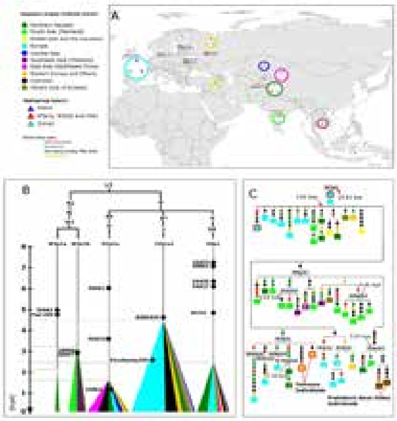
1. Decoding the health-protective roles of lncRNA in centenarians

To illustrate the potential roles of lncRNA in human healthy aging, we obtained and analyzed the RNA sequencing data of peripheral blood samples from two longevity cohorts, consisting 76 centenarians (CENs), 54 centenarian-children (F1) and 41 spouses of centenarian-children (F1SP). We identified eight lncRNAs that were differentially CENs compared to F1SPs. Among them, we found that the overexpression of either THBS1-IT1 or THBS1-AS1, two lncRNAs with increased expression in CENs, can remarkably reduce expression of p16 and p21, and decrease the activity of senescent related β-galactosidase, suggesting that THBS1-IT1 and THBS1-AS1 can delay cellular senescence. Collectively, we provided the first comprehensive analysis of lncRNA expression in longevous populations, and our results hinted that the lncRNAs with expression differences in CENs are potential protective factors in human healthy aging **(Jiang et al. 2021, *Briefings in Bioinformatics*).**

2. Demic diffusion of spread of Indo-European languages to northern Pakistan

Based on mitogenome sequencing data of 213 Indo-European speakers in north Pakistan, as well as mitochondrial DNA (mtDNA) data of both contemporary and ancient samples from north Pakistan and surroundings, the analyses showed that maternal genetic components of Indo-European speaking populations in northern Pakistan mainly come from Western Eurasia. Haplogroups W3a1a and J1b1a1 may be related to the migration of early Indo-European language speakers, indicating that the diffusion of Indo-European languages to South Asia may not only restricted to simple cultural expansion, but also accompanied by population migration. Our study also showed the corridor role of northern Pakistan in the diffusion of Indo-European languages to South Asia **(Rahman et al. 2021, *European Journal of Human Genetics*).**



Phylogeographic Analysis of Western Eurasian Genetic Components in Northern Pakistani Populations
【Rahman et al. 2021, *European Journal of Human Genetics*】

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工作人员（Staff)

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肖富辉 博士 副研究员
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李玉春 博士 副研究员
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郑俊娟 博士 助理研究员
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Yuhong Li, Associate researcher
Zia Ur Rahman 博士 特别研究助理
Zia Ur Rahman, Associate researcher
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Shaoyan Pu, Assistant researcher
杨利琴 硕士 实验师
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马思雨 硕士 助理实验师
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夏天睿 硕士 研究实习员
Tianrui, Xia, Research trainee
赵梦婧 硕士 研究实习员
Mengjing Zhao, Research trainee

研究生（Graduate Students)

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郜宗亮 Zongliang Gao 2021

硕士研究生

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王霞燕 Xiayan Wang 2020
姚亚冬 Yadong Yao 2020
周青青 Qingqing Zhou 2020
张润峰 Runfeng Zhang 2021
唐传芳 Chuanfang Tang 2021

生物多样性基因组学研究

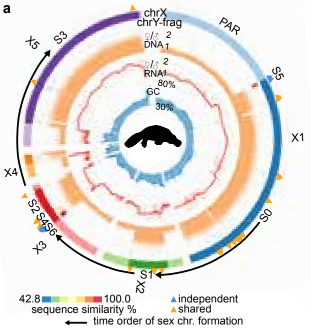
张国捷，中国科学院昆明动物研究所客座研究员，哥本哈根大学生物系终身教授，中国国家基因库副主任。长期担任 *Nature, Science, Genome Research, Current Biology* 等顶尖国际期刊和各国基金会评审委员。目前已在 *Science, Nature, Cell, Science Advances, Nature Communication, PNAS, Current Biology* 等国际高影响力杂志发表论文 160 余篇。2021 年，课题组发布了鸭嘴兽和针鼹的参考基因组，揭示了现生哺乳动物最近共同祖先的基因组演化信息，对理解哺乳类发生的适应演化提供了重要的系统框架；解析了原始辐鳍鱼类的塞内加尔多鳍鱼、匙吻鲟、弓鳍鱼和鳄雀鳝以及非洲肺鱼基因组，从不同演化节点揭示了脊椎动物水生到陆生的演化之谜；建立新算法对狨猴基因组进行解析，分别组装两条同源染色体，建立二倍体物种完美基因组新标准。在 ***Nature*** (2), ***Cell*** (2), ***Nature Communications*** (1), ***PNAS*** (1), ***GigaScience*** (3) 等国际刊物发表 SCI 文章 19 篇。

实验室主页： http://zhanggjlab.org/

重要成果及产出：

1. C. Yang[1], Y. Zhou[1], S. Marcus[1], G. Formenti, L. A. Bergeron, Z. Song, X. Bi, J. Bergman, M. M. C. Rousselle, C. Zhou, L. Zhou, Y. Deng, M. Fang, D. Xie, Y. Zhu, S. Tan, J. Mountcastle, B. Haase, J. Balacco, J. Wood, W. Chow, A. Rhie, M. Pippel, M. M. Fabiszak, S. Koren, O. Fedrigo, W. A. Freiwald, K. Howe, H. Yang, A. M. Phillippy, M. H. Schierup, E. D. Jarvis, **G. Zhang*** , Evolutionary and biomedical insights from a marmoset diploid genome assembly, Nature, 2021, 594, 227-233 .
2. X. Bi[1], K. Wang[1], L. Yang[1], H. Pan[1], H. Jiang[1], Q. Wei[1], M. Fang, H. Yu, C. Zhu, Y. Cai, Y. He, X. Gan, H. Zeng, D. Yu, Y. Zhu, H. Jiang, Q. Qiu, H. Yang, Y. E. Zhang, **W. Wang***, M. Zhu*, S. He* and **G. Zhang*** , Tracing the genetic footprints of vertebrate landing in non-teleost ray-finned fishes, Cell, 2021, 184, 1377-1391 e1314.
3. Y. Zhou[1], L. Shearwin-Whyatt[1], J. Li[1], Z. Song, T. Hayakawa, D. Stevens, J. C. Fenelon, E. Peel, Y. Cheng, F. Pajpach, N. Bradley, H. Suzuki, M. Nikaido, J. Damas, T. Daish, T. Perry, Z. Zhu, Y. Geng, A. Rhie, Y. Sims, J. Wood, B. Haase, J. Mountcastle, O. Fedrigo, Q. Li, H. Yang, J. Wang, S. D. Johnston, A. M. Phillippy, K. Howe, E. D. Jarvis, O. A. Ryder, H. Kaessmann, P. Donnelly, J. Korlach, H. A. Lewin, J. Graves, K. Belov, M. B. Renfree, F. Grutzner*, Q. Zhou* and **G. Zhang*** , Platypus and echidna genomes reveal mammalian biology and evolution, Nature, 2021, 592, 756-762.
4. P. A. O'Brien, N. Andreakis, S. Tan, D. J. Miller, N. S. Webster, **G. Zhang***, D. G. Bourne* , Testing cophylogeny between coral reef invertebrates and their bacterial and archaeal symbionts, Molecular Ecology , 2021, 30, 3768-3782 .
5. L. A. Bergeron*, S. Besenbacher, J. Bakker, J. Zheng, P. Li, G. Pacheco, M. S. Sinding, M. Kamilari, M. T. P. Gilbert, M. H. Schierup, **G. Zhang*** , The germline mutational process in rhesus macaque and its implications for phylogenetic dating, Gigascience, 2021, 10, 1-14.
6. X. Bi, **G. Zhang*** , Ancestral developmental potentials in early bony fish contributed to vertebrate water-to-land transition, Zoological Research, 2021, 42, 135-137 .

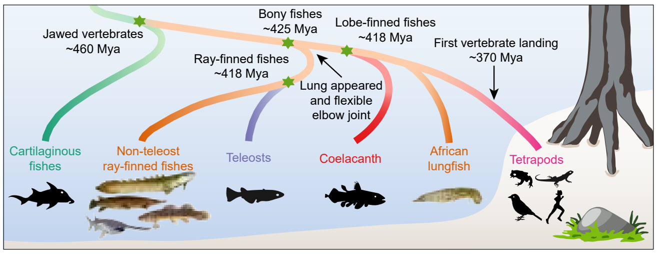
1. 解析哺乳动物祖先染色体



基于最新的测序技术绘制了鸭嘴兽和针鼹的高质量基因组，并据此与人、有袋类动物、鸟类和爬行类等多种动物基因组进行比较追溯，最终跨越 1.8 亿年，重建了现生哺乳动物共同祖先的基因组图谱。研究团队发现，单孔目物种的 5 条 X 染色体与其他绝大多数哺乳动物的 X 染色体序列并不相似，但有一部分序列跟鸟类的性染色体同源。推翻了此前学界认为的单孔目 5 对性染色体由两个古老的单孔目类群杂交产生这一假说，提出单孔目中的多对性染色体更可能是通过多对古老的常染色体相互之间发生了非同源片段的交换，即转座异位事件形成。（Zhou *et al*., 2021, *Nature* ）

2. 解开脊椎动物从水生到陆生的演化之谜

本研究通过对多鳍鱼基因组以及其他三种原始辐鳍鱼的基因组的解析，揭示了登陆的遗传基础在硬骨鱼类祖先已经出现。研究发现，能够增加骨骼运动灵活性的滑膜关节在早期鱼类中已经存在，调控这些功能相关的遗传基础甚至更早起源。通过比较基因组学的分析，发现在这些远古鱼类的嗅觉感受器中同时存在着两种类型的嗅觉受体，除了具有鱼类都拥有的检测水溶性分子的嗅觉受体之外，还有能够检测空气分子的嗅觉受体。这与它们的空气呼吸能力相一致。与此同时，在远古鱼类中高表达的基因显著富集在血管新生通路，这也解释了在这些远古鱼类里的肺或者鱼鳔表面为何密布血管，从而有助于氧气在肺部的扩散及运输。另外一些肺特异性表达的基因在软骨鱼就已经出现，这也暗示着“原肺”形成的分子基础在鱼类登陆前就已经建立。从鱼类的一心房一心室再到人的两心房两心室，心脏结构趋向于完善，而功能也变得更加复杂。研究人员找到了这一演化过程产生的功能创新相关遗传证据，并且新发现的一个基因调控元件与人类心脏疾病相关。（Bi *et al*., 2021, *cell*）



3. 解密狨猴二倍体遗传信息差异

研究团队利用家系基因组测序数据，组装出普通狨猴（*Callithrix jacchus*）的基因组，利用被测个体的父母本的测序数据进行遗传信息区分，使用新算法可以完美地将两条同源染色体分别组装出来，从而获得全部染色体的遗传数据。本研究对二倍体物种完美基因组提出了新的标准，即二倍体细胞中的两套基因组应分别独立组装到染色体水平并含有极少的测序漏洞，本次研究也论证了实现这一目标的可行性。高质量的狨猴基因组也利用这个物种作为动物模型的医学研究提供重要遗传数据。（Yang *et al*. 2021, *Nature*）

Biodiversity Genomics Lab

Dr. Guojie Zhang, Head of Biodiversity Genomics Group, Kunming Institute of Zoology, CAS, full professor in University of Copenhagen and Associate Director of the China National GeneBank. Dr. Zhang has published more than 160 articles, including *Science, Nature, Cell, Science Advances, Nature Communications, PNAS* and *Current Biology*. In 2021, we generated reference genomes of the platypus (*Ornithorhynchus anatinus*) and echidna (*Tachyglossus aculeatus*), allowing us to detect the ancestral and lineage-specific genomic changes that shape both monotreme and mammalian evolution.；we presented genome sequences of the bichir, paddlefish, bowfin, and alligator gar, providing insights for mechanisms underlying water-to-land transition；we applied a trio-binning approach to assemble a high-quality, diploid reference genome for the common marmoset, establishing the perfect genome standard and implicating the potentials for the use of marmoset as a non-human primate model system in biomedical research.19 high profile SCI papers were published, including ***Nature*** (2), **Cell** (2), ***Nature Communications*** (1), ***PNAS*** (1), ***GigaScience*** (3).

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1. Analysis of mammalian ancestral chromosomes

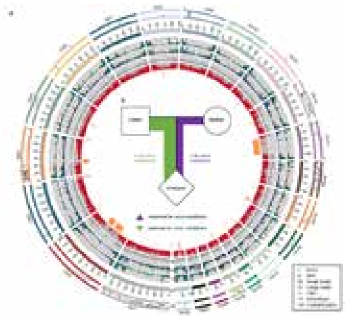
Based on the latest sequencing technologies, the team mapped the high-quality genomes of the platypus and echidna, and compared them with the genomes of various animals such as humans, marsupials, birds and reptiles, successfully reconstructed the genome map of the common ancestor of living mammals over a span of 180 million years. The research team found that the monotreme's five X chromosomes were different from the X chromosome sequences of most other mammals, but some were homologous to the sex chromosomes of birds. The disvovery overturned the previous hypothesis that five pairs of sex chromosomes of monotreme were generated by hybridization of two ancient monotreme groups. The team proposed that the mutiple sex chromosomes in monotreme are most likely derived from the fusion and translocation of non-homologous fragments between ancestral autochromosomes, known as translocation events, which resulted in the formation of current five pairs of sex chromosomes.(Zhou *et al*., 2021, *Nature*)

2. The evolution of vertebrates from aquatic to terrestrial

This study reveals that the genetic basis for water-to-land transition was present in the ancestors of teleost fish by analyzing the genome sequence of bichir and the other three actinopterygians. This study also found synovial joints, which increaseskeletal mobility, were already present in early fish, and the genetic basis for regulating these functions originated even earlier. Through comparative genomic analysis, the researchers found two types of olfactory receptors in these ancient fish, one is to detect water-soluble molecules and the other is to detect air molecules, which is consistent with their ability to breathe the air. At the same time, genes that are highly expressed in ancient fish are significantly enriched in angiogenesis pathways, which may contribute to diffusion and transportation of oxygen in the lungs, explaining why the surfaces of the lungs or swim bladders in ancient fish are covered with blood vessels. Other lung-specific genes have also been found in cartilaginous fish, suggesting that the molecular basis for "proto-lung" formation was established before the fish landing. The coevolution of the cardiopulmonary system is important for vertebrate landing. From one atrium and one ventricle of fish to two atrium and two ventricles of human, the heart's structure tends to be perfect, and its functions become more complex. The researchers found genetic evidence for functional innovations arising from this evolutionary process and confirmed that a newly identified gene regulatory element is associated with human heart disease. (Bi *et al*., 2021, *cell*)

3. Deciphering the differences in diploid genome of marmoset

By using a trio-binning approach, the team present a high-quality, diploid reference genome, with both haplotypes assembled independently at the chromosome level, for the common marmoset (*Callithrix jacchus*), an primate model system that is widely used in biomedical research. At the same time, the comparison of parental genome sequences also refreshed people's understanding of the genetic information differences between parents. By analying genes related to growth and development, the study demonstrated the prospect of developing marmoset as a non-human primate model for medical studies. (Yang *et al*. 2021, *Nature*)



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适应性进化与进化医学

吕雪梅，博士，研究员，博士生导师，适应性进化与进化医学学科组负责人。主要从事适应性进化的群体基因组学研究，以物种和细胞群体水平的变异和进化为核心，探讨中性进化和自然选择等进化驱动力的对群体动态演化相对作用，从而揭示从遗传和表观变异的累积、到适应性改变的形成和进化一系列过程的基本规律。解析了肿瘤细胞群体的进化及其基本理论，揭示了肿瘤内部极大量的遗传多样性和进化规律，提示了肿瘤治疗需要寻求新的策略；揭示了体细胞 DNA 甲基化异质性的动态变化及生物学意义，为更好的理解在肿瘤进化过程中表观组学动态演变及其功能意义奠定基础。2020 年起牵头承担科技部重点研发项目新冠应急专项，围绕新冠病毒基因组进化规律与动态演变研究技术体系创建与应用开展研究，与本项目骨干成员陆剑、郑永唐、吴仲义、陈华等团队紧密合作，取得一系列研究成果和进展，研究论文发表在 *Science Bulletin*、*NSR* 等期刊，并建立新冠病毒分型和追踪的数据库和网站工具。

重要成果及产出：

1. Yongsen Ruan, Zhida Luo, Xiaolu Tang, Guanghao Li, Haijun Wen, Xionglei He, Xuemei Lu*, Jian Lu*, Chung-I Wu*.On the founder effect in COVID-19 outbreaks – How many infected travelers may have started them all? National Science Review, 2020, Accepted. IF17.584
2. Chunyan Li#, Melisa Olave#, Yali Hou#, Geng Qin#, Ralf F. Schneider, Zexia Gao, Xiaolong Tu, Xin Wang, Furong Qi, Alexander Nater, Andreas F. Kautt, Shiming Wan, Yanhong Zhang, Yali Liu, Huixian Zhang, Bo Zhang, Hao Zhang, Meng Qu, Shuaishuai Liu, Zeyu Chen, Jia Zhong, He Zhang, Lingfeng Meng, Kai Wang, Jianping Yin, Liangmin Huang, Byrappa Venkatesh*, Axel Meyer*, **Xuemei Lu*,** Qiang Lin*.Genome sequences reveal global dispersal routes and suggest convergent genetic adaptations in seahorse evolution. Nature Communications, 2021, 12(1), IF15.805
3. Guanghao Li#, Zuyu Yang#, Dafei Wu, Sixue Liu, Xuening Li, Tao Li, Yawei Li, Liji Liang, Weilong Zou, Chung-I Wu, Hurng-Yi Wang*, **Xuemei Lu*.** Evolution under spatially heterogeneous selection in solid tumors. Molecular Biology and Evolution, 2021-12-02,online, IF18.670
4. MingShan Wang#, JinJin Zhang#, Xing Guo#, Ming Li#, Rachel Meyer#, Hidayat Ashari#, ZhuQing Zheng, Sheng Wang, MinSheng Peng, Yu Jiang, Mukesh Thakur, Chatmongkon Suwannapoom, Ali Esmailizadeh1, Nalini Yasoda Hirimuthugoda, Moch Syamsul Arifin Zein, Szilvia Kusza, Hamed Kharrati-Koopaee, Lin Zeng, YunMei Wang, TingTing Yin, MinMin Yang, MingLi Li, **XueMei Lu**, Emiliano Lasagna, Simone Ceccobelli, Humpita Gamaralalage Thilini Nisanka Gunwardana, Thilina Madusanka Senasig, Shao-Hong Feng, Hao Zhang, Abul Kashem Fazlul Haque Bhuiyan, Muhammad Sajjad Khan, Gamamada Liyanage Lalanie Pradeepa Silva, Le Thi Thuy, Okeyo A. Mwai,Mohamed Nawaz Mohamed Ibrahim, Guojie Zhang, Kai-Xing Qu, Olivier Hanotte, Beth Shapiro,Mirte Bosse*, DongDong Wu*, JianLin Han* and YaPing Zhang*. Large-scale genomic analysis reveals the genetic cost of chicken domestication, BMC Biology, (2021) 19:118, IF 8.182
5. Xiaolu Tang#, Ruochen Ying#, Xinmin Yao#, Guanghao Li, Changcheng Wu, Yiyuli Tang, Zhida Li, Bishan Kuang, Feng Wu, Changsheng Chi, Xiaoman Du, Yi Qin, Shenghan Gao, Songnian Hu, Juncai Ma, Tiangang Liu, Xinghuo Pang, Jianwei Wang, Guoping Zhao, Wenjie Tan*, Yaping Zhang*, **Xuemei Lu*,** Jian Lu*, Evolutionary analysis and lineage designation of SARS-CoV-2 genomes, Science Bulletin, 2021,66(22), IF7.658

1. 揭示海马印 - 太起源及其全球扩散的时空路径与适应进化机制

首次明确了印 - 太交汇区的印 - 澳群岛是全球海马的起源中心；原创性地发现了在地质、洋流驱动下海马全球扩散路径的时空特征及生态适应与进化机制，提出了印 - 太海马类群由古特蒂斯海和南非好望角两条路径先后进入大西洋的新观点；发现海马 bmp3 基因可能调控了棘刺性状的独立进化。

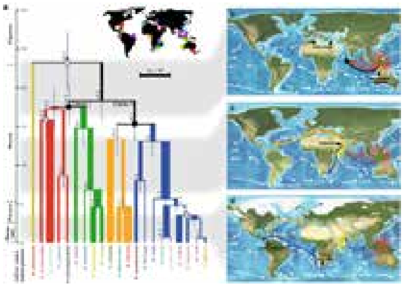

图 1. 全球优势海马类群的群体分化及其洋流驱动下的扩散时空路径特征

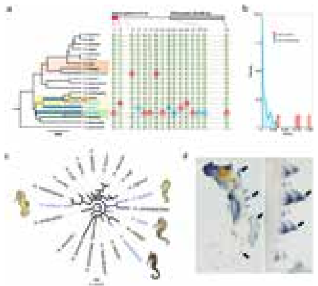

图 2. 海马棘刺表型独立进化机制及 Crispr-cas9 体系验证 bmp3 基因功能

【Li CY et al., 2021, ***Nature Communications***, IF15.805】

2. 新冠病毒基因组演化分析及谱系划分

通过大规模分析 SARS-CoV-2 基因组变异数据，课题组与合作单位根据突变频率与变异位点连锁性筛选出代表性 SNV，划分出 130 个病毒谱系，绘制出单倍型亲缘关系网络图。谱系分析还发现各支病毒有各自独特的分布模式，与社会的地理条件、交通运输、防疫政策等相关，该研究囊括了目前出现的绝大多数新冠基因组变异并整理了谱系关系，阐明其中各个谱系时空分布的规律，搭建出新冠病毒演化的大体框架，对理解病原体变异规律、新冠流行病学追踪、预测病毒的演化方向有重要意义。

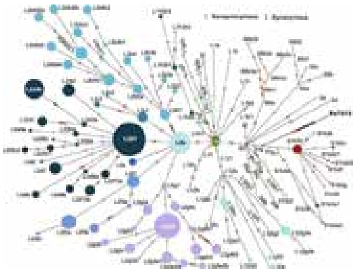

图 1. 基于 206 个分型标记位点的 130 个亚谱系的单倍型网络

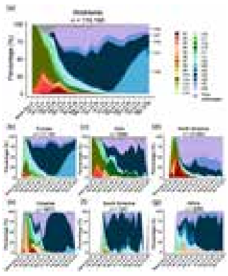

图 2. 谱系 / 亚谱系的时空分布

【Tang XL et al., 2021, ***Science Bulletin***, IF7.658】

Adaptive Evolution and Evolutionary Medicine

Dr. Xuemei Lu, Professor, Principal Investigator, The recent studies of our group are about the fundamental paradigms of ecological and evolutionary biological processes such as speciation, adaptive evolution, adaptive phenotypic change of cells, etc. There are three scenes used for sparkling the research: 1) species level, 2) population level, and 3) cell population level. Basing on ecological and evolutionary theory and population genetics, together with system biology approaches and multi-omics methods, we have developed a somatic cell-based experimental evolutionary system to investigate the issues, which are hard to record and analyze in natural populations.

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1. Genome sequences reveal global dispersal routes and suggest convergent genetic adaptations in seahorse evolution

Seahorses have a circum-global distribution in tropical to temperate coastal waters. Yet, seahorses show many adaptations for a sedentary, cryptic lifestyle: they require specific habitats, such as seagrass, kelp or coral reefs, lack pelvic and caudal fins, and give birth to directly developed offspring without pronounced pelagic larval stage, rendering long-range dispersal by conventional means inefficient. Here we investigate seahorses' worldwide dispersal and biogeographic patterns based on a de novo genome assembly of Hippocampus erectus as well as 358 re-sequenced genomes from 21 species. Seahorses evolved in the late Oligocene and subsequent circum-global colonization routes are identified and linked to changing dynamics in ocean currents and paleo-temporal seaway openings. Furthermore, the genetic basis of the recurring "bony spines" adaptive phenotype is linked to independent substitutions in a key developmental gene. Analyses thus suggest that rafting via ocean currents compensates for poor dispersal and rapid adaptation facilitates colonizing new habitats.

2. Evolutionary analysis and lineage designation of SARS-CoV-2 genomes

The pandemic due to the SARS-CoV-2 virus, the etiological agent of Coronavirus Disease 2019 (COVID-19), has caused immense global disruption. With the rapid accumulation of SARS-CoV-2 genome sequences, however, thousands of genomic variants of SARS-CoV-2 are now publicly available. To improve the tracing of the viral genomes' evolution during the development of the pandemic, we analyzed single nucleotide variants (SNVs) in 121,618 high-quality SARS-CoV-2 genomes. We divided these viral genomes into two major lineages (L and S) based on variants at sites 8782 and 28144, and further divided the L lineage into two major sublineages (L1 and L2) using SNVs at sites 3037, 14408, and 23403. Subsequently, we categorized them into 130 sublineages (37 in S, 35 in L1, and 58 in L2) based on marker SNVs at 201 additional genomic sites. This lineage/sublineage designation system has a hierarchical structure and reflects the relatedness among the subclades of the major lineages. We also provide a companion website (www.covid19evolution.net) that allows users to visualize sublineage information and upload their own SARS-CoV-2 genomes for sublineage classification. Finally, we discussed the possible roles of compensatory mutations and natural selection during SARS-CoV-2's evolution. These efforts will improve our understanding of the temporal and spatial dynamics of SARS-CoV-2's genome evolution.

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Ouedraogo Raogo Blaise
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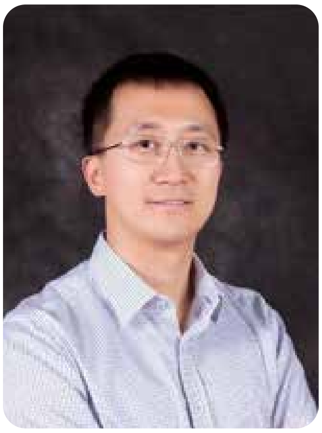

行为遗传和进化

王国栋，博士，研究员，博士生导师。入选中组部万人计划青年拔尖人才，中国科学院青年促进会优秀会员，云南省中青年学术和技术带头人。获 2019 年度中国科学院青年科学家奖，作为发起人之一创建家犬基因组研究国际联盟。现任中国动物学会动物行为学分会第二届理事会理事（2019 年 11 月 -2023 年 11 月）和中国科学院昆明动物研究所人类疾病的家犬模型省创新团队带头人（2019- 至今）。主要研究方向为群体遗传、适应性进化、复杂表型和行为的遗传机制等研究。以第一作者和通讯作者（含并列）在 *Nat Genet*、*Nat Commun*、*Cell Res*、*PNAS*、*Mol Biol Evol* 和 *Nucl Acids Res* 等 SCI 杂志发表论文 28 篇。获 Sanofi-Cell Research 优秀论文和第三届中国科协优秀科技论文，研究结果被 *Nature*、*The New York Times*、*The Guardian*、*National Geographic*、*Scientific American* 等国际杂志报道。

重要成果及产出：

1. Zhang, S. J.[1], **Wang, G. D.**[1], Ma, P. C.[1], Zhang, L. L., Yin, T. T., Liu, Y. H., Otecko, O. N., Wang, M., Ma, Y. P., Wang, L., Mao, B. Y.*, Savolainen, P.*, and Zhang, Y. P.*. Genomic regions under selection in the feralization of the dingoes. ***Nat Commun*** 2020.11 (1):671.
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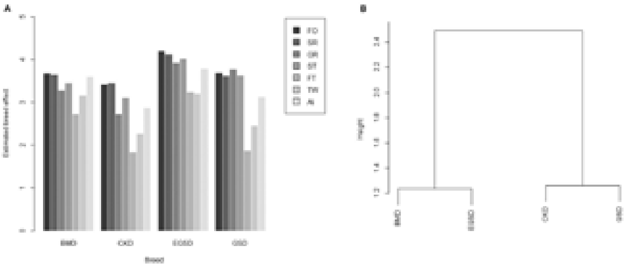
4. Ostrander, E. A.*[1], **Wang, G. D.**[1], Larson, G., vonHoldt, B. M., Davis, B. W., Jagannathan, V., Hitte, C., Wayne, R. K., Zhang, Y. P.*, Dog, K. C., Dog10K: an international sequencing effort to advance studies of canine domestication, phenotypes and health. ***Natl Sci Rev*** 2019, *6* (4), 810-824.
5. **Wang, G. D.**[1], Zhai, W.[1], Yang, H. C.[1], Wang, L.[1], Zhong, L., Liu, Y. H., Fan, R. X., Yin, T. T., Zhu, C. L., Poyarkov, A. D., Irwin, D. M., Hytonen, M. K., Lohi, H., Wu, C. I., Savolainen, P.*, Zhang, Y. P.*, Out of southern East Asia: the natural history of domestic dogs across the world. ***Cell Res*** 2016, *26* (1), 21-33.
6. **Wang, G. D.**[1], Zhai, W.[1], Yang, H. C., Fan, R. X., Cao, X., Zhong, L., Wang, L., Liu, F., Wu, H., Cheng, L. G., Poyarkov, A. D., Poyarkov, N. A., Jr., Tang, S. S., Zhao, W. M., Gao, Y., Lv, X. M., Irwin, D. M., Savolainen, P., Wu, C. I.*, Zhang, Y. P.*, The genomics of selection in dogs and the parallel evolution between dogs and humans. ***Nat Commun*** 2013, *4*, 1860.

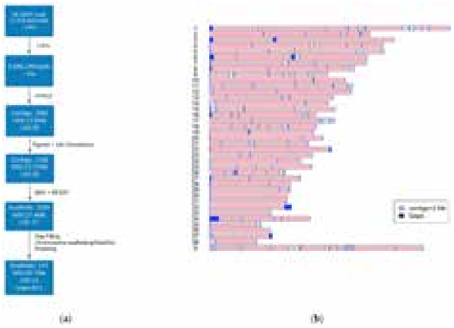
1. 行为学探究昆明犬起源



本研究选取公安部昆明警犬基地的四种警用犬，德国牧羊犬（GSD）、德国牧羊犬 DDR 工作系（EGSD）、马里努阿犬（BMD）和昆明犬（CKD）进行打分行为测试。对测试结果进行多因素方差分析（ANOVA），结果显示品种、性别和年龄会影响个体的行为测试打分，因此在建立品种的行为范式时我们剔除了年龄和性别。通过分析我们发现 EGSD 在各项测试中都具有较高的品种效应（breed effect）得分，而 CKD 在各项测试中得分最低。为了进一步量化 CKD 和其他品种犬行为范式的相似性，我们使用了基于欧式距离的聚类进行层次聚类分析，聚类结果显示 CKD 和 GSD 行为范式具有相似性。因此证明昆明犬的的起源可能来自于 GSD 和昆明土狗的杂交，而非 EGSD。

(Li, Jin-Xiu et al. 2021 ***Current zoology***)

2. 组装 Dog10k_Boxer_Tasha_1.0 基因组



当前已发表的家犬基因组是 2005 年使用 sanger 全基因组鸟枪测序法测得的 boxer(Tasha)。基于当时的技术限制，该基因组存在大量的空缺，组装错误以及序列缺失。Tasha 作为现发表参考基因组的供体，研究团队获得了它的血液，更新了 CanFam 参考基因组。

使用 PacBio 和 10x Chromium long-reads 组装的 Dog10k_Boxer_Tasha_1.0 其连续性显着增加。CanFam3.1 的 contig size 仅为 267 kb，而 Dog10k_Boxer_Tasha_1.0 的 contig N50 为 27.3 Mb，序列连续性增加了 100 倍以上。 Dog10k_Boxer_Tasha_1.0 基因组序列相对于 CanFam3.1 组装的改进不仅仅是片段连续性更好，同时填补了 CanFam3.1 版本中的缺失序列，最重要的是矫正了部分基因区域的组装错误。

(Jagannathan Vidhya et al. 2021 ***Genes***)

Genetics and Evolution of Behavior

Prof. Guodong Wang, researcher, Ph.D. Supervisor. The 2019 Young Scientist Award of the Chinese Academy of Sciences and as one of the initiators to create the Dog10K Consortium. Recently year we focused on genomic evolution, adaptive evolution, the genetic basis of complex traits and behavior. Research progress published on Nat Genet, Nat Commun, Cell Res, PNAS, Mol Biol Evol, Nucl Acids Res and other science citation index (SCI) journals.

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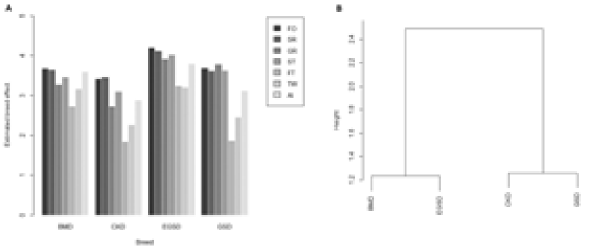
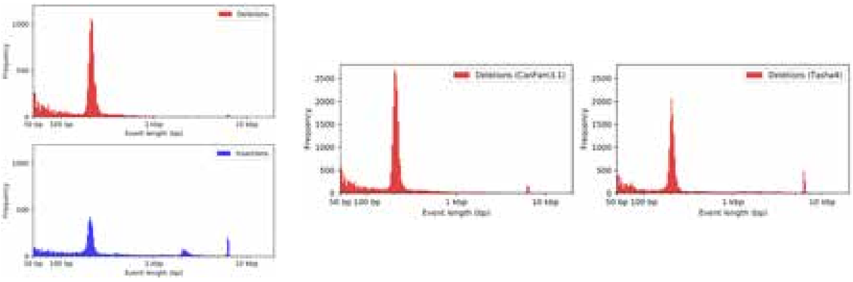
1. Behavioral evidence for the origin of Chinese Kunming dog



Inspired by the confirmed genetic basis of breed-based behavioral stereotypes and the existed heritability of behavioral traits estimated in Swedish Army dogs, a hypothesis was proposed that CKD might have a similar behavioral stereotype to its original breed. The evidence from the comparison of behavioral stereotypes implied CKD might origin from the hybrid between Kunming indigenous village dogs and GSD.

(Li, Jin-Xiu et al. 2021 ***Current zoology***)

2. Dog10K_Boxer_Tasha_1.0: A Long-Read Assembly of the Dog Reference Genome



Genetic studies in the dog have relied on a draft reference genome of a purebred female boxer dog named “Tasha” initially published in 2005. Derived from a Sanger whole genome shotgun sequencing approach coupled with limited clone-based sequencing, the initial assembly and subsequent updates have served as the predominant resource for canine genetics for 15 years. While the initial assembly produced a good-quality draft, as with all assemblies produced at the time, it contained gaps, assembly errors and missing sequences, particularly in GC-rich regions, which are found at many promoters and in the first exons of protein-coding genes. Here, we present Dog10K_Boxer_Tasha_1.0, an improved chromosome-level highly contiguous genome assembly of Tasha created with long-read technologies that increases sequence contiguity >100-fold, closes >23,000 gaps of the CanFam3.1 reference assembly and improves gene annotation by identifying >1200 new protein-coding transcripts. The assembly and annotation are available at NCBI under the accession GCF_000002285.5.

(Jagannathan Vidhya et al. 2021 ***Genes***)

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神经系统的发育机制与演化

毛炳宇，博士，研究员，中德马普青年科学家小组组长，遗传资源与进化国家重点实验室副主任。先后获得国家自然科学基金委杰出青年基金、重点项目等资助。实验室主要以小鼠、非洲爪蟾和文昌鱼为动物模型研究神经系统的早期发育机制及其演化。

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重要成果及产出：

1. **Ma P# , Li Y#, Wang H,Mao B*** . (2021)Haploinsufficiency of the TDP43 ubiquitin E3 ligase RNF220 leads to ALS-like motor neuron defects in the mouse. ***Journal of Molecular Cell Biology*** , 13(5), 374–382.
2. **Ma P#**, **Mao B***,(2021) The many faces of the E3 ubiquitin ligase, RNF220, in neural development and beyond. ***Development, Growth & Differentiation***, DOI: 10.1111/dgd.12756.
3. **Wang H#, Yang C, Li Y,** Zhao S, **Ma P*,Mao B*.** (2021)RNF220-mediated ubiquitination promotes aggresomal accumulation and autophagic degradation of cytoplasmic Gli via HDAC6 . ***Biochemical and Biophysical Research Communications,***557 ,323-328.
4. Zhang Q#, Zhang L, Huang Y, **Ma P, Mao B**, Ding Y,Song N* (2021)Satb2 regulates the development of dopaminergic neurons in the arcuate nucleus by Dlx1. ***Cell Death and Disease*** 2021,12:879.
5. Lv Z#,Gong L,Ren Y,Chen Y, Wang Z,Liu L,Li H,Chen X,Li Z, Luo H,Jiang H,Zeng Y,Wang Y,Wang K, Zhang C, Jiang H, Wan W, Qin Y,Zhang J, **Zhu L**,Shi W,He **S,Mao B**,Wang W*,Kong X*,Li Y*.(2021) Large-scale sequencing of flatfish genomes provides insights into the polyphyletic origin of their specialized body plan. ***Nature Genetics***, 2021.

1. 揭示 RNF220 调控肌萎缩侧索硬化症相关蛋白 TDP43 稳定性的新机制

泛素连接酶 RNF220 通过调控不同靶蛋白不同类型的泛素化修饰参与多个神经系统发育过程的调控。虽然 RNF220-/- 小鼠出生致死，但是约 1/3 的 RNF220+/- 小鼠成年后表现出进行性的运动障碍，最后瘫痪而死。开放场和转棒等行为学分析发现，RNF220+/- 小鼠的运动能力显著降低。通过组织切片和病理学染色分析发现，RNF220 在成年小鼠的脊髓运动神经元中特异表达，且其蛋白主要定位在细胞质中；与野生型小鼠相比，RNF220+/- 小鼠脊髓运动神经元细胞中的 TDP43 蛋白表现出由细胞核到细胞质的转定位现象且蛋白水平增多；RNF220+/- 小鼠的腓肠肌肌纤维的直径变小，表现出萎缩现象且肌肉出现去神经支配现象。因此，RNF220+/- 小鼠表现出类似人肌萎缩侧索硬化症（ALS）的行为和病理学特征。体内外的生化分析发现，RNF220 通过促进 TDP43 蛋白 K48 类型的经典泛素化修饰参与 TDP43 蛋白稳定性的调控。该研究揭示了 ALS 相关蛋白 TDP43 稳定性调控新机制，丰富了人们对 ALS 致机理的认识（***J Mol Cell Biol***，2021）。

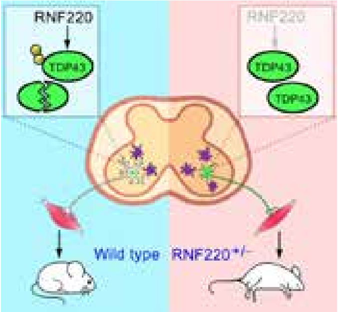

图 1. RNF220 通过 TDP43 调控脊髓运动神经元功能。
Fig 1. RNF220 regulates TDP43 stability in spinal motor neurons.

2. Shh 信号通过 RLIM/ZC4H2/RNF220 正反馈调节自身活性与小脑发育

Shh 信号在小脑发育与髓母细胞瘤发生中具有重要作用。我们之前的工作表明，RNF220 在小脑颗粒细胞中通过调控表观遗传因子 EED 的稳定性而激活 Shh 信号，在小脑颗粒细胞增殖调控中具有重要作用。在 Shh 信号激活的小鼠自发髓母细胞瘤模型中，RNF220 蛋白的水平升高，但这一过程是如何调控的并不清楚。在本研究中，我们发现 ZC4H2 对于小脑 Shh 信号的激活与小脑发育同样是必需的，而 Shh 信号同样可在转录后水平稳定 ZC4H2。进而我们发现 ZC4H2 是泛素连接酶 RLIM 的靶蛋白，RLIM 可促进 ZC4H2 的 K11/K63 特异性的多泛素化，提高其稳定性。而 RLIM 是 Shh 信号的直接靶基因，可被 Shh 信号激活。本研究阐明了在小脑发育与髓母细胞瘤发生过程中 Shh 信号通过 RLIM-ZC4H2-RNF220-EED 这一通路，正反馈提高 Shh 信号活性的分子机制，论文已被 ***J Mol Cell Biol*** 杂志接收。

Mechanisms of Neural Patterning and Evolution

Dr. Bingyu Mao, Principal Investigator, Ph. D. (1998, Shandong University, China). The molecular mechanisms of neural patterning and how these mechanisms evolved during vertebrate origin are the focuses of our lab. We use mouse, the amphibian *Xenopus* and the cephalochordate amphioxus as our model animals.

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1. Haploinsufficiency of the TDP43 ubiquitin E3 ligase RNF220 leads to ALS-like motor neuron defects in the mouse

TDP43 pathology is seen in a large majority of amyotrophic lateral sclerosis (ALS) cases, suggesting a central pathogenic role of this regulatory protein. Clarifying the molecular mechanism controlling TDP43 stability and subcellular location might provide important insights into ALS therapy. The ubiquitin E3 ligase RNF220 is involved in different neural developmental processes through various molecular targets in the mouse. Here, we report that the RNF220$^{+/-}$ mice showed progressively decreasing mobility to different extents, some of which developed typical ALS pathological characteristics in spinal motor neurons, including TDP43 cytoplasmic accumulation, atrocytosis, muscle denervation, and atrophy. Mechanistically, RNF220 interacts with TDP43 *in vitro* and *in vivo* and promotes its polyubiquitination and proteasomal degradation. In conclusion, we propose that RNF220 might be a modifier of TDP43 function *in vivo* and contribute to TDP43 pathology in neurodegenerative disease like ALS.

2. Sequential stabilization of RNF220 by RLIM and ZC4H2 during cerebellum development and Shh group medulloblastoma progression

Sonic hedgehog (Shh) signaling is essential for the proliferation of cerebellar granule neuron progenitors (CGNPs), and its misregulation is linked to various disorders, including cerebellar cancer medulloblastoma (MB). During vertebrate neural development, RNF220, a ubiquitin E3 ligase, is involved in spinal cord patterning by modulating the subcellular location of Glis through ubiquitination. RNF220 is also required for full activation of Shh signaling during cerebellum development in an epigenetic manner through targeting EED. ZC4H2 was reported to be involved in spinal cord patterning by acting as an RNF220 stabilizer. Here, we provided evidence to show that ZC4H2 is also required for full activation of Shh signaling in CGNP and MB progression by stabilizing RNF220. In addition, we found that the ubiquitin E3 ligase RLIM is responsible for ZC4H2 stabilization through direct ubiquitylation, through which RNF220 is also thus stabilized. RLIM is a direct target of Shh signaling and is also required for full activation of Shh signaling in CGNP and MB cell proliferation. We further provided clinical evidence to show that the RLIM-ZC4H2-RNF220 cascade is involved in Shh-group MB progression. Disease-causative human RLIM and ZC4H2 mutations affect their interaction and regulation. Therefore, our study shields light on the regulation of Shh signaling during cerebellar development and MB progression, and provides insights into neural disorders caused by RLIM or ZC4H2 mutations.

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哺乳动物胚胎发育

郑　萍，博士，研究员，课题组长。2009 年入选中国科学院“百人计划”。云南省高端科技人才，中国科学院王宽诚人才奖“西部学者突出贡献奖”获得者。实验室主要研究方向包括：1）干细胞维持遗传物质稳定性的调控机制；2）灵长类精原干细胞的基础生物学及其在基因修饰技术中的应用研究；3）灵长类早期胚胎发育。

重要成果及产出：

1. **Wang L**#, **Li J**#, Zhou H, **Zhang W**, Gao J, **Zheng P***. A novel lncRNA Discn fine-tunes replication protein A (RPA) availability to promote genomic stability. Nat Communications, 2021,12(1):5572.
2. Qin DD#, Zhou JK#, **He XC**#, Shen XY#, **Li C**, Chen HZ, Yan LZ, Hu ZF, Li X, Lv LB, Yao YG*, Wang Z*, Huang XX*, Hu XT*, **Zheng P***. Depletion of giant ANK2 in monkeys causes drastic brain volume loss. Cell Discovery, 2021, 7(1):113.

1. 鉴定了调控干细胞基因组稳定性的 全新 lncRNA Discn

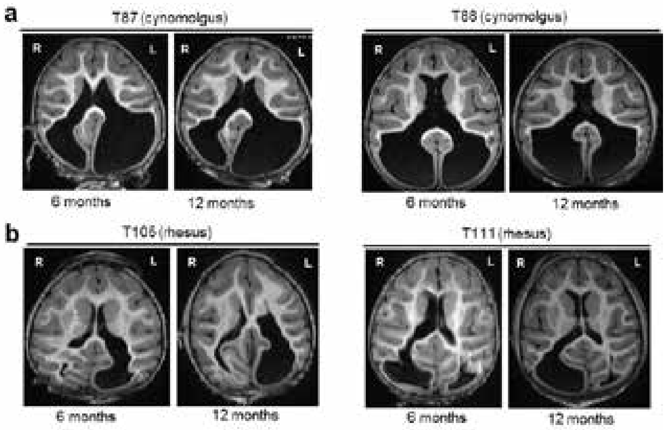
干细胞具很强的基因组稳定性维持能力，但机制远未清楚。通过转录组分析，我们在胚胎干细胞和多种成体干细胞中鉴定到一个尚未注释的 lncRNA，命名为 DISCN。DISCN 主要在干细胞中表达，且其表达响应 DNA 损伤处理。功能研究发现，DISCN 对维持胚胎干细胞和神经干细胞的基因组稳定性非常关键。在小鼠中敲除 DISCN，可导致新生鼠死亡。幸存的成年个体神经功能也严重受损，在学习记忆、情感及运动能力中表现出显著缺陷。机制分析发现，DISCN 定位于核仁中，通过 DISCN-Ncl-RPA 轴维持核质中自由 RPA 的蛋白量。RPA 蛋白是细胞 DNA 复制、DNA 损伤反应的限速因子。因此，干细胞通过高表达 DISCN，显著提升自由 RPA 的含量，从而显著增强其基因组稳定性。该工作揭示了基因组稳定性维持机制的进化。

【Wang L et al. 2021, ***Nature Communications***】

2. 巨型 ANK2 基因敲除猴揭示啮齿类和灵长类脑发育的分子调控差异

巨型 ANK2 基因主要表达于神经系统，遗传关联分析提示它与人类自闭症的发生相关。小鼠中敲除巨型 ANK2 不影响脑结构，但会轻度损伤社交功能。我们利用基因编辑技术，构建了巨型 ANK2 基因敲除食蟹猴（2 只）和猕猴（2 只）模型。但磁共振影像分析发现，敲除巨型 ANK2 基因均导致食蟹猴和猕猴大脑发育异常，侧脑室异常增大，灰质体积大量减少。但这些脑结构变化不影响大脑基本功能，基因敲除猴具有正常的睡眠 - 觉醒周期、社交互动和环境探索行为。 该研究揭示了巨型 ANK2 基因在灵长类大脑发育中的重要作用，及其功能的物种进化差异，并为研究脑功能重组和可塑性提供了极佳模型。

【Qin DD et al. 2021, ***Cell Discovery***】



Mammalian Embryonic Development

Dr. Ping Zheng, Principal Investigator, joined in Kunming Institute of Zoology, Chinese Academy of Sciences in 2009. The laboratory studies 1) how stem cells safeguard their genomic stability, 2) the biology of primate spermatogonia stem cells, and 3) the early embryogenesis of non-human primates. We use mouse, monkey and tree shrew as animal models.

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1. A novel lncRNA Discn fine-tunes replication protein A (RPA) availability to promote stem cell genomic stability

Stem cells (SCs) possess superior stable genome compared to their differentiated progenies. The underlying mechanisms remain poorly defined. Here we identified an un-annotated lncRNA DISCN which is predominantly expressed in embryonic stem cells (ESCs) and tissue stem cells (e.g. neural stem/progenigor cells, NSPCs). Loss of DISCN led to massive genome instability in cultured mouse ESCs and NSPCs. Notably, knock out DISCN in mice resulted in newborn death as well as brain dysfunctions in survived adults due to the DNA double strand break accumulation and associated inflammatory reactions. Mechanistically, DISCN localizes in nucleolus where it binds to Ncl and sequesters Ncl at nucleolus. This prevents Ncl from translocating into nucleoplasm and avoids excessive Ncl-RPA association. Thus, DISCN sustains the RPA availability central to replication stress response. These findings have implications for understanding cancer cell biology and the evolution of genomic stability regulation. (***Nature Communications***, 2021,12(1):5572)

2. Depletion of giant ANK2 in monkeys causes drastic brain volume loss

Giant ankyrin 2 (ANK2) is a neuro-specific isoform of ANK2. Genetic studies proposed it as a strong candidate involved in nonsyndromic autism spectrum disorders (ASDs). Here we specifically depleted the giant ANK2 in two cynomolgus monkeys and two rhesus monkeys. Surprisingly, depletion of this isoform did not cause core ASDs symptoms. Rather, mutant monkeys displayed typical abnormalities in brain development, including significant enlargement of lateral ventricles and gray matter loss. Consistent and marked volumetric losses were predominantly located in left visual area 1, left visual area 2, left anterior visual area, left ventral temporal cortex and right medial frontal cortex. Intriguingly, mutant monkeys had normal basic brain functions manifested by unperturbed sleep-wake cycles, social interaction, and environmental exploration. Our studies revealed the key roles of giant ANK2 in primate brain development, and uncovered the evolutionary divergence of giant ANK2 between rodents and primates. (***Cell Discovery,*** 2021, 7(1):113)

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谢 恒	Xie, Heng	2018
陶慧玲	Tao, Huiling	2019
孟夏朵	Meng, Xiaduo	2020
董玉萍	Dong, Yuping	2020
金 洁	Jin, jie	2020

表观遗传与发育调控

焦保卫，博士，研究员，博士生导师。2013 年国家海外高层次引进人才，2014 年云南省高端人才，2019 年云南省产业技术领军人才。兼任中国细胞生物学学会理事，云南省细胞生物学学会第五届理事会秘书长。长期从事乳腺发育、乳腺癌、乳腺（癌）干细胞的研究。 研究团队发现 SGCE 在乳腺癌干细胞耐药中的新机制，以及 TAR DNA 结合蛋白 43 (TDP-43) 在乳脂分泌过程中的作用。目前已经在 *Cell*、*PNAS*、*Nature Communications*、*Advanced Science* 等国际期刊杂志发表论文 30 余篇。

重要成果及产出：

1. **Xiyin Li**[1], **Hairui Wang**[1], Xing Yang[1], Xiaoqi Wang, **Lina Zhao**, **Li Zou**, **Qin Yang**, Zongliu Hou, Jing Tan, **Honglei Zhang***, Jianyun Nie*, and **Baowei Jiao***. GABRP sustains the stemness of triple-negative breast cancer cells through EGFR signaling. ***Cancer Lett***. 2021 Aug 28;514:90-102. IF 8.64
2. **Haibo Xu**[1], **Lina Zhao**[1], **Xu Feng** , **Yujie Ma** , **Wei Chen** , **Li Zou** , **Qin Yang** , Jihong Sun , Hong Yu* , **Baowei Jiao*.** Landscape of genomic imprinting and its functions in the mouse mammary gland. ***J Mol Cell Biol***. 2021 Feb 15;12(11):857-869. IF 6.688

发明专利：

1. 焦保卫，赵丽敏，柯浩，易萍，邹丽，杨钦 . TDP-43 基因在预测产妇泌乳量方面的应用 . 专利号：ZL201911086725.6（2021.3.9 授权）
2. 焦保卫，赵丽娜，陈策实，邱婷 . 抑制 SGCE 的试剂的应用 . 专利号：ZL202010309986.6 (2021.3.30 授权)
3. 焦保卫，赵丽娜，陈策实，邱婷 . SGCE 基因作为三阴性乳腺癌标志物的应用 . 专利号：ZL202010309979.6（2021.6.25 授权)

1. GABRP 通过 EGFR 信号维持三阴性乳腺癌细胞的干性

由于缺乏特定的治疗靶点，三阴性乳腺癌 (TNBC) 的有效治疗方案相对较少。表皮生长因子受体 (EGFR) 信号在 TNBC 中高度活跃，并与不良预后相关。大多数能显著改善肺癌和结肠癌预后的 EGFR 拮抗剂在乳腺癌中的临床效果有限。然而，限制 TNBC 中 EGFR 的表达是提高 EGFR 拮抗剂临床疗效的潜在策略。本研究中，我们发现 - 氨基丁酸 A 型受体 π 亚基 (GABRP) 作为一种富集于 TNBC 干细胞的膜蛋白，与 EGFR 相互作用并显著维持其表达，从而维持 TNBC 细胞干性和介导化疗耐药。沉默 GABRP 可诱导 EGFR mRNA 及蛋白水平下调以减弱 TNBC 干性，并增强其对紫杉醇、阿霉素、顺铂等化疗药物的敏感性。另外，我们还发现一种 FDA 批准用于辅助治疗癫痫发作的药物瑞替加滨，可以增加 TNBC 对吉非替尼的敏感性。总体而言，我们的研究结果表明，GABRP 可以通过调节 EGFR 的表达维持 TNBC 的干性，这表明 GABRP 可能是一个潜在的治疗靶点，可以解决 TNBC 中 EGFR 抑制剂耐药。

【Li XY et al. 2021 ***Cancer Lett***, IF=8.64】

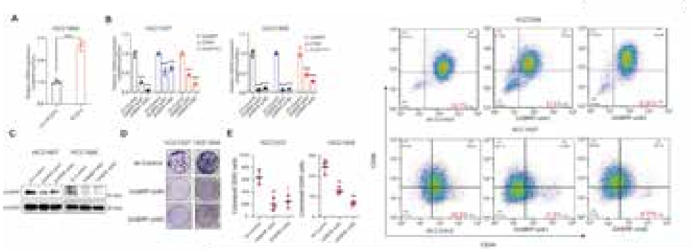

图 1. GABRP 敲降抑制三阴性乳腺癌细胞的干性

2. 基因组印迹及其在小鼠乳腺中的功能

基因组印迹是 DNA 的表观遗传修饰，基因表达受母本或父本遗传的等位基因调控。胎盘和胚胎中的印迹基因 (IGs) 对生长调节和营养供应至关重要。然而，尽管乳腺是一种重要的营养传递器官，但有关乳腺基因组印迹的研究仍然有限。在本研究中，我们发现在小鼠乳腺发育过程中，IGs 的数量和表达水平都有所下降。IG 的表达具有谱系特异性，与乳腺发育和泌乳相关。对单细胞 RNA 测序数据的 meta 分析显示，乳腺 IGs 在一个调控细胞干性和分化的网络中共同表达，这在我们的功能研究中得到了证实。因此，我们的数据表明，IGs 对乳腺干细胞的自我更新至关重要，IG 下降与乳腺成熟相关。

【Xu HB et al. 2021 ***J Mol Cell Biol***, IF= 6.688】

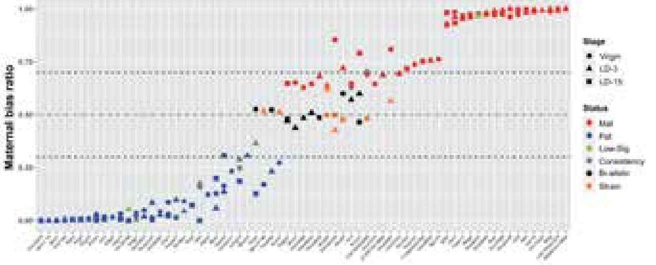

图 2. 小鼠乳腺中的印迹基因

Epigenetic and Developmental Regulation

Dr. Baowei Jiao, Principal Investigator, doctoral supervisor. The research team is mainly interested in mammary gland development, breast cancer, normal and breast cancer stem cell. Research team found a novel mechanism of SGCE in breast cancer stem cell chemoresistance and the role of TDP-43 in milk lipid secretion. Currently, over 30 papers have been published in international journals, such as *Cell, PNAS, Nature Communications, Advanced Science.*

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1. GABRP sustains the stemness of triple-negative breast cancer cells through EGFR signaling

we found that the gammaaminobutyric acid type A receptor π subunit (GABRP), as a membrane protein enriched in TNBC stem cells, interacted with EGFR and significantly sustained its expression, resulting in stemness maintenance and chemotherapy resistance. Silencing GABRP induced down-regulation of EGFR signaling, which hindered cell stemness and enhanced sensitivity to chemotherapies, including paclitaxel, doxorubicin, and cisplatin. We also identified that retigabine, an FDA-approved drug for adjunctive treatment of seizures, increased the sensitivity of EGFR to gefitinib in gefitinib-resistant cells. 【Li XY et al. 2021 ***Cancer Lett***, IF=8.64】

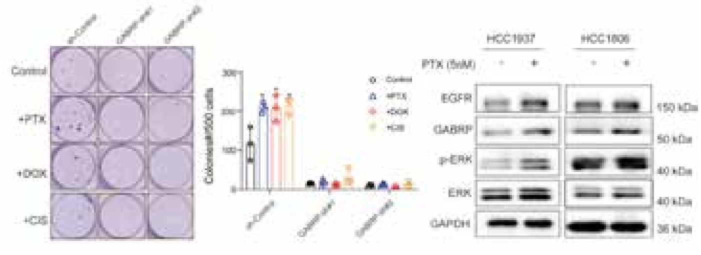

Fig 3. Loss of GABRP increases chemotherapy drug sensitivity in TNBC

2. Landscape of genomic imprinting and its functions in the mouse mammary gland

we found that both the number of IGs and their expression levels decreased during development of the mouse mammary gland. IG expression was lineage-specific and related to mammary gland development and lactation. Meta-analysis of single-cell RNA sequencing data revealed that mammary gland IGs were co-expressed in a network that regulated cell stemness and differentiation, which was confirmed by our functional studies. Accordingly, our data indicated that IGs were essential for the self-renewal of mammary gland stem cells and IG decline was correlated with mammary gland maturity. Taken together, our findings revealed the importance of IGs in a poorly studied nutrition-related organ, i.e. the mammary gland, thus providing a reference for further studies on genomic imprinting. 【Xu HB et al. 2021 ***J Mol Cell Biol***, IF= 6.688】

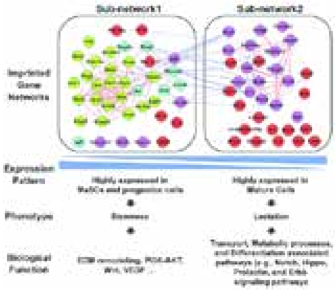

Fig 4. The Pattern of mammary gland development regulated by imprinted gene network

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灵长类进化遗传与发育

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重要成果及产出：

1. **Dong-Dong Wu***, Xiao-Guang Qi, Li Yu, Ming Li,Zhi-Jin Liu, Anne D. Yoder, Christian Roos,-Takashi Hayakawa, Jeffrey Rogers, Tomas MarquesBonet, Bing Su, Yong-Gang Yao,Ya-Ping Zhang, Guojie Zhang*,Initiation of the Primate Genome Project, ***ZOOLOGICAL RESEARCH***, 2022, 43(2): 147−149.
2. Ming-Shan Wang† , Jin-Jin Zhang†, Xing Guo†, Ming Li†, Rachel Meyer†, Hidayat Ashari†,Zhu-Qing Zheng, Sheng Wang, Min-Sheng Peng, Yu Jiang, Mukesh Thakur,Chatmongkon Suwannapoom, Ali Esmailizadeh, Nalini Yasoda Hirimuthugoda,Moch Syamsul Arifin Zein, Szilvia Kusza, Hamed Kharrati-Koopaee, Lin Zeng, Yun-Mei Wang,Ting-Ting Yin, Min-Min Yang, Ming-Li Li, Xue-Mei Lu, Emiliano Lasagna, Simone Ceccobelli,Humpita Gamaralalage Thilini Nisanka Gunwardana, Thilina Madusanka Senasig, Shao-Hong Feng,Hao Zhang, Abul Kashem Fazlul Haque Bhuiyan, Muhammad Sajjad Khan,Gamamada Liyanage Lalanie Pradeepa Silva, Le Thi Thuy, Okeyo A. Mwai26,Mohamed Nawaz Mohamed Ibrahim, Guojie Zhang, Kai-Xing Qu, Olivier Hanotte, Beth Shapiro,Mirte Bosse*, **Dong-Dong Wu***, Jian-Lin Han* and Ya-Ping Zhang*,Large-scale genomic analysis reveals the genetic cost of chicken domestication. ***BMC Biology***, (2021) 19:118.
3. Yan Li *, **Dong-Dong Wu** , Finding unknown species in the genomes of extant species. ***JOURNAL OF GENETICS AND GENOMICS***, 48 (2021) 867e871.
4. **Lin Zeng#,** He-Qun Liu#, Xiao-Long Tu#, Chang-Mian Ji#, Xiao Gou#, Ali Esmailizadeh, Sheng Wang, Ming-Shan Wang, Ming-Cheng Wang, Xiao-Long Li, Hadi Charati, Adeniyi C. Adeola, Rahamon Akinyele Moshood Adedokun, Olatunbosun Oladipo, Sunday Charles Olaogun, Oscar J. Sanke, Mangbon Godwin F., Sheila Cecily Ommeh, Bernard Agwanda, Jacqueline Kasiiti Lichoti, Jian-Lin Han, Hong-Kun Zheng, Chang-Fa Wang*,Ya-Ping Zhang*, Laurent A. F. Frantz*, **Dong-Dong Wu*.** Genomes reveal selective sweeps in kiang and donkey for high-altitude adaptation. ***ZOOLOGICAL RESEARCH,*** 2021, 42(4): 450−460.
5. **Yong Shao*,** †, Xiao-Bo Wang*, Mei-Ling Zhang *, Yan Liu *, Sheng Wang,Bao-Lin Zhang, Min-Min Yang, Ming-Hai Yang, Ting Jia, Tian-Chun Pu, Yan Lu,He Liu, Zhe Xu, Bo Li, Ning Liu, Violet Magoma Onsongo, **Dong-Dong Wu** ,Cheng-Lin Zhang †, Jue Ruan † & Yan Li †,Long-read genome sequencing provides molecular insights into scavenging and societal complexity in spotted hyena Crocuta crocuta,***Molecular Biology and Evolution,*** doi/10.1093/molbev/msac011/6509522,2022.

1. 发起灵长类基因组计划

解析和重构灵长类祖先到现代人类演化过程中的基因组变异图谱，是理解人类演化生物学的关键一步。在过去的几十年里，灵长类进化支系由于其独特的系统发育位置和重要性，一直是演化基因组学研究的热点。少数灵长类支系的比较基因组学研究已经拓宽了研究者对灵长类基因组演化特征多样性的认知，揭示了一系列基因组变异参与和调控人类表型的发育和演化。然而，到目前为止，仅仅不超过10%的灵长类物种的基因组被测序，人类和非人灵长类基因组演化和变异历史的研究仍然存在相当大的缺口。为了填补这一缺口，我们率先发起了灵长类基因组计划，利用全新的三代长读段基因组测序技术，产生和增加高质量灵长类参考基因组的数量。我们在这里概括和总结了灵长类基因组计划中需要解决的某些重要科学问题和将来的一些考虑。我们预计，大尺度的现存灵长类物种更广泛的分类单元的基因组抽样和比较，将极大地帮助我们理解人类表型和疾病的演化、灵长类物种形成和适应的基因组机制，最终有助于灵长类动物的保护和利用。

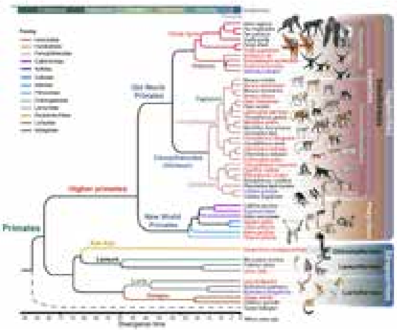

图1. 灵长类基因组计划

2. 基因组层面揭示藏野驴和藏家驴的高原适应

在过去的几百年里，西藏家驴已经适应了青藏高原的高海拔环境。有趣的是，与马科动物关系密切的藏野驴也栖息在这一地区。已有报道已经证明特定基因和适应渐渗在不同谱系中对青藏高原低氧环境适应的重要性。在本研究中我们评估了藏家驴和藏野驴适应青藏高原的生物途径是否相同，以及是否发生了适应性渐渗。我们从一个藏野驴个体上组装了基因组，并分析了5头藏野驴和93头藏家驴（其中24头来自青藏高原）的基因组。分析表明，在藏野驴的EPAS1位点存在一个强的硬选择性扫描。然而，在西藏的家驴中，另一种基因，即EGLN1，可能与它们对高海拔的适应有关，猜测与它们对高海拔的适应有关。此外，杂交分析没有发现藏家驴和藏野驴种间基因流动的证据。研究结果表明，虽然藏家驴到达青藏高原进化时间较短，且有一个与藏家驴亲缘关系较近的物种已经适应了低氧环境，但藏家驴并不是通过基因混合适应环境，而是通过另一种生物途径进化适应环境的。

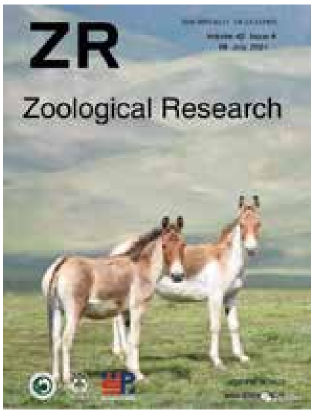

图2. 基因组层面揭示藏野驴和藏家驴在高海拔适应方面的选择性清除现象

Primate Evolutionary Genetics and Development

Dr. Dong-Dong Wu, Principal Investigator.

Dong-Dong Wu obtained his B.S at the Fudan University in 2006, and received his Ph.D from Kunming institute of Zoology, Chinese Academy of Sciences in 2011. He performed studies of artificial selection on domestic animals, particularly high altitude adaptation of domestic animals in Tibet. He has published more than 40 research papers in *Nat Genet, Cell Res, Genome Biol, Mol Biol Evol* etc, as first author or co-corresponding author.

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1. Initiation of the Primate Genome Project

A crucial step for understanding human evolution is to identify the genomic changes that occurred during primate evolution,thus allowing investigators to reconstruct the ancestral states preceding the human condition. In the past several decades, the primate clade has been a research focus in genome sequencing due to its unique phylogenetic position and key importance. Comparative genomic analyses of several primate lineages have radically expanded our knowledge on the tempo and mode of different features in primate genome evolution, revealing many genomic innovations contributing to the development and evolution of human phenotypes. However, with less than 10% of primate species currently sequenced, a considerable gap remains regarding the evolutionary history of every base pair in human and non-human primate (NHP) genomes. To fill this gap, we propose to organize and establish the Primate Genome Project (PGP) to scale up the number of high-quality reference genome assemblies for primate species using cutting-edge sequencing technologies. We outline here the possible paths going forward and some of the major questions to be addressed within this ambitious project. We anticipate that genomic comparisons, including broader taxon sampling of extant primate species, will significantly contribute to our understanding of the evolution of human phenotypes and diseases and the genomic mechanisms of primate speciation and adaptation, which will ultimately assist in primate conservation efforts. Currently, the genomes of a dozen representative NHP species from 22 genera have been published (Ensembl v103), with 72% of genera not yet sequenced. These high-quality genomes will provide rapid information for comparisons in the context of primate phylogeny to reconstruct the primate tree of life and clarify the genomic changes underlying the speciation and adaptation processes of major primate lineages. We anticipate that a detailed evolutionary landscape will be disclosed for all genomic variations across primate lineages from chromosomal rearrangements to single base-pair substitutions. This landscape will inform the evolutionary patterns of structural variations, segmental duplications, protein-coding genes, and non-coding regulatory elements. Conservation genomic analyses of population data will be highly informative regarding genomic diversity and recent demographic history, which are crucial parameters for evaluating the conservation status of species (Orkin et al., 2021). We expect that the PGP will generate a rich resource for primate lineage genomics over the next few years. Given the advances in sequencing technologies, it is important to initiate interdisciplinary cooperation and joint data analysis by integrating expertise in primatology, conservation, biomedicine, genomics, and evolutionary biology. Therefore, we welcome researchers to join the consortium and contribute to this necessary and timely research.

2. Genomes reveal selective sweeps in kiang and donkey for high-altitude adaptation

Over the last several hundred years, donkeys have adapted to high-altitude conditions on the Tibetan Plateau. Interestingly, the kiang, a closely related equid species, also inhabits this region. Previous reports have demonstrated the importance of specific genes and adaptive introgression in divergent lineages for adaptation to hypoxic conditions on the Tibetan Plateau. Here, we assessed whether donkeys and kiangs adapted to the Tibetan Plateau via the same or different biological pathways and whether adaptive introgression has occurred. We assembled a de novo genome from a kiang individual and analyzed the genomes of five kiangs and 93 donkeys (including 24 from the Tibetan Plateau). Our analyses suggested the existence of a strong hard selective sweep at the EPAS1 locus in kiangs. In Tibetan donkeys, however, another gene, i.e., EGLN1, was likely involved in their adaptation to high altitude. In addition, admixture analysis found no evidence for interspecific gene flow between kiangs and Tibetan donkeys. Our findings indicate that despite the short evolutionary time scale since the arrival of donkeys on the Tibetan Plateau, as well as the existence of a closely related species already adapted to hypoxia, Tibetan donkeys did not acquire adaptation via admixture but instead evolved adaptations via a different biological pathway.

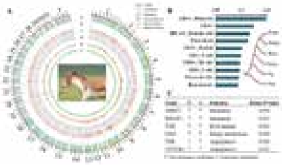

Fig 3. Genome evolution in kiangs

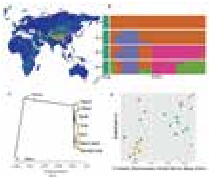

Fig 4. Population genetics analysis of kiangs and domestic donkeys

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大脑进化发育与生理功能

盛能印，博士，研究员，博士生导师。中国科学院“百人计划”、云南省“云岭高层次人才”获得者。长期从事神经科学相关研究工作，包括中枢神经系统发育形成和神经突触信息传递作用分子机制。已经在 *Cell*、*Developmental Cell*、*PNAS*、*Nature Communications* 等国际学术期刊发表论文 17 篇。目前实验室以小鼠、蜜袋鼯、貂和猕猴为模型，主要研究：（1）大脑胼胝体结构的进化发育和功能调控；（2）大脑皮层沟回结构的进化发育与功能调控；（2）神经突触进化发育遗传机制与神经精神疾病的内在联系及分子机制。

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重要成果及产出：

1. Luo R, Fan Y, Yang J, Ye M, Zhang DF, Guo K, Li X, Bi R, Xu M, Yang LX, Li Y, Ran X, Jiang HY, Zhang C, Tan L, **Sheng N**, Yao YG*. (2021) A novel missense variant in ACAA1 contributes to early-onset Alzheimer’s disease, impairs lysosomal function, and facilitates amyloid-β pathology and cognitive decline. ***Signal Transduct Target Ther*** 6(1):325.

在哺乳类动物的演化过程中，最显著的改变则是由大脑所决定的高级认知功能，大脑结构和功能调控的复杂性被认为是人类区别于其他物种的重要原因。我们研究组重点关注大脑半球对侧连接的重要结构胼胝体、大脑皮层沟回结构进化发育、神经突触环路功能进化的遗传机制，以及这些功结构的进化发育与大脑生理、病理调控的内在联系。

1. 大脑胼胝体结构的进化发育

在动物演化过程中，胼胝体是从胎盘哺乳类开始出现的连接对侧大脑的神经纤维结构，主要是由皮层 2-3 层胼胝体投射神经元（CPN）产生的对侧轴突神经束所组成。在人类大脑中其缺失或发育异常往往导致认知功能障碍，与自闭症等神经精神疾病密切相关。整合哺乳类（包括单孔类、和、有袋类和胎盘哺乳类）基因组比较分析，我们发现中在胎盘哺乳类动物中进化出近 32 万个新的保守非编码元件（Placental Conserved Noncoding Elements，PCNEs）。因此，我们进一步整合小鼠 CPN 关键发育期（E15.5 天）的 RNA-seq 和 ATAC-seq 组学数据，利用生物信息学分析构建其分子调控网络，筛选出在 E15.5 天 CPN 中潜在的活性开放的 PCNEs 约 2.1 万个，其中有 1000 多个 PCNE 调控 200 多个已知的胼胝体发育和疾病关键基因，包括 FoxG1、Pou3f2、Pou3f3、Cux2、Nfix 等转录因子。我们将这些 PCNEs 克隆至 Stagia3 报告载体中，通过宫内电转将其转染至 CPN 中，考察其开放性，进一步结合 CRISPR 表观调控技术，增强或抑制其活性，研究对胼胝体发育的影响，以及调控的下游基因和作用机制。

为深入研究从有袋类 - 胎盘哺乳类进化过程中，基因组进化在胼胝体进化发育中的作用机制，我们以蜜袋鼯和小鼠为研究对象，收取胼胝体发育关键时期的胚胎皮层组织，利用单细胞组学测序，包括 RNA-seq、CUT&Tag-seq、ATAC-seq 等，分析大脑皮层神经元细胞谱系和开放的顺时调控元件（CREs）的差异性，并进一步深入研究细胞谱系进化与基因调控网络进化的内在联系。

2. 大脑皮层沟回结构的进化发育

皮层沟回结构是人类大脑的重要特征，其发育形成异常与诸多神经疾病密切相关。研究表明在哺乳类演化过程中，大脑皮层沟回形成经历多次起源。我们首先以非洲兽总目（Afrotheria）、劳亚兽总目（Laurasiatheria）和灵长目（Primate）三支哺乳类为研究对象，根据皱褶指数选取其中有脑回和无脑回的物种，采用趋同进化分析方法研究其基因组中受到共同正选择的基因，发现诸多分子与神经发育和功能相关。貂是目前研究沟回发育的主要动物模型，因此我们利用三代基因组测序组装了高质量的水貂基因组序列，与此同时，我们收取了水貂皮层发育关键节点及成年沟和回组织，利用 RNA-seq、ChIP-seq、ATAC-seq 组学分析，研究沟和回之间基因表达调控网络的差异，以期解析大脑皮层沟回结构形成的分子机制，结合小鼠动物模型，探究其发育紊乱与神经发育疾病的关系。

3. 神经突触进化发育和功能调控机制

动物大脑除了宏观结构上的变化，突触环路的微进化也是其功能表型多样性的重要物质基础。目前研究发现，诸多灵长类 / 人类特有基因在皮层沟回等形态结构进化调控中发挥重要作用，但对于神经突触进化调控的特有基因知之甚少。BTN3A 亚家族是灵长类特有的免疫球蛋白超家族成员，我们前期工作发现其中的 BTN3A2 为精神分裂症易感基因，并可以调控突触传递活性。我们利用生物信息学手段，系统分析了 BTN 家族成员的基因演化历史，并发现 BTN3A 家族在大脑中具有较强的表达，因此我们以海马培养脑片为研究系统，利用膜片钳电生理技术研究 BTN3A 家族分子对兴奋性和抑制性突触传递活性的影响，以解析该灵长类特有基因家族对神经突触进化调控作用机制。此外，我们构建了 BTN3A2 的基因敲入小鼠模型，行为学实验表明，该小鼠的工作记忆能力受损，但没有表现出自闭、社交障碍等相关神经行为缺陷；电生理结果显示在海马神经元中异位表达可以影响突触前神经递质释放，从而调控兴奋性突触传递活性；分子细胞实验则鉴定出 BTN3A2 分子可以与 Nrxn 等突触前黏附分子相互作用，因此我们将深入研究其中的分子机制，以从分子 - 突触 - 环路 - 整体动物多个层次，系统解析该灵长类特有基因在神经突触进化和功能调控中的作用。

Brain evolutionary development and physiological function

Prof. Nengyin Sheng, Principal Investigator, joined in Kunming Institute of Zoology, Chinese Academy of Sciences in 2017. The research of Sheng's lab focuses on central nervous system (CNS) and will study the following topics using mice, ferret, sugar glider and rhesus monkey as model systems: (1) The mechanism and function of corpus callosum evolutionary development; (2) The mechanism and function of evolution and development of cortical gyrification; (3) The genetic bases underlying evolution and development of synapse, and its internal relationship with neuropsychiatric disorders.

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During the evolution of mammals, the most significant change is the acquirement of high-level cognitive abilities determined by the brain. The complexity of brain structures and function regulations is considered to be the most significant character to distinguish *Homo sapiens* from other species. Our research group focuses on studying the genetic mechanisms underlying brain evolution and development, especially the corpus callosum, an important structure of the contralateral connection of the cerebral hemisphere, the gyrification structure of cerebral cortex and the synaptic circuit, as well as the internal relationship of their proper regulation with brain physiological functions and pathological conditions.

1. The evolutionary development of corpus callosum

In the process of animal evolution, the corpus callosum is a nerve fiber structure connecting the contralateral brain that appeared from placental mammals, and is mainly composed of contralateral axon nerve bundles produced by the corpus callosum projection neurons (CPN) of the 2-3 cortical layers. Integrative and comparative analyses of mammalian genomes, we find that nearly 320,000 new conservative non-coding elements in placental mammals (PCNEs). Therefore, we further integrate the available RNA-seq and ATAC-seq omics data of the key developmental period of mouse CPN (E15.5 days). Using bioinformatics analyses to construct its molecular regulatory network, we identify about 21,000 open and potential active PCNEs potential in E15.5 CPNs, among which there are more than 1,000 PCNEs regulating around 200 known key genes for the corpus callosum development, as well as its related disease, including critical transcription factors such as FoxG1, Pou3f2, Pou3f3, Cux2, and Nfix. We clone these PCNEs into the Stagia3 reporter vector, transfected them into CPN by in utero electroporation to investigate their openness. Furthermore, combining with CRISPR epigenetic regulation technology to enhance or inhibit their activity, we study the effect on the development of the corpus callosum, and the regulatory downstream genes and functional mechanism.

In order to in-depth study the genomic mechanism for the corpus callosum evolutionary development during marsupial-placental mammals evolution, we use honey gliders and mice as the research models to collect embryonic cortex tissues during the critical period of corpus callosum development and use single cell omics sequencing, including RNA-seq, CUT&Tag-seq, ATAC-seq, etc., to analyze the detailed differences including cerebral cortical neuronal cell lineages and open clockwise regulatory elements (CREs). We further study the internal relationship underlying evolution of the cell lineage and genetic regulatory network.

2. The evolutionary development of cortical gyrification

The cortical folding is an important feature of the human brain, and its abnormal development is closely related to many neurological diseases. We first take the three branches of Afrotheria, Laurasiatheria and Primate as the research objects. According to the gyrification index, we selecte species with and without brain gyrus, and use convergent evolution analysis to identify the genes subjected to common positive selection. We find that many genes are indeed related to neurodevelopment and function. Ferret is currently the main animal model for studying gyrus and sulcus development. Therefore, we use three-generation genome sequencing to assemble high-quality mink genome sequences. At the same time, we collected the gyrus and sulcus tissues during key stages of mink cortex development as well as adult ones. Using RNA-seq , ChIP-seq, ATAC-seq omics analyses, we study the difference in gene expression and regulatory network between the sulcus and gyrus, in order to analyze the molecular mechanism of the gyrification structure of the cerebral cortex. Combining with mice models, we will explore the relationship of its abnormal development with neural developmental disorders.

3. Neural synaptic evolution and brain function

Besides the macrostructure changes of animal brains, the microevolution of synaptic circuits is also the important material basis for the diversity of its functional phenotypes. The BTN3A subfamily is a member of the immunoglobulin superfamily unique to primates. Our previous work found that BTN3A2 is a susceptibility gene for schizophrenia and can regulate synaptic transmission activity. We systematically analyze the genetic evolution history of BTN family members and find that the BTN3A family has a strong expression in the brain. Therefore, we use hippocampal cultured slices as the research system and apply patch clamp electrophysiological technology to study the effect of BTN3A family molecules on the evolutionary regulation of neuronal synapses. In addition, we constructed a knock-in mouse model of BTN3A2. We combine neural behavioral, electrophysiological recording, molecular and cellular tools to study the function and molecular mechanism of this primate specific gene underlying synaptic evolution at the levels of from molecular, synaptic circuit to overall animal.

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进化发育生物学

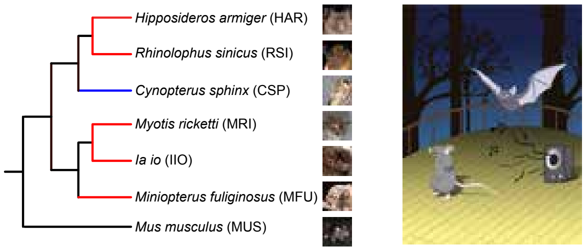
刘　振，博士，研究员，博士生导师，国家优秀青年基金获得者，省万人计划青年拔尖人才。主要以非模式动物为研究对象，结合比较基因组学、进化遗传学和功能基因组学的理论和方法，从进化发育生物学的角度揭示动物适应性复杂性状的分子遗传机制。目前以第一或通讯作者在 *Science, Science Advances, PNAS, Current Biology, Molecular Biology and Evolution* 等国际著名期刊发表研究论文二十余篇。

重要成果及产出：

1. **He K[1], Liu Q[1], Xu DM[1], Qi FY[1], Bai J, He SW, Chen P, Zhou X, Cai WZ, Chen ZZ, Liu Z*, Jiang XL*, Shi P*.** (2021). Echolocation in soft-furred tree mice**. *Science* 372: eaay1513.**
2. **Xu DM**[1], **Yang CP**[1], **Shen QS**[1], Pan SK[1], **Liu Z**[1], Zhang TZ[1], **Zhou X**, Lei ML, **Chen P**, **Yang H**, **Zhang T**, **Guo YT**, Zhan XJ*, Chen YB*, **Shi P***. (2021). A single mutation underlying phenotypic convergence for hypoxia adaptation on the Qinghai-Tibetan Plateau. ***Cell Research*** 31:1032-1035.
3. **Liu Z**[1], **Chen P**[1], **Li YY**[1], **Li MW**, **Liu Q**, Pan WL, **Xu DM**, **Bai J**, Zhang LB*, Tang J*, **Shi P*** (2021). Cochlear hair cells of echolocating bats are immune to intense noise. ***Journal of Genetics and Genomics*** 48:984-993.
4. **Guo YT**, **Zhang J**, **Xu DM**, Tang LZ*, **Liu Z***. (2021). Phylogenomic relationships and molecular convergences to subterranean life in rodent family Spalacidae. ***Zoological Research*** 42: 671−674.

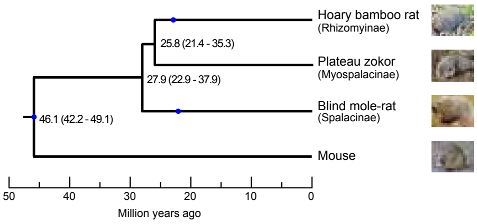
1. 回声定位蝙蝠耳蜗毛细胞的抗噪声机制研究

高强度噪音会引起耳蜗毛细胞损伤和凋亡，进而导致哺乳动物听力严重受损。然而自然界中的回声定位蝙蝠却可以长期暴露于高强度声音而听力不受影响。通过比较回声定位和非回声定位蝙蝠的耳蜗转录组，发现细胞凋亡、DNA 损伤、线粒体损伤、免疫及炎症反应等过程可能参与调控回声定位蝙蝠抗噪音机制。体外功能实验发现，在回声定位蝙蝠耳蜗高表达的转录因子 ILS1 可能是回声定位蝙蝠抗噪声的重要分子因素之一。 传统的噪音性听力损失研究多集中在利用模式动物进行耳蜗毛细胞损伤及再生的分子机制解析，而该研究则通过比较经历不同适应演化过程的非模式动物蝙蝠，发现哺乳动物耳蜗毛细胞在针对强噪声时可以形成适应性选择进化，从而加深了人们对耳蜗毛细胞和噪声关系的理解。



2. 鼹形鼠科的系统基因组学与营地下生活的分子趋同研究

啮齿目鼹形鼠科（Spalacidae）的所有物种都是地下生活的，演化出了多样的营地下生活的特征。然而，该科中三个亚科（Myospalacinae、Smalacinae 和 Rhizomyinae）间的系统发生关系及其适应地下生活的分子基础仍然知之甚少。本研究对银星竹鼠（*Rhizomys pruinosus*）进行了全基因组测序及组装，系统基因组分析支持 Myospalacinae 和 Rhizomyinae 亲缘关系更近，并且发现鼹形鼠科的三个亚科是在一个相对较短的时间跨度下分化出来的（~200 万年）。与具有相似分化时间的非地下对照组相比，鼹形鼠科与非洲鼹鼠存在显著多的趋同基因，这些趋同基因在血管形态发生和氧化应激反应等功能类别中富集，提示着它们可能参与到了鼹形鼠科适应低 O2- 高 CO2 的地下环境的演化过程中。



Evolutionary Developmental Biology

Prof. Zhen Liu, Principal Investigator. Evolutionary developmental biology is like a bridge to mediate the evolutionary biology and developmental biology for understanding the genetic basis of phenotypic changes macroevolutionarily. Using bats as a research model, we focus on the following major questions: (1) what are the roles of molecular variations on the developmental mechanisms for the origin and elaboration of adaptive phenotypes in evolutionary process? (2) what are the relative roles of chance and necessity in evolution for the developmental mechanisms of adaptive phenotypes?

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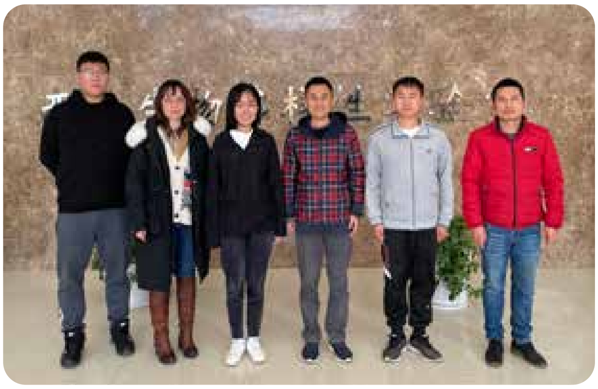
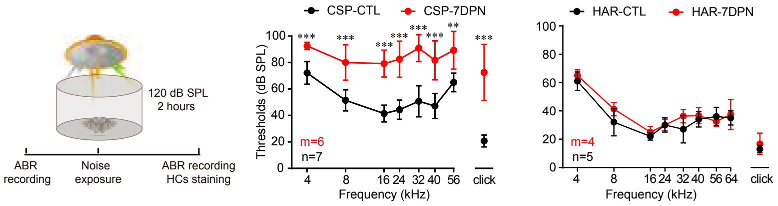


1. Cochlear hair cells of echolocating bats are immune to intense noise

Exposure to intense noise can damage cochlear hair cells, leading to hearing loss in mammals. Echolocating bats, however, are naturally exposed to continuous intense sounds from their own and neighboring sonar emissions for maintaining sonar directionality and range. Here, we propose the presence of intense noise resistance in cochlear hair cells of echolocating bats against noise-induced hearing loss (NIHL). To test this hypothesis, we performed noise exposure experiments for laboratory mice, one nonecholocating bat species, and five echolocating bat species. Contrary to nonecholocating fruit bats and mice, the hearing and the cochlear hair cells of echolocating bats remained unimpaired after continuous intense noise exposure. The comparative analyses of cochleae transcriptomic data showed that several genes protecting cochlear hair cells from intense sounds were overexpressed in echolocating bats. Particularly, the experimental examinations revealed that ISL1 overexpression significantly improved the survival of cochlear hair cells. Our findings support the existence of protective effects in cochlear hair cells of echolocating bats against intense noises, which provides new insight into understanding the relationship between cochlear hair cells and intense noises, and preventing or ameliorating NIHL in mammals.



2. Phylogenomic relationships and molecular convergences to subterranean life in rodent family Spalacidae

It has long known that the rodent family Spalacidae belongs to typically subterranean mammals. However, the phylogenetic relationship among its three subfamilies and the molecular mechanisms for them adapting to underground life remain poorly explored, especially at the genome-wide scale. By *de novo* sequencing a bamboo rat (*Rhizomys pruinosus*) genome, we inferred the phylogenomic relationship among these subfamilies of the spalacids and supported a sister relationship between Myospalacinae and Rhizomyinae, which represents a conclusive phylogenomic relationship among three subfamilies of Spalacidae. Our genome-wide convergent evolution analyses revealed that the convergent genes between the spalacids and the African subterranean mole-rats are enriched in some functional categories that are relate to the adaptation to the hypoxic-hypercapnic underground environment.

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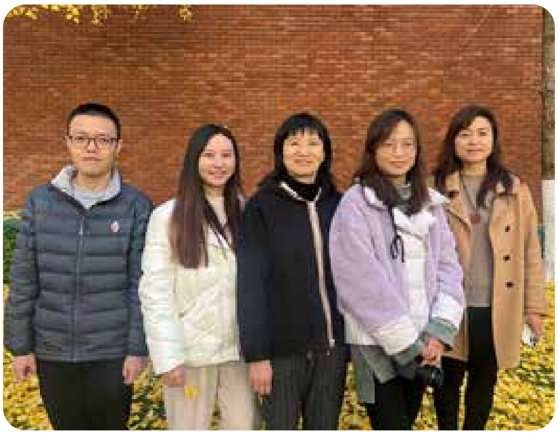


昆明野生动物细胞库

昆明野生动物细胞库（简称昆明细胞库）成立于 1986 年，是以保存动物的遗传资源和遗传多样性为主要目的的细胞库。现已保存有 367 种动物的细胞系 2428 株 20000 余份。 大多数为哺乳动物的细胞系，其中包括 60 种国家级重点保护动物的细胞系。目前，昆明细胞库是国家生物医学实验细胞资源库、中国科学院生物遗传资源库、中国西南野生生物种质库的成员单位之一，也是遗传资源与进化国家重点实验室的成员单位之一。

重要成果及产出：

1. Yuan Yin*, Hui-Zhong Fan*, Bo-Tong Zhou*, Yi-Bo Hu*, Guang-Yi Fan*, **Jin-Huan Wang***, Fan Zhou*, **Wen-Hui Nie***, Chen-Zhou Zhang et al. Molecular mechanisms and topological consequences of drastic chromosomal rearrangements of muntjac deer. **Nature Communications**, 2021, 12: 6858. (*These authors contributed equally)
2. Weera Thongnetr, Wiwat Sangpakdee, Alongklod Tanomtong, **Wenhui Nie**, Sayam Raso, Krit Pinthong.The chromosomal homology between dusky langur (Trachypithecus obscurus Ried, 1837) and human (Homo sapiens) revealed by chromosome painting. **Nucleus**, 2021, doi.org/10.1007/s13237-021-00381-0.

1. 细胞资源的收集和保藏

2021 年度 , 昆明细胞库利用从野外采集以及从其他途径获得的动物材料，共新建各类动物细胞系 130 株 , 其中包括眼镜王蛇、普通鸬鹚、大足鼠耳蝠、普通伏翼、针尾鼹和北白颊长臂猿等 19 种野生动物的细胞系 77 株 , 建立家养动物、人和实验动物的正常细胞系和肿瘤细胞系 53 株。复苏和扩增各类动物细胞系 583 株次。

2. 对外服务

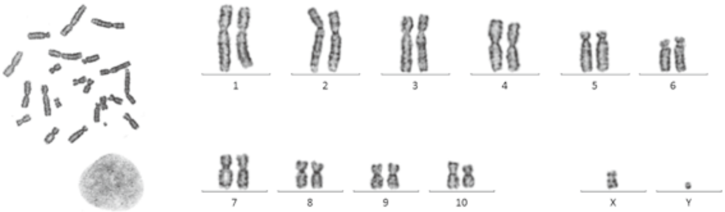
在 2021 年度，昆明细胞库为全国各地的 191 家单位，其中高等院校 84 家，科研院所 22 家，企业 85 家的研究人员提供各类野生和家养动物细胞系、人及常见实验动物的各类正常组织来源的细胞系、肿瘤细胞系及培养液共计 890 株次。除提供细胞服务外， 我们还提供了核型分析和 STR 检测等技术服务 58 株次， 以及通过电话、邮件及现场指导等方式提供大量的细胞培养技术咨询。

3. 青海沙蜥的核型分析

爬行动物的性别决定是爬行动物研究中的一个关键问题。青海沙蜥雌雄个体的形态差异较大， 但是否存在性染色体的分化还未知。为了满足课题组的研究需求，我们开展了来自四个不同采集地的青海沙蜥 17 个个体的染色体制备和核型分析的工作。结果表明两个区域的青海沙蜥雌雄个体的染色体形态一致，而另外两个区域的青海沙蜥雌雄个体中有一条染色体形态有差异。这种差异是否是性染色体有分化还有待进一步研究。

4. 蜜袋鼯不同组织来源细胞系的建立

蜜袋鼯是一种原产于澳大利亚和新几内亚地区的有袋动物，是为数不多的具有类似于人类手指的哺乳动物之一。蜜袋鼯的身体两侧拥有滑行膜，从手关节延伸到脚踝，有利它们在树林间滑行。利用课题组提供的蜜袋鼯，我们为课题组成功建立了五种不同组织来源的蜜袋鼯体细胞系，并完成了蜜袋鼯的核型分析工作， 为课题组开展后续研究储备了细胞材料。

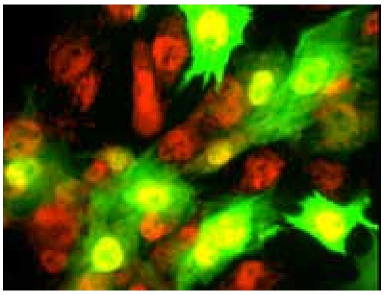


Kunming Wild Animal Cell Bank

In order to protect animalgenetic resource and genetic diversity, Kunming wild animal cell bank was established in Kunming Institute of Zoology, Chinese Academy of Science in 1986. Up to now 2428 cell lines from 367 species have been preserved in our cell bank. Most cell lines are derived from mammals. Among the species, 60 species are national protected animals in China. Now it is one branch of National Biomedical Experimental Cell ResourceBank for Sci-Tech, Biological Genetic Resource Bank of CAS, China Germplasm Bank of Wild Species, and State Key Laboratory of Genetic Resources and Evolution.

1. The collection and preservation of cell lines

In 2021, 130 cell lines from various wild animals, domestic animals and humans had been established and frozen. Among these cell lines, 77 cell lines were derived from 19 species of wild animals such as King Cobra, Great Cormorant, Rickett's big-footed bat, Common pipistrelle; Long-tailed mole and Northern white-cheeked gibbon etc.; 53 cell lines were established from domestic animals, experimental animals and humans. Four hundred and fifty-one of frozen-stored cell lines were also resuscitated and subcultured.



2. Cell lines service and technical service

In 2021, Kunming Cell Bank have provided cell services 890 times, such as wild and domestic animal cell lines, tumor cell lines and culture medium for researchers from 191 units across the country, including 84 universities, 22 research institutes and 85 enterprises.In addition to providing cell services, we also have provided technical services like karyotype analysis and STR test for 58 times, as well as a large number of cell culture technical advice through telephone, email and on-site guidance.

3. Karyotype analysis of Vlangal' s toad-headed agamas

Sex determination in reptiles is a key issue in reptile research. For Vlangal's toad-headed agamas, there are great morphological differences between male and female, but whether there is sex chromosome differentiation is unknown. In order to meet the research needs of the research group, we carried out chromosome preparation and karyotype analysis of 17 individuals of Vlangal's toad-headed agamas from four different collection sites.The results showed that the chromosome morphology of male and female in the two regions was the same, while in the other two regions, one chromosome morphology was different between male and female indivduals.Whether this difference is sex chromosome differentiation remains to be further studied.

4. Establishment of cell lines from the sugar glider

The sugar glider is a marsupial native to Australia and New Guinea, one of the few mammals with human-like fingers.The sugar gliders have membranes on both sides of their bodies that extend from the knuckles of the hands to the ankles, allowing them to glide between the trees. Using the tissues of the glider provided by the research group, we successfully established five somatic cell lines from different tissues for the research group, and completed the karyotype analysis of the sugar glider. The cell materials were reserved for the research group to carry out follow-up research.

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重要在研项目

序号	项目名称	项目来源	项目类别	负责人	执行期	总经费（万元）	参与类型
1	第二次青藏高原综合科学考察研究任务五（生物多样性保护与可持续利用）	科技部	科技基础资源调查专项	施　鹏	2019-2024	18993	主持
2	高黎贡山南段代表性脊椎动物种质资源调查收集与保存	科技部	科技基础资源调查专项	柴　静	2021-2026	274	参与
3	社交障碍的神经环路机制与干预研究	科技部	科技创新 2030 重大项目	张亚平	2021-2026	4000	主持
4	“ 猕猴介观神经联接图谱 ” 项目课题二：《猕猴全脑空间转录组图谱绘制和细胞类型鉴定》	科技部	科技创新 2030 重大项目	罗　鑫	2021-2026	1004.308	参与
5	中国健康长寿人群多队列的系统研究	科技部	国家重点研发计划	孔庆鹏	2018-2022	2820	主持
6	灵长类多能干细胞基因组稳态调控网络及增强策略	科技部	国家重点研发计划	郑　萍	2021-2026	2329	主持
7	新冠病毒基因组进化规律与动态演变研究技术体系创建与应用	科技部	国家重点研发计划	吕雪梅	2020-2022	450	主持
8	非人灵长类与树鼩脑疾病模型创建与关键技术研究	科技部	国家重点研发计划	毛炳宇	2021-2024	300	主持
9	生猪高产优质高效性状形成的分子调控网络	科技部	国家重点研发计划	谢海兵	2021-2026	1140	参与
10	中国长寿家系人群健康老龄调控因子甄别研究	科技部	国家重点研发计划	李功华	2019-2022	530	参与
11	病原变异及其跨物种传播的回溯和演进方法体系构建	科技部	国家重点研发计划	吕雪梅	2021-2024	513	参与
12	利用多组学技术解析社交与情感的遗传基础和调控网络	科技部	国家重点研发计划	王国栋	2019-2024	438	参与
13	企鹅物种进化树，进化格局以及对地质环境变迁的响应	科技部	国家重点研发计划	张国捷	2018-2021	228	参与
14	灵长类大脑进化分子机制的转基因猕猴研究	基金委	重点项目	宿　兵	2018-2022	340	主持
15	多能干细胞高效调控 DNA 复制压力反应的关键 lncRNA 鉴定与功能分析	基金委	重点项目	郑　萍	2020-2024	312	主持
16	回声定位蝙蝠高频听力适应性进化的遗传发育机制	基金委	重点项目	施　鹏	2020-2024	303	主持
17	高原湖泊水质变化过程中鲫鱼复合体种群体多样性变化及其生态适应性	基金委	联合基金项目	吕雪梅	2020-2023	231	主持

序号	项目名称	项目来源	项目类别	负责人	执行期	总经费（万元）	参与类型
18	全球视角下全基因组数据解析家鸡的起源和扩散	基金委	联合基金项目	吴东东	2020-2023	230	主持
19	猕猴大脑发育调控的三维基因组解析与灵长类脑进化的遗传机制研究	基金委	联合基金项目	宿 兵	2021-2024	227	主持
20	剪接因子 SFPQ 对三阴性乳腺癌中 Erα 的转录调控研究	基金委	联合基金项目	焦保卫	2019-2022	220	主持
21	阿尔茨海默症（AD）转基因树鼩模型的创建及有效性评价	基金委	联合基金项目	郑 萍	2018-2021	204	主持
22	鲤科鱼类肌间刺系统演化及其在滇池金线鲃遗传机制	基金委	联合基金项目	杨君兴	2018-2021	200	主持
23	哺乳动物的趋同演化	基金委	优秀青年科学基金项目	刘 振	2020-2022	130	主持
24	基于线粒体基因组和 Y 染色体遗传信息追溯美洲印第安人的源流历史	基金委	国际合作	孔庆鹏	2017-2021	235	主持
25	动物复杂性状的进化创新与重塑	中科院	B 类先导专项培育项目	施 鹏	2021-2022	800	主持
26	驯化动植物对高寒环境的适应及基因资源利用	中科院	A 类先导专项	彭旻晟	2018-2022	1160	参与
27	高原湿地垫脚石式廊道生态修复技术与示范 (子课题 2)	中科院	A 类先导专项	杨君兴	2019-2023	1145	参与
28	猪育种示范基地建设与完善	中科院	A 类先导专项	张亚平	2019-2024	1130	参与
29	关键区域的高通量、连续覆盖生物多样性监测与评估	中科院	A 类先导专项	Douglas W Yu	2018-2023	1094.23	参与
30	气候环境变化对典型动物及种群的影响	中科院	A 类先导专项	车 静	2018-2023	1060.29	参与
31	高原人群适应高寒环境的遗传资源发掘	中科院	A 类先导专项	孔庆鹏	2018-2022	686.31	参与
32	西南山地旗舰动物生态廊道设计技术与示范	中科院	A 类先导专项	蒋学龙	2019-2023	621.54	参与
33	两栖类生物多样性格局及其与季风气候的关系	中科院	B 类先导专项	柴 静	2018-2023	398.72	参与
34	鸟类不同类群间及与病毒间的协同演化机制研究	中科院	B 类先导专项	张国捷	2018-2023	300	参与
35	宿主比较基因组与共进化	中科院	重点部署项目	彭旻晟	2019-2021	480	主持

序号	项目名称	项目来源	项目类别	负责人	执行期	总经费（万元）	参与类型
36	建立哀牢山自然保护区快速生物多样性监测方法	中科院	重点项目	Douglas W Yu	2017-2022	400	主持
37	家犬强迫症疾病模型初探	中科院	前沿重点项目	王国栋	2019-2023	300	主持
38	自闭症食蟹猴模型的创建	中科院	西部之光交叉团队	郑萍	2019-2021	200	主持
39	西部之光引进人才项目——吕雪梅	中科院	西部之光	吕雪梅	2019-2021	200	主持
40	江西鄱阳湖流域山区水系分布的大鲵种质资源调查及保护创新研究	中科院	科技服务网络计划（STS 计划）区域重点项目	车静	2021-2023	990	主持
41	非洲动物多样性格局及动物资源研究与利用课题 -3	中科院	中非联合研究中心项目	蒋学龙	2021-2023	200	主持
42	现生鸟类多样性演化历史及机制研究	中科院	国际合作项目	张国捷	2019-2022	270	主持
43	非洲猪科动物种质和遗传资源	中科院	国际合作项目	彭旻晟	2021-2024	240	主持
44	云南跨境生物监测预警技术体系研究及应用	云南省	重大科技专项计划	施鹏	2021-2024	2000	主持
45	云南高原湖泊特有四大名鱼的保育及其深度发掘利用研究	云南省	对外科技合作专项	杨君兴	2020-2023	300	主持
46	云南省领军人才项目——宿兵	云南省	领军人才项目	宿兵	2020-2024	920	主持
47	云南省云岭学者（2020）——孔庆鹏	云南省	高层次人才培养支持计划	孔庆鹏	2020-2025	200	主持
48	云南省云岭学者（2019）——施鹏	云南省	高层次人才培养支持计划	施鹏	2019-2024	200	主持
49	春城科技领军人才专项——孔庆鹏	昆明市	春城科技领军人才专项	孔庆鹏	2021-2024	1000	主持
50	昆明长水国际机场威胁性鸟类防控中心项目	企业合作	横向项目	杨晓君	2018-2021	295	主持

发表论文

（蓝色标注：实验室是文章第一完成单位；加粗：标注实验室的人员；通讯作者 *；共同第一作者 ^{1}）

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授权专利

专利号	专利名称	类别	授权日期	完成人（固定人员）
ZL201911086725.6	TDP-43 基因在预测产妇泌乳量方面的应用	发明专利	2021-03-09	焦保卫，邹 丽，杨 钦
ZL202010309986.6	抑制 SGCE 的试剂的应用	发明专利	2021-03-30	焦保卫，赵丽娜
ZL202010309979.6	SGCE 基因作为三阴性乳腺癌标志物的应用	发明专利	2021-06-25	焦保卫，赵丽娜
CN201710949841.0	一种基于多样性指数和区域范围关系的幂法则标度模型预测微生物群落结构的方法	发明专利	2021-06-26	马占山
CN201711289534.0	一种基于多样性指数与时空关系的幂法则标度模型预测微生物群落结构变化的方法	发明专利	2021-05-14	马占山
CN201711223008.4	一种基于 Hill numbers 与时间关系的幂法则模型预测微生物群落结构的方法	发明专利	2021-09-17	马占山
CN201611126939.8	基于人体菌群互作网络分析评估机体健康和诊断疾病的方法	发明专利	2021-12-17	马占山
CN201611127036.1	人体微生物互作网络中正负作用比值在评估人体健康和疾病诊断中的应用	发明专利	2021-12-17	马占山
CN201611126940.0	一种应用 β 稳定性分析单细胞测序数据的方法	发明专利	2021-12-03	马占山，李连伟

获奖

省部级奖励

序号	成果名称	类型	等级	完成人	完成情况
1	乳腺癌异质性的分子机制研究	云南省科学技术奖——自然科学奖	三等奖	焦保卫、柯 浩、赵丽敏	独立完成
2	大动物高效基因编辑与体细胞克隆技术的创新与应用	云南省科学技术奖——技术发明奖	一等奖	魏红江，赵红业，卿玉波，王 文，陈 翔，成文敏，李鸿辉，贾宝瑜，王 配，曾伟奇，赵 恒，角德灵，徐凯祥	非第一完成人（非独立完成）
3	暗色唇鱼人工繁殖与产业化推广	云南省科学技术奖——科学技术进步奖	三等奖	潘晓赋、艾祖军、范 伟、刘 兴、王云峰、程 乐、杨君兴	第一完成人（非独立完成）

荣誉称号

姓名	年度	奖项	类型
杨君兴	2021	云南“最美科技工作者”称号	省级

第二章 开放合作交流

开放课题

课题编号	申请人	职 称	申请人所在单位	项目名称	资助经费（万元）
GREKF21-01	Damon Lesmeister	Research Scientist	USDA Forest Service and Oregon State University	Connecting Earth Observation to Biodiversity and Ecosystems II	8.5
GREKF21-02	陈进民	副教授	安徽师范大学	锄足蟾超科的物种多样性分布格局研究	8.5
GREKF21-03	钟树荣	副教授	昆明医科大学	云南孟高棉语族人群的母系遗传历史研究	8.5
GREKF21-04	杨连东	副研究员	中国科学院水生生物研究所	鱼类平扁体型适应的趋同进化研究	8.5
GREKF21-05	陆 剑	研究员	北京大学	新冠病毒的进化和传播	8.5
GREKF21-06	易 斌	讲师	红河学院	微生物菌群构建和多样性维持机制研究	8.5
GREKF21-07	夏王晓	讲师	西安医学院	海月水母水螅体向水母体转化的细胞和分子基础研究	8.5
GREKF21-08	金志刚	教授	浙江师范大学	DDX3X 介导的应激颗粒在突触调控中的机制研究	8.5
GREKF21-09	刘 洋	教授	陕西师范大学	啮齿动物视色素的表型进化及分子机制研究	8.5
GREKF21-10	黄庆国	副研究员	公安部昆明警犬基地	警犬高兴奋性形成的遗传机制研究	8.5
GREKF21-11	王 滔	讲师	昆明医科大学第二附属医院	胰腺癌与 IPMN 差异性转录组学研究	8.5
GREKF21-12	吉学平	研究馆员	云南省文物考古研究所	云南早期现代人遗传多样性的古 DNA 研究	8.5
GREKF21-13	郭 琨	讲师	昆明医科大学	猕猴精原干细胞发育及分化过程中基因表达调控的研究	8.5
GREKF21-14	陈忠良	副教授	贵州医科大学	lncRNA956 维持小鼠胚胎干细胞基因组稳定的分子机制	8.5

参加学术会议

序号	会议名称	会议时间	会议地点	报告人（参会人）
1	2021 年八学会新春联谊会暨学术会议	2021.01.15-16	云南 安宁	吕章夏、白慧掀
2	Biology & Genomics of Social Insects	2021.03.30-04.01	线上	张国捷
3	中国整合生物样本学大会	2021.04.09	上海	尹婷婷
4	肿瘤动物模型创制及应用研究室学术讲座	2021.04.12	四川 成都	焦保卫
5	中国细胞生物学学会 2021 年全国学术年会	2021.04.12-16	重庆	焦保卫、杨　星、刘　霁、邵海莉
6	2021 动物学前沿论坛“动物基因资源多样性与利用”	2021.04.23-25	浙江 宁波	王　文
7	“生猪高产优质高效性状形成的分子调控网络”研讨会	2021.05.29-31	北京	赵丽娜
8	第三届青年生命科学论坛	2021.06.04-06	北京	尹婷婷、柳延虎
9	第十七届全国昆虫区系分类学术研讨会暨第五届传粉昆虫学术研讨会	2021.06.11-14	线上	李学燕，董志巍
10	第十一届全国核酸学术讨论会	2021.07.02-05	辽宁 大连	焦保卫、王　慧、缪佳雨
11	现代水产种业培训班暨云南水产种业发展论坛	2021.07.14-15	云南 景洪	殷艳慧、潘晓赋、王晓爱、吴安丽、张源伟
12	云南省水产学会休闲渔业分会（云上若海俱乐部）和遗传育种分会成立大会暨休闲渔业产业发展论坛	2021.07.28-29	云南 昆明	黄新迪、潘晓赋、王晓爱、盛　丹、吴安丽、何宇娇
13	中国昆虫学会“全国第四届甲虫进化分类与多样性学术研讨会”	2021.07.09-11	云南 大理	李学燕
14	The 2nd AsiaEvo Conference	2021.08.16-19	线上	车　静、张国捷、刘薇薇、徐　伟
15	第十四届神经生物学大会	2021.09.16-19	重庆	马鹏程、李雨薇

序号	会议名称	会议时间	会议地点	报告人（参会人）
16	COP15 NGO 平行论坛	2021.09.27-28	云南 昆明	车静
17	2021 棒棰岛肿瘤及血液病前沿论坛	2021.10.13-15	辽宁 大连	焦保卫
18	中国昆虫学会年会	2021.10.13-16	陕西 西安	李学燕、刘薇薇
19	第九届中国西部动物学学术研讨会	2021.10.15-17	重庆	吴云鹤、陈进民、王识之、张少杰
20	第十届中国乳腺癌高峰论坛	2021.10.15-17	辽宁 沈阳	焦保卫
21	香山科学会议	2021.10.18-19	北京	车静
22	高黎贡山陆生野生动物疫源疫病监测网络建设座谈会	2021.10.22	云南 昆明	吴云鹤
23	中国动物学会原生动物学分会第十一次会员代表大会暨第二十一次学术讨论会	2021.10.22-26	山东 青岛	文建凡、吕章夏、白慧掀、程姣妮、邓琪、沈洁
24	第十届神经细胞生物学前沿研讨会	2021.10.26-28	湖北 武汉	盛能印
25	中国动物学会动物行为学分会第四届（2021）学术年会暨全国动物行为学第八次研讨会	2021.10.28-31	上海	周其俊
26	云南省昆虫学会第十一次会员代表大会暨 2021 年学术年会	2021.10.29-31	云南 曲靖	李学燕、何金武、刘薇薇
27	亚欧两栖爬行动物多样性与保护国际学术大会暨中国动物学会两栖爬行动物学分会 2021 年度学术大会	2021.11.02	四川 成都	车静、柴静、张栋儒、吴云鹤、Alex Plimo Karuno
28	昆明医科大学学术交流会	2021.11.03	云南 昆明	文建凡
29	深圳国家基因库学术交流	2021.11.03	广东 深圳	尹婷婷
30	南方海洋科学与工程广东省实验室（广州）学术交流	2021.11.03	广东 广州	尹婷婷
31	中国生物化学与分子生物学会 2021 年全国学术会议	2021.11.25-28	云南 昆明	郑萍、张伟道、马怀孝、王林、唐敏、宁雨琪、陶慧玲、孙春丽、金洁、李聪、龚道华、董玉萍、孟夏朵
32	International Frontiers Forum on Animal Genetics, Breeding, and Reproduction (2021)	2021.12.03	湖北 武汉	谢海兵

邀请专家报告

序号	专家姓名	单位	职称	报告题目	报告时间
1	周浙昆	中国科学院西双版纳热带植物园	研究员	青藏高原新生代植物多样性与高原环境的协同演化	2021.01.05
2	陈华	中国科学院北京基因组所	研究员	Inferring demographic history using allele frequency spectrum and hidden Markov models	2021.03.16
3	徐书华	中科院 - 马普学会计算生物学伙伴研究所	研究员	群体基因组学	2021.03.16
4	邹征廷	中国科学院动物研究所	研究员	序列演化异质性和系统发育分析的深度学习初探	2021.05.28
5	李海鹏	中国科学院上海营养与健康研究所	研究员	Genomic inference of a human super bottleneck in the Early Stone Age	2021.05.28
6	葛斯琴	中国科学院动物研究所	研究员	昆虫的形态与功能	2021.07.12
7	David Irwin	University of Toronto	教授	Evolution of Proinsulin and Proglucagon Genes in Vertebrates	2021.07.13
8	胡荣贵	中国科学院分子细胞科学卓越创新中心	研究员	Ubiquitin (Ub) & Retinoic Acid (RA) Signaling in Autism Spectrum Disorders (ASD)	2021.11.17
9	刘默芳	中国科学院上海生物化学与细胞生物学研究所	研究员	男性不育与肿瘤发生	2021.11.17
10	彭勇	四川大学华西医院	教授	肝癌中 pre-miRNA 的核质转运调控	2021.11.17
11	宋微波	中国海洋大学	院士	进展中的纤毛虫学研究：一个微观世界的窗口	2021.12.16
12	陈婷	北京生命科学研究所	研究员	Surface perspective on aging and autoimmune disease	2021.12.31

第三章 人才队伍培养

新增人才称号

序号	姓名	荣誉称号	项目来源	获得年份
1	郑 萍	中青年科技创新领军人才	国家	2021
2	郑 萍	国家高层次人才特殊支持计划科技创新领军人才	国家	2021
3	马鹏程	中青年学术和技术带头人后备人才	云南省	2021
4	曾 琳	中青年学术和技术带头人后备人才	云南省	2021
5	刘 振	“西部之光”交叉团队	中科院	2021
6	董 锋	“西部之光”青年学者项目	中科院	2021
7	高 云	技术支撑人才	中科院	2021
8	尹婷婷	青年创新促进会会员	中科院	2021
9	罗 鑫	青年创新促进会会员	中科院	2021
10	马鹏程	青年创新促进会会员	中科院	2021
11	赵丽娜	青年创新促进会会员	中科院	2021
12	张 涛	青年创新促进会会员	中科院	2021
13	柳延虎	青年创新促进会会员	中科院	2021
14	高 伟	特别研究助理资助项目	中科院	2021

在读研究生及博士后

序号	导师	硕士生	博士生	博士后
1	Douglas W Yu		李宗煦、罗明洁	
2	车 静	曹如君、THET MYAT OO、冯小刚、卢宸祺、于中斌、万 涵、荀 皓	张 毅、ALEX PLIMO KARUNO、FELISTA KASYOKA KILUNDA、侯绍兵、徐 伟、董文捷、余传鑫、易木荣	
3	佴文惠	高简奥、王浩博		
4	蒋学龙	SAMSON MABEYA OURU、SAMBAYA BRIAN ANOTO、胡文豪、李弈仙、陈春妮、汪思远、张 敏	牛晓炜、KENNETH OTIENO ONDITI、于秋鹏、胡文强、何水旺	
5	饶定齐	何圆圆		
6	李学友	王金宇		
7	焦保卫	邵海莉、黄吉鹏、缪佳雨、杨 超、王 毯	郭 璐、杨 旭、邹 丽、刘 霈	
8	孔庆鹏	翁崇峻、赵 龙、王霞燕、张润峰、姚亚冬	葛明侠、王昊天、尹藩乾、苏 倩、敖鸿舜、郜宗亮	
9	李功华	周青青		
10	刘 振	国天日	蒋继滨	
11	吕雪梅	魏婉宜、何晓艺、李丰邑、廖思洁、张 蕾、何 昊	陈泽宇、冯 璥、闫 凯、魏昀旸、RAOGO BLAISE OUEDRAOGO、REX FRIMPONG ANANE、张 昕、李梓锋	
12	马占山	杨 旭	李文迪、MD MOTIUR RAHMAN、陈红菊、肖琬蒙、乔玉亭	
13	毛炳宇	杨陈成、陈锦芳、马玉竹、李 伟	朱 良、李雨薇、茶靖美	
14	盛能印	吴月春、易琳昀、李 熹、杨 锐、张 浩、赵 阳	叶雅馨、刘娅敏、卜宇飞、万 梨	
15	施 鹏	华秦杨、马苑硕、陈施培、饶 琦、李雪凤、周 豪、吕颜洁	刘 奇、白 婧、陈 杰、郭媛婷、蔡婉芷、华 绒、周 鑫、陈 鹏、姚晓晴、杨 陆	刘广帅 陈中正
16	王国栋	吴青琴、曾 敏、冯馨瑶、程 欣、钱辰畅	张少杰	

序号	导师	硕士生	博士生	博士后
17	王 文	李 俊	毛初阳、关 晴	胡 平 余甜甜
18	文建凡	JIMOH SULIAT ABIKE	HAYAT ULLAH、程姣妮、邓 琪	
19	吴东东	VIOLET MAGOMA ONSONGO、陈勇璇、李彦旭、甘 爽、骆阿云、陆一铮	田航宇、张佳进、张锦锦、庄晓琳、刘 宁、雅 文、涂小龙	王 胜 王 坤
20	宿 兵	张 悦、刘 凯、罗文皓、陈凯敏、周 慧	郑王山、郭永博、孟晓宇、岳 天、周 斌、曾雪芮、张凤云、吴海旭	
21	祁学斌	张伟杰、徐嘉浩		
22	张晓明	赵银辉		
23	杨君兴	吴可心、施 敏	孙 超、潘晓赋、殷艳慧、车星锦、龙 静、刀 微	
24	潘晓赋	朱 龙		
25	杨晓君	姚舜禹、赵 岩	王 洁、高建云	
26	吴 飞	何 林		
27	张国捷	钟文江	张霞芳、戴学勤、左大双	高琼华
28	张亚平	LAMECK AJUMA ODONGO、母昌概、王凤娟、丁梦婷、吴然燃、岑道机、刘利生	沈全宽、戴珊珊、黎武略、颜 晨、许明敏、马 成、张越东、周博闻、汪 轩、伍胤桥、李应菊、刘 行、王 蓉、孙伟杰、李 婕、陶 林、施 贤、秦婉婷、石田培、郭 超、耿伟航	李锦秀
29	高 云	牛文静、曹学娜、宋修成		
30	彭旻晟	SUSAN MUTHONI MAINA、NJUKI RUTH NJERI、姜香香		
31	郑 萍	谢 恒、陶慧玲、董玉萍、孟夏朵	姜方洁、孙春丽、龚道华、李 聪、宁雨琪、金 洁、唐 敏	杨亚娟

研究生优秀论文奖

序号	姓名	获奖等级	期刊	IF	作者排序
1	刘奇	一等奖	Science	51.433	并列第一作者

毕业研究生一览表

序号	姓名	学位	攻读专业	导师姓名	毕业日期
1	蔡望	博士	动物学	Douglas W Yu	2021.01
2	吴云鹤	博士	动物学	Douglas W Yu、车静	2021.01
3	MD MIZANUR RAHMAN	博士	动物学	车静	2021.01
4	付婷婷	博士	遗传学	车静	2021.07
5	高伟	博士	遗传学	车静	2021.01
6	吴甜甜	硕士	生物工程	佴文惠	2021.07
7	ALOIS WAMBUA MWEU	硕士	动物学	蒋学龙	2021.07
8	胡哲畅	硕士	动物学	蒋学龙	2021.07
9	宋文宇	博士	动物学	蒋学龙	2021.01
10	刁显红	硕士	细胞生物学	焦保卫	2021.07
11	ZIA UR RAHMAN	博士	遗传学	孔庆鹏	2021.01
12	郜宗亮	硕士	遗传学	孔庆鹏	2021.07
13	顾康蜀云	硕士	病理学与病理生理学	孔庆鹏	2021.01
14	郭丽云	硕士	药学	孔庆鹏	2021.07
15	郭荣慧	硕士	遗传学	孔庆鹏	2021.01
16	韩一鸣	硕士	生物工程	孔庆鹏	2021.07
17	陶鑫灵	硕士	生物工程	吕雪梅	2021.07
18	茶靖美	硕士	细胞生物学	毛炳宇	2021.07
19	王绘山	博士	细胞生物学	毛炳宇	2021.07

序号	姓名	学位	攻读专业	导师姓名	毕业日期
20	张龙龙	博士	细胞生物学	毛炳宇	2021.01
21	王雪琪	硕士	生物学	彭旻晟	2021.07
22	黄家卉	硕士	生物工程	祁学斌	2021.07
23	唐 杰	硕士	生物工程	盛能印	2021.01
24	易雅星	硕士	神经生物学	盛能印	2021.07
25	陶 乐	硕士	遗传学	施 鹏	2021.07
26	姚晓晴	硕士	药学	施 鹏	2021.07
27	张 涛	博士	遗传学	施 鹏	2021.01
28	朱 磊	博士	遗传学	施 鹏	2021.07
29	张湘泉	硕士	生物工程	王国栋	2021.07
30	陈海涛	博士	遗传学	王 文	2021.01
31	李 冀	硕士	遗传学	王 文	2021.07
32	刘 威	博士	遗传学	王 文	2021.01
33	王 宝	博士	遗传学	王 文	2021.01
34	吕章夏	博士	细胞生物学	文建凡	2021.01
35	ADEOLA OLUWAKEMI AYOOLA	博士	遗传学	吴东东	2021.07
36	王永琴	硕士	遗传学	宿 兵	2021.07
37	袁佳妙	博士	遗传学	宿 兵	2021.07
38	黄新迪	硕士	动物学	杨君兴	2021.07
39	单鹏飞	博士	动物学	杨晓君	2021.07
40	王继山	博士	动物学	杨晓君	2021.07
41	DAVID HERIEL MAUKI	博士	遗传学	张亚平	2021.07
42	李建波	博士	遗传学	张亚平	2021.07
43	刘 露	硕士	生物学	张亚平	2021.01
44	路 恒	硕士	遗传学	张亚平	2021.07
45	施 贤	硕士	生物工程	张亚平、高 云	2021.07
46	李竞争	博士	细胞生物学	郑 萍	2021.01

工作人员名单

（按姓名拼音首字母排序）

学术带头人

Douglas W Yu	车静	蒋学龙	焦保卫	孔庆鹏	刘振
吕雪梅	马占山	毛炳宇	盛能印	施鹏	王国栋
王文	文建凡	吴东东	宿兵	杨君兴	杨晓君
张国捷	张亚平	郑萍			

工作人员

Adeniyi Charles Adeola	Zia Ur Rahman	白慧掀	鲍万冬	蔡星	曾琳
柴静	常云艳	常洲	戴红娟	邓家坤	董锋
董志巍	佴文惠	高建云	高伟	高云	郭彦
郝军军	何水旺	何文彬	和耀喜	侯东敏	胡哲畅
辉洪	季吟秋	金洁琼	李朝翠	李春梅	李功华
李桂梅	李建波	李连伟	李梦成	李梦雯	李权
李欣然	李学燕	李学友	李玉春	李玉宏	李毓劲
廖爱文	刘贵春	刘倩	刘淑伟	刘薇薇	柳延虎
罗杰	罗荣松	罗鑫	吕雪	吕章夏	马怀孝
马鹏程	潘晓赋	彭旻晟	浦绍艳	饶定齐	邵永
沈文菁	盛丹	苏伟婷	孙长杰	谭玉莲	田航宇
涂小龙	王洪娇	王绘山	王慧	王洁	王金焕
王林	王识之	王晓爱	王晓阳	王运梅	韦建福
吴安丽	吴春莹	吴飞	吴汝念	吴云鹤	伍和启
肖富辉	谢国丽	谢海兵	薛敏	岩道	杨春燕
杨晖	杨利琴	杨敏敏	杨钦	杨䖔	殷利夺
尹婷婷	余琴	张宝林	张栋儒	张海林	张树润
张涛	张伟道	张晓明	张源伟	张越	张云春
赵洁	赵丽娜	赵明茹	赵若苹	赵士萍	郑俊娟
周其俊	周通	周鑫	周中银	朱春玲	朱建国
朱玮璟	邹丽				

2021年度报告
ANNUAL REPORT

遗传资源与进化国家重点实验室　中国科学院昆明动物研究所

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