CSCB
中国细胞生物学学会
CHINESE SOCIETY FOR CELL BIOLOGY

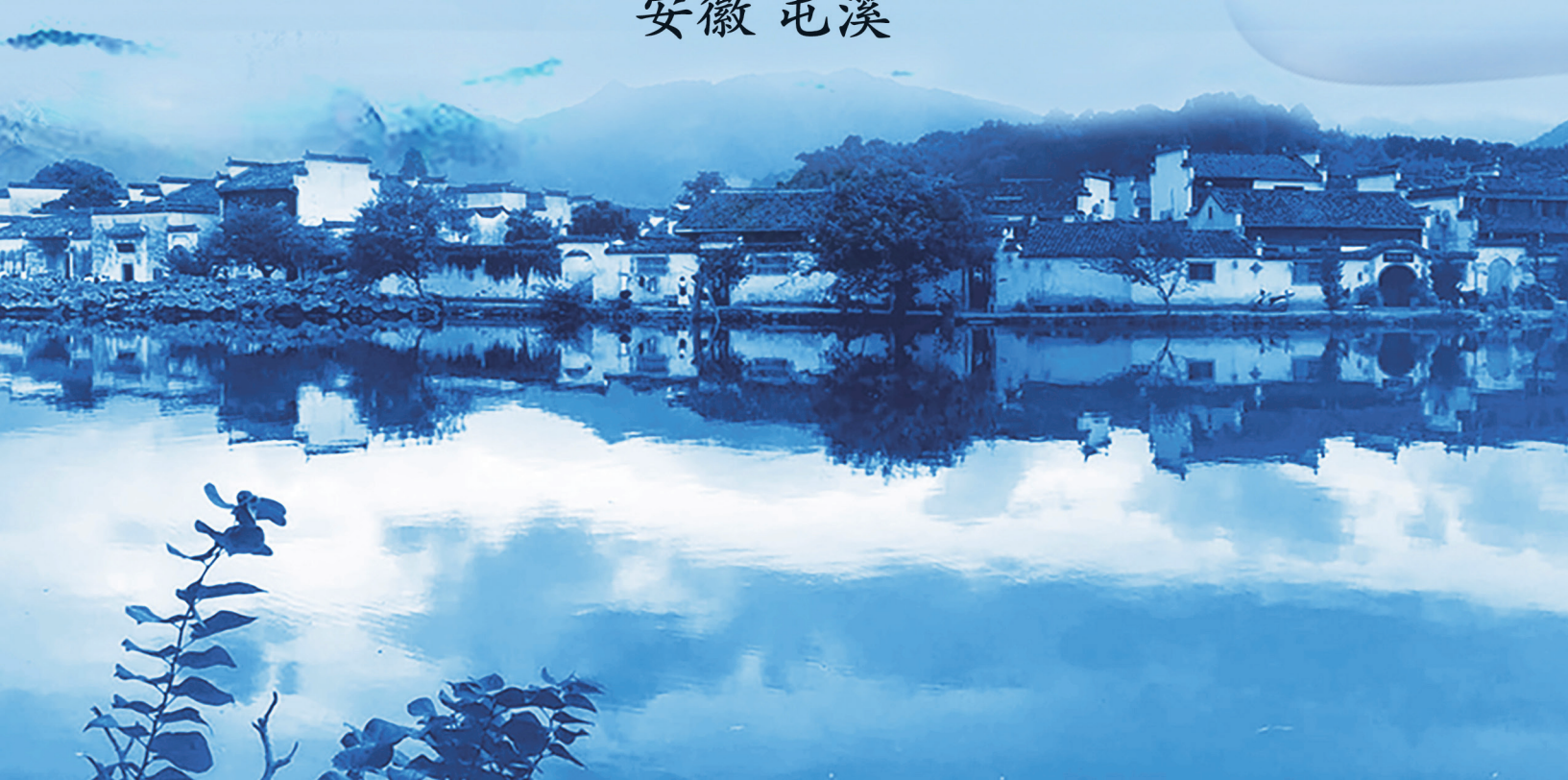
CSBMB
中国生物化学与分子生物学会
The Chinese Society of Biochemistry and Molecular Biology

EPIGENETIC RETREAT
暨第十五次全国基因功能与表观遗传调控学术研讨会

会议手册

2023年10月15-18日

安徽 屯溪



目　录

Epigenetic Retreat 暨第十五次全国基因功能与表观遗传调控学术研讨会

会议（第二轮）通知

（2023 年 10 月 15 日-18 日，安徽屯溪）

由中国细胞生物学学会染色质生物学分会与中国生物化学与分子生物学会基因专业委员会联合主办，“Epigenetic Retreat 暨第十五次全国基因功能与表观遗传调控学术研讨会”定于 2023 年 10 月 15 日-18 日在安徽省黄山市屯溪举行。

本次会议主要包括四个主题：1. 染色质结构与功能；2.表观遗传修饰与基因表达调控；3.RNA 功能与调控；4.表观遗传与人类健康。会议将为基因表达调控与表观遗传学相关研究领域的知名学者与青年科技人员提供相互交流的平台，共享当前相关领域的前沿热点与最新进展，以促进同行间的相互交流与合作。会议规模约为 200 人。诚挚欢迎基因表达调控与表观遗传学相关研究领域的专家、学者和研究生积极参会、踊跃投稿。

会议时间：2023 年 10 月 15 日-18 日（16 日早上开幕；18 日中午离会）
会议地点：安徽省黄山市昱城皇冠假日酒店
主办单位：中国细胞生物学学会染色质生物学分会
　　中国生物化学与分子生物学会基因专业委员会
会务承办：悠选会务展览服务（上海）有限公司

一、组织委员会

主　　席：翁杰敏

副 主 席：蓝斐、陈玲玲、陈勇

成　　员：（按姓氏汉语拼音排序）

（基因分会）曹晓风，陈德桂，陈 佳，陈玲玲，陈 炜，陈 勇，丁春明，杜海宁，何向伟，惠静毅，金勇丰，孔道春，蓝 斐，李海涛，李 晴，李珊珊，林圣彩，刘默芳，刘向宇，逯 杨，孟飞龙，莫 玮，彭小忠，翁杰敏，吴 旻，吴 强，杨建华，姚红杰，余希岚，张强锋，周大旺，周金秋，朱 冰，朱卫国

（染色质分会）蔡 勇、高绍荣、巩志忠、韩俊宏、胡 苹、颉 伟、蓝 斐、李国红、李国亮、李海涛、李 晴、刘 喆、沈 立、沈晓骅、石 磊、汤富酬、王 纲、王 玺、翁杰敏、吴 旻、吴 强、许兴智、臧建业、张 勇、赵 颖、朱 冰、陶永光、杨 娜、汪方炜、吴旭东、林承棋、胡德庆、梁凯威、李 兵、谢 敬、于 明、杨 鹏、宋晓元、俞洋、丁 勇、陆发隆、孙前文、陈 凯、陈柱成、李珊珊、李元元、罗卓娟、王占新、朱卫国

三、会议日程及专题

10 月 15 日	11:00-20:00	参会签到	黄山市 昱城皇冠假日酒店
10 月 16 日	8:50-12:00	开幕式 & 报告	含午餐
	13:00-21:30	报告 & 墙报交流	含晚餐
10 月 17 日	8:50-17:30	报告	含午餐
	18:00-	全员晚宴	
10 月 18 日	8:50-12:00	报告 & 闭幕式	含午餐

四、征文内容及摘要提交

学术交流形式：本次会议以大会报告、青年科学家报告以及墙报的形式进行学术交流，大会报告人由学术委员会推荐邀请，青年科学家报告人由导师推荐或自荐进行遴选，摘要墙报采取自愿报名的方式在报名网页提交，会议将从中遴选出一些作为会议报告。

>>摘要提交要求

1、摘要提交采用邮件提交至 chromatin@cscb.org.cn，标题注明 Epigenetic Retreat

2、摘要内容需和会议的交流内容一致。请根据摘要内容选择合适的专题。摘要将根据所属专题进行编号。

3、摘要的文件格式是：WORD。

4、摘要字数需控制在一页之内（约 350 字）。

5、表格图片图例等不应出现在摘要中。

6、摘要提交截止日期：9 月 15 日

>>墙报提交要求

1、墙报提交采用在线提交的方式，注册并登录后方可提交墙报。

2、请自制墙报带至会场，尺寸要求：高 120 cm，宽 90 cm；墙报语言为中文或英文。

3、会议期间，学会将统一展示墙报并开展评选。

4、墙报提交截止日期：9 月 20 日

五、会议费用

（一）注册费标准（包括会议费、资料费、会议期间就餐费等）　　自理：住宿费及交通费

参会人员类别	8 月 1 日-9 月 30 日	现场注册 缴费
正式会员	1900 元	2200 元
非正式会员	2100 元	2400 元
学生会员	1400 元	1700 元
非学生会员	1500 元	1800 元

1. 会议报名方式：https://www.cscb.org.cn/meeting/EpigeneticRetreat2023/（正在逐步完善中）

或微信扫描下方二维码注册，填写参会表单。（方式二选一，请勿重复注册）

扫描二维码

因场地限制，注册名额有限，额满即止。
报名注册相关问题可邮件 reservation@youshr.com，可索取团队报名表

2. 缴费方式：在线缴费（推荐）和银行汇款。
（1）支付宝/微信缴费 （推荐）：https://www.cscb.org.cn/payment_conference/116.html
（2）银行转账：(汇款时需要备注姓名，单位和参加会议的名称)
户　名：中国细胞生物学学会
账　号：03392400040009251
开户行：农行徐汇区枫林支行

注意事项：
1) 请缴费后将参会人名、汇款凭证、开票信息发送邮件至财务邮箱 treasure@cscb.org.cn，以便核对查询。
2) 电子发票：在核对缴款完成后的 15 个工作日内电子发票将直接发到邮箱。
3) 退费说明：缴费后不能参会者,于 2023 年 8 月 31 日（含）之前申请退费的,将扣除 200 元后退还余款；2023 年 9 月 1 日之后将不再退款。

六、会议住宿交通

大会地址：安徽省黄山市昱城皇冠假日酒店（黄山市屯溪区徽州大道 1 号）

住宿及房型　　（房费前台自付）

昱城皇冠假日酒店	双床房　480 元/间晚	高级房 含早
	大床房　480 元/间晚	高级房 含早
黄山市屯溪区徽州大道 1 号		

***请注册时一并提交住宿需求，会务组会进行预留，无须自行联系酒店预定，住宿人自行前往酒店办理入住登记及付费开票。**

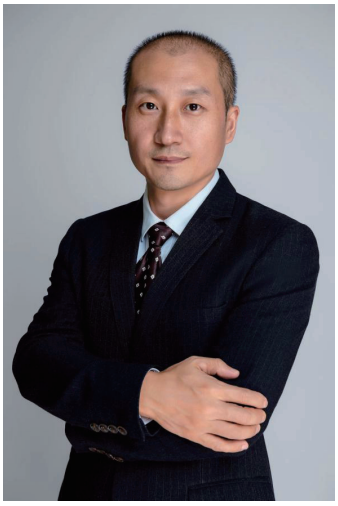
Epigenetic Retreat 暨第十五次全国基因功能与表观遗传调控学术研讨会组委会
中国细胞生物学学会染色质生物学分会
中国生物化学与分子生物学会基因专业委员会
二零二三年八月

⊙特邀嘉宾（按姓氏首字母排序）

石雨江 YUJIANG GENO SHI

复旦大学特聘教授
复旦大学生物医学研究院实验室主任
复旦大学附属中山医院双聘教授
国际知名表观遗传学家

创建复旦大学生物医学研究院表观遗传与衰老研究中心，主要从事表观遗传学前沿研究，发现了第一个组蛋白去甲基化酶 LSD1/KDM1A，开创并奠定了组蛋白去甲基化的生物化学与生物物理学基础，并对其生物学功能的阐明作出了关键性的贡献。目前课题组的主要研究方向包括：1）表观遗传学的基础研究，包括发现新型表观遗传标记，探索新型表观遗传酶及其功能研究；2）糖尿病、肥胖与肿瘤等疾病的表观遗传机理研究；3）衰老与长寿的表型组学及表观遗传学机理研究；4）抗衰计算生物学及新型的长寿 & 衰老模式生物创建与研究，在 Nature、Cell 等期刊发表研究论文 60 余篇。



徐彦辉

复旦大学附属肿瘤医院研究员
生物医学研究院兼职教授
科技部重点研发计划首席科学家

先后获得国家杰出青年科学基金、长江学者特聘教授、国家万人计划领军人才等人才项目支持。长期从事基因表达调控的研究，面向分子生物学国际科学前沿问题，揭示了转录起始多个复杂过程的分子机制，回答了“基因转录如何启动”这一生命领域根本性科学问题，被认为是分子生物学领域的重大突破性进展。目前课题组的主要研究方向主要包括：1，转录起始的机制研究，希望综合利用结构生物学、生物化学、生物物理等方法，系统的阐释转录起始这一极其复杂且重要的生物学过程；2，构建蛋白质抗体库作为独特的研究工具，开发同时靶向多种蛋白质的测序新方法，在单细胞、发育、病理等层面解析生物大分子在细胞层面的复杂相互作用和功能，所取得的发现不仅可以指导深入的分子生物学研究，也可应用在基础研究和临床诊治等众多方面。作为通讯作者在 Science（5）、Nature（2）、Cell 等期刊上发表了 40 多篇论文，研究成果获得教育部高等学校科学研究优秀成果奖自然科学一等奖。

中国细胞生物学学会科研诚信管理暂行办法

第一章　总则

第一条 为贯彻落实中共中央办公厅国务院办公厅《关于进一步加强科研诚信建设的若干意见》（厅字〔2018〕23 号），监督引导广大细胞科技工作者自觉遵守《科技工作者道德行为自律规范》（中国科协九届常务四次会议审议通过），加强学会科研诚信建设，营造学会风清气正的创新环境和学术氛围，将科研诚信工作纳入常态化管理，特制定本管理办法。

第二条 本办法适用于中国细胞生物学学会会员，学会下设分支机构，以及所有参与学会组织的学术活动、申请学会奖项或资助项目的单位或个人。

第三条 伦理工作委员会全面负责学会科研伦理、诚信管理工作，切实发挥审议、评定、受理、调查、监督、咨询等作用。

第二章　科研诚信规范

第四条 遵守中华人民共和国公民道德准则；

遵守诚实守信原则，在数据采集分析、公布科研成果等方面坚持实事求是，不得故意挑选、剔除实验数据；做好实验记录和原始实验数据的保存工作；

遵守公平原则，对竞争者和合作者做出的贡献给予合理认同和评价；

尊重知识产权，保障对研究成果做出实质性贡献的专业人员的署名权；

遵守声明与回避原则，严谨自律，对不熟悉的专业问题谨言慎行，对可能发生利益冲突时有义务声明，必要时应当回避。

第五条 在申请学会项目、奖项中，应当保证所有申请材料的真实、准确，并明确区分自己和他人的工作对研究成果的贡献。

第六条 在学术研究中应检索相关文献或了解相关研究成果，在发表论文或以其他形式科研报告中引用他人观点、成果时应在文后如实列出。不应当以盲目增加文献被引率为目的，进行不适当的自我引用。

第七条 研究成果应当首先经过同行评议的程序发表，或在科学共同体内进行其他形式的交流，

不得一稿多投。

第八条　在参与学会各种推荐、评审活动中，应客观、公正地进行评议，尊重被评议人的尊严和学术自主性，尊重不同学术观点，不得收受被评议人及其利益相关方赠予的有碍公正评议的礼物或其他馈赠。

第九条　在参加学会学术交流活动中，投稿论文摘要一旦被会议组织者录用，论文作者或其代表应根据会议要求，到会参加交流。

第十条　尊重研究对象 (包括人类和非人类研究对象)，自觉遵守科研伦理规范，开展研究前要按有关规定获得单位伦理委员会的审查批准。对于涉及克隆、转基因、基因组编辑等具有不确定性的新技术研究，应当遵守国家相关法律规定以及国际公认的生命伦理原则及规范。

第三章　科研失信行为处理

第十一条　科研失信行为，是指在科学研究及相关活动中发生的违反科学研究行为准则与规范的行为，包括：

（一）抄袭、剽窃、侵占他人研究成果或项目申请书；

（二）编造研究过程，伪造、篡改研究数据、图表、结论、检测报告或用户使用报告；

（三）买卖、代写论文或项目申请书，虚构同行评议专家及评议意见；

（四）以故意提供虚假信息等弄虚作假的方式或采取贿赂、利益交换等不正当手段获得科研活动审批，获取科技计划项目（专项、基金等）、科研经费、奖励、荣誉、职务职称等；

（五）违反科研伦理规范；

（六）违反奖励、专利等研究成果署名及论文发表规范；

（七）其他科研失信行为。

第十二条　学会伦理工作委员会设立科研失信行为投诉举报邮箱，受理科研失信行为的投诉举报，进行调查并给出处理建议。

第十三条　科研失信人员，一经调查证实，如系会员，取消会员资格。如有在学会任职， 经学会常务理事会议审议，一并取消。因失信行为获得奖励、荣誉的，将取消学会授予荣誉或推荐资格。

第十四条　学会伦理工作委员会负责建立科研失信行为监管档案，将涉及科研失信行为的个人

或单位记录在案，并可依据情节严重程度向学会会员通报或学术委员会向外界通报批评。根据需要提供查询或向相关国家监督管理部门移交或报备。

第十五条　学会会员在失信调查和认定阶段具有申辩权。对已认定的失信行为或惩戒处理有异议的，可向学会伦理工作委员会提出申诉。

第十六条　举报人应据实举报。若涉嫌诬告，经伦理工作委员会认定，依据情节严重程度取消其 2-5 年内学会会员资格以及学会任职，禁止参与任何学会举办的学术会议和活动。

第四章　附则

第十七条　本办法经学会常务理事会通过后执行，由学会伦理工作委员会负责解释。第十八条　本办法自发布之日起实施。

⊙摘要集

Active DNA demethylation promotes cell fate specification and the DNA damage response

Wei Wu

Neurons harbor high levels of single-strand DNA breaks (SSBs) that are targeted to neuronal enhancers, but the source of this endogenous damage remains unclear. Using two systems of postmitotic lineage specification—induced pluripotent stem cell–derived neurons and transdifferentiated macrophages— we show that thymidine DNA glycosylase (TDG)–driven excision of methylcytosines oxidized with ten-eleven translocation enzymes (TET) is a source of SSBs. Although macrophage differentiation favors short-patch base excision repair to fill in single-nucleotide gaps, neurons also frequently use the long patch subpathway. Disrupting this gap-filling process using anti-neoplastic cytosine analogs triggers a DNA damage response and neuronal cell death, which is dependent on TDG. Thus, TET-mediated active DNA demethylation promotes endogenous DNA damage, a process that normally safeguards cell identity but can also provoke neurotoxicity after anticancer treatments.

Outward-oriented sites within clustered CTCF boundaries are key for intraTAD chromatin interactions and gene regulation

Qiang Wu

Center for Comparative Biomedicine, Institute of Systems Biomedicine, Shanghai Jiao Tong University, Shanghai 200240, China

E-mail: qiangwu@sjtu.edu.cn

CTCF plays an important role in adjusting insulation at TAD boundaries, where clustered CBS (CTCF-binding site) elements are often arranged in a somewhat tandem array with a complex divergent or convergent orientation. Here using cPcdh and HOXD loci as a paradigm, we look into the clustered CTCF TAD boundaries and find that, counterintuitively, outward-oriented CBS elements are crucial for inward enhancer-promoter interactions as well as for gene regulation. Specifically, by combinatorial deletions of a series of putative enhancer elements in vivo or CBS elements in vitro, in conjunction

with chromosome conformation capture and RNA-seq analyses, we show that deletions of outward-oriented CBS elements weaken the strength of intraTAD promoter-enhancer interactions and enhancer activation of target genes. Our data highlight the crucial role of outward-oriented CBS elements within the clustered CTCF TAD boundaries and have interesting implications on the organization principles of clustered CTCF sites within TAD boundaries.

Keywords: CBS orientation, cohesin, CTCF, enhancer, gene regulation, HOXD, Protocadherin, TAD boundary

Mechanistic Insights into Chromosome Folding by Cohesin

Zhubing Shi

School of Life Sciences, Westlake University; Westlake Laboratory of Life Sciences and Biomedicine, Hangzhou, Zhejiang 310024

In the interphase nuclei of mammalian cells, chromosomes are folded into topologically associating domains (TADs) and loops at the sub-megabase scale, thereby regulating various essential cellular processes, including gene expression, DNA recombination and DNA damage repair. The structure maintenance of chromosome (SMC) complex cohesin and the architectural protein CCCTC-binding factor (CTCF) play a fundamental role in the organization of TADs and loops. Using single-molecule imaging, we demonstrate that cohesin, typically functioning as a dimer, compacts DNA by bidirectional loop extrusion at an average rate of 0.5 kilobases per second, which depends on NIPBL and ATP hydrolysis. Biochemical and structural analysis showed that DNA is trapped by cohesin and NIPBL in the folded state, and NIPBL together with trapped DNA promotes ATP-mediated engagement of cohesin's ATPase head domains, thereby stimulating its ATPase activity. CTCF acts as a polar barrier of cohesin, which contributes to the formation of TAD boundaries. CTCF blocks cohesin-mediated DNA compaction when its N terminus encounters cohesin, while it accelerates cohesin translocation when its C terminus faces cohesin. The YDF motif and the basic linker ahead of the zinc fingers in CTCF are vital for cohesin arrest. Cohesin can traverse nucleosomes but not dCas9 and dCas12a ribonucleoproteins during DNA compaction. Like CTCF, dCas9 and dCas12a ribonucleoproteins are also polar roadblocks to cohesin. They arrest cohesin only when the proto-spacer adjacent motif (PAM) is oriented towards translocated cohesin. Furthermore, R-loops, which can bind to cohesin and CTCF, attenuate DNA compaction by cohesin, suggesting a barrier role of R-loops in hindering cohesin translocation. Collectively, these findings provide mechanistic insights into how cohesin, in concert with CTCF and R-loops, shape interphase chromosomes.

CRISPR tools for studying chromatin organization in living cells

Haifeng Wang

School of Life Sciences, Tsinghua University

The CRISPR techniques provide powerful toolkits for us to probe chromatin structure, function and dynamics. We developed the CRISPR-Genome Organization (CRISPR-GO) platform for programmable control of spatial genome organization, and the CRISPR live-cell fluorescence in situ hybridization (LiveFISH) platform for DNA and RNA live-cell imaging.

The CRISPR LiveFISH provides a method using synthesized fluorescent oligonucleotide probes to visualize the real-time dynamics of DNA and RNA in diverse cell types, including primary patient cells. In addition, LiveFISH tracks the real-time movement of DNA double-strand breaks induced by gene editing and endogenous chromosome translocations. Finally, combining Cas9 and Cas13 systems, LiveFISH allows for simultaneous visualization of genomic DNA and RNA transcripts in living cells. Thus, the CRISPR LiveFISH enables real-time live imaging of DNA and RNA dynamics during genome editing, transcription, and rearrangements in single cells. The CRISPR-GO system allows one to efficiently manipulate the spatial positioning of desired genomic locus relative to specific nuclear compartments in the nucleus, including the nuclear periphery, Cajal bodies, and promyelocytic leukemia (PML) bodies. Genomic positioning via CRISPR-GO is inducible and reversible, and can be programmed to target different genomic sequences. Targeting some genomic loci to the nuclear periphery or to Cajal bodies repressed gene expression.

Centromere Weakening Drives Efficient Chromosome Fusion in S. pombe

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Each eukaryotic species has a stable karyotype, which is faithfully maintained through generations. Recent breakthrough in synthetic biology has achieved drastic chromosome fusions in multiple organisms, suggesting that species can tolerate massive changes in karyotype. How chromosome fusion occurs under natural conditions and how it affects species evolution remain to be explored.

Here, we report the finding of a novel function of centromere in maintaining karyotype stability in

the fission yeast S. pombe. Genetically compromised centromere(s), via reducing the level of CENP-A/Cnp1 incorporation, efficiently induces telomere-telomere fusion, resulting in a stable new karyotype--reducing the haploid chromosome number from three to two. Consequentially, the need in the number of functional centromeres reduces from three to two, compensating for the reduction in CENP-A incorporation. Analysis of the chromosome fusion sites showed that telomere-telomere fusions are carried out by homologous recombination at the sub-telomeric homologous modules. Surprisingly, the patterns of chromosome fusion in cells within a single colony may vary, indicating that chromosome fusion occurs independently and efficiently the daughter cells derived from the same parental cell.

Together, these results support a model that the stability of chromosomal architectures is directly affected by centromere structure/function, and that a possible functional crosstalk exists between centromere and telomere.

The nucleosome-independent role of histones

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Histones are the most abundant nuclear proteins and act as the constitutive components of chromatin. The majority of previous studies have focused on their nucleosome-dependent functions. Whether nuclear histones have nucleosome-independent roles remains elusive. Here, we reveal a nucleosome-independent function of H2A-H2B. H2A-H2B interacts with a nuclear envelope protein Sad1 in fission yeast. Although Sad1 binds H2A-H2B in a manner structurally similar to the canonical H2A-H2B chaperones, the Sad1-histone interaction does not directly affect nucleosome assembly and H2A.Z distribution. Instead, H2A-H2B functions as a modulator for Sad1 to enhance Sad1's functionality. Histone binding boosts the interaction between Sad1 and HDACs, and promotes the LLPS ability of Sad1. Our results and some recent studies highlight the intriguing notion that the H2A-H2B dimer could have broader nucleosome-independent functions than previously thought.

Functions of protein phosphatases in transcriptional control

Fei Chen

Eukaryotic transcription requires orchestrated phosphorylation and dephosphorylation of the C-terminal repeat domain (CTD) of RPB1, the largest subunit of RNA polymerase II (Pol II), and several key transcription regulators including DSIF. In mammals, phosphorylation of 52 heptad repeats of Pol II CTD at Ser5 and Ser2 have been well known regulations of transcription initiation and elongation, respectively. Unlike the extensive studies of phosphorylation, understanding the dephosphorylation of Pol II and other transcription regulators is limited. PP2A and PP1 are the most abundant phosphatases in cells. We previous reported the roles of PP2A, within the context of INTAC, in dephosphorylating Pol II and DSIF and transcriptional control. In this talk, I will present our recent progress in elucidating functions of PP1 in transcription.

LINE-1 5'UTRs function as enhancers to regulate naïve pluripotency

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LINE-1s are the major clade of retrotransposons with autonomous retrotransposition activity. Despite the potential genotoxicity, LINE-1s are highly activated in early embryos. Here we show that a subset of young LINE-1s, L1Md_Ts, are marked by the RNA polymerase II elongation factor ELL3, and function as enhancers in mouse ESCs. ELL3 depletion dislodges the DNA hydroxymethylases TET1 and the corepressor SIN3A from L1Md_Ts, but increases the enrichment of the Bromodomain protein BRD4, leading to loss of 5hmC, gain of H3K27ac, and up-regulation of the L1Md_T nearby genes. Specifically, ELL3 occupies and represses the L1Md_T-based enhancer located within Akt3, which encodes a key regulator of AKT pathway. ELL3 is required for proper ERK activation and efficient shutdown of naïve pluripotency through inhibiting Akt3 during naïve-primed transition. Our study reveals the enhancer function of subset of young LINE-1s controlled by ELL3 in

transcription regulation and mouse early embryo development.

Key words: ELL3, LINE-1, enhancer, Akt3, early development

H3.3 Ser31 phosphorylation consolidates heterochromatin for retrotransposon silencing and X chromosome inactivation

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Heterochromatin is crucial for silencing repetitive elements and restraining gene expression during development. Dysfunctions of heterochromatic state closely associate with the pathogenesis of

various human diseases. Increasing evidences show that the histone variant H3.3 plays key important roles in heterochromatin formation and retrotransposon silencing. However, the molecular mechanism underlying H3.3-primed heterochromatin formation remains elusive. Here, we demonstrate that the phosphorylation of H3.3 unique residue Ser31, which is absent from canonical histones H3.1/H3.2, is essential to the instatement of H3K9me2/3-associated heterochromatin during both retrotransposon silencing and X chromosome inactivation. Mechanistically, Ser31-phosphorylated H3.3 facilitates H3.3K27me3 recognition by the Polycomb protein CBX2/7, which further recruits KAP1-SetDB1, enabling the formation of H3K9me2/3-associated heterochromatin across the genome. Expression of the nonphosphorylatable H3.3 (H3.3S31A) or the CBX7 mutant that is defective in H3.3 pSer31 recognition (CBX7R22A) leads to global reduction of H3K9me3, along with the derepression of multiple types of retrotransposons. Importantly, these mutants also lead to defective assembly of H3K9me2/3 heterochromatin at the inactivated X chromosome in differentiated female mouse cells, implying the significance of H3.3 Ser31 phosphorylation in the transition from facultative to constitutive heterochromatin during X chromosome inactivation. Taken together, our results reveal a mechanism of heterochromatin consolidation regulated by the histone variant H3.3 and its phosphorylation.

RNA poly(A) 尾表观遗传调控

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Poly(A) 尾是在真核生物中绝大部分 mRNA 的 3’末端通过非模板来源方式添加的一段序列。然而受限于检测技术，poly(A) 尾信息在常规转录组测序的时候都被丢弃了，其编码的调控信息所知甚少。我们建立了全转录组 poly(A) 尾准确测序新方法，意外发现 poly(A) 尾内部有着广泛的 U、C 和 G 等非 A 碱基修饰。Poly(A) 尾中非 A 碱基修饰的种类、数量和位置以及 poly(A) 尾的长度提供了巨量的信息编码空间，提示 poly(A) 尾可能编码了重要的 RNA 表观遗传调控信息。利用我们开发的新方法，我们揭示了人类早期胚胎中 mRNA poly(A) 尾巴介导的母源 mRNA 重塑，并证明其对人类胚胎第一次细胞分裂至关重要。

关键词：（poly(A) 尾，非 A 碱基修饰，RNA 表观调控）

Mechanism of the allosteric activation of deacetylase SIRT1

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Increasing the activity of the NAD-dependent mammalian deacetylase sirtuin 1 (SIRT1) has proved to be an effective therapeutic strategy for conditions such as aging, metabolic disorders, and inflammation. Many sirtuin-activating compounds (STACs) have been reported for SIRT1, such as the natural STAC resveratrol and the synthetic STACs SRT1720 and ac1. However, whether the mechanism of STAC-mediated SIRT1 activation involves direct interactions between STACs and the substrate, or whether this interaction cause SIRT1 to undergo allosteric activation remains controversial. Here, we used all-atom molecular dynamics (AAMD), steered molecular dynamics (SMD), and replica exchange molecular dynamics (REMD) simulations to explore the conformational space involved in the allosteric regulations of SIRT1 concerning various substrates and STACs. We report on the global dynamic and thermodynamic landscapes of SIRT1 allosteric activation, which were consistent with the experimental data. We found that there are more than one mechanism governing the allosteric activation of SIRT1, depending on the interacting mode between STACs and the substrates. Based on the two criteria for the high efficiency activation mechanism of SIRT1 revealed by our simulations and experimental data, a high-throughput molecular docking strategy was developed and several compounds activating the SIRT1-catalyzed deacetylation were identified. In vitro and in cell activities of these newfound STACs were examined and the possible regulating mechanisms were analyzed. Recently, we solved the structure of SIRT1 in complex with its negative regulator, which provide more insights into the regulatory mechanism of SIRT1 activity. In summary, our results provide sound evidence regarding the allosteric activation of SIRT1 and should facilitate the development of authentic STACs of SIRT1 for the benefit of human health.

Evolutionarily conserved function of polycomb in suppressing mobile genetic elements through licensing Hisone expression

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As the most abundant elements in the genome, retrotransposons have thrived in almost all animals throughout evolution and comprise more than 37% of the human genome. The mobilizations of retrotransposons cause DNA breaks, gene mutations and genomic instability, thereby being largely considered detrimental. Remarkably, despite the correlation between retrotransposon activation and disease (sterility, cancer and other pathological conditions) being identified, little is known about how the mobilizations of retrotransposons are controlled during somatic development in host. Here, we determined a highly conserved mechanism that prevent transposon activation and mobilization. By tracking transposition events, we identified one of Polycomb proteins, playing a pivotal role in silencing transposon mobility during both Drosophila and mouse development. Polycomb was characterized as a major hallmark that specifically binds to the DNA sequences of histone gene cluster and initiate histone expression. Upon polycomb depletion, the decreased Histone production will subsequently cause less deposition of both H3K9me3 and H3K36me2 in transposon sequences, resulting in their activation and mobilization. Without the protection of Polycomb, uncontrolled transposon will cause DNA breaks and defects in both fly hindgut and mouse liver, leading to shorter life span and embryonic lethality of Drosophila and mouse, respectively. Our finding highlights that with the endless arms race between hosts and transposons happening during evolution, the key factors will also be evolved to suppress transposon activity during somatic development.

甲藻表观遗传学调控规律初探

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甲藻，是一类具有双鞭毛和独特细胞核（甲藻核，dinokaryon）的单细胞真核生物。相较于其他真核生物，甲藻具有巨大的基因组（可达 200G），染色体在整个细胞周期都处于高度浓缩螺旋状态（胆固醇液晶态）。此外，甲藻染色体中缺乏典型真核生物核小体的基本组分 - 组蛋白，分析表明，甲藻组蛋白调控功能在长期进化过程中逐渐退化，被其他表观遗传调控机制所取代。本报告将简要介绍我们前期的研究发现：甲藻中复杂多样的核酸（DNA/RNA）修饰将部分弥补组蛋白的功能缺失，在染色质功能调节和基因表达调控中起着关键作用，从而形成一种新颖的表观遗传学调控网络。

Multiple functions of one long noncoding RNA

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Our previous study showed that Synage, a long noncoding RNA (lncRNA), is highly expressed in the cytoplasm of cerebellar neurons and is involved in the regulation of synaptic stability in the cerebellum. However, the role of lncRNA Synage in Purkinje neurons and granule neurons and its molecular mechanism remain unclear. Here we used Cre-loxP system to generate Synage conditional knockout mice in cerebellar Purkinje neurons or granule neurons. Both conditional knockout mice resulted in cerebellar atrophy, loss of Purkinje neurons and granule neurons, decreased synaptic stability of cerebellar cortex, and motor function injury. We are currently dissecting the underlying mechanism of the multiple functions of Synage in cerebellar neurons and synapsis. The study of lncRNA Synage in cerebellar Purkinje neurons and granule neurons enriches our understanding of the function and mechanism of lncRNAs in cerebellum and contributes to understanding the important role of lncRNAs in cerebellum.

Lysine 2-hydroxyisobutyrylation of NAT10 promotes cancer metastasis in an ac4C-dependent manner

Bin Li

Posttranslational modifications add tremendous complexity to proteomes, however, gaps remain in knowledge regarding the function and regulatory mechanism of newly discovered lysine acylation modifications. A panel of non-histone lysine acylation patterns was compared in metastasis models and clinical samples, and 2-hydroxyisobutyrylation (Khib) was focused on due to its significant upregulation in cancer metastases. By the integration of systemic Khib proteome profiling in 20 paired primary esophageal tumors and metastatic tumors with CRISPR/Cas9 functional screening, lysine 823 in NAT10 (NAT10 K823) was identified as a substrate for Khib and found to functionally contribute to metastasis. Mechanistically, NAT10 is posttranslationally modified by Khib and that this PTM increases NAT10's stability. NAT10 promotes metastasis by increasing NOTCH3 mRNA stability in an N4-acetylcytidine (ac4C)-dependent manner. Furthermore, the lead compound #7586-3507 inhibited the function of NAT10 and showed efficacy in tumor models in vivo at low concentration. Together, our findings bridge newly identified lysine acylation modifications with RNA modifications, which provides novel insights into epigenetic regulation in human cancer. Pharmacological inhibition of NAT10 K823 Khib modification constitutes a potential antimetastasis strategy.

Unannotated microprotein EMBOW regulates the interactome and chromatin and mitotic functions of WDR5

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The conserved WD40-repeat protein WDR5 interacts with multiple proteins both inside and outside the nucleus. However, it is currently unclear whether, and how, the distribution of WDR5 between complexes is regulated. Here, we show that an unannotated microprotein EMBOW dually encoded in the human SCRIB gene interacts with WDR5 and regulates its binding to multiple interaction partners, including KMT2A and KIF2A. EMBOW is cell-cycle regulated, with two expression maxima at late G1 phase and G2/M phase. Loss of EMBOW decreases WDR5 interaction with KIF2A, aberrantly shortens the spindle length, prolongs G2/M phase and delays cell proliferation. On the other hand, loss of EMBOW increases WDR5 interaction with KMT2A, leading to WDR5 binding to off-target genes, erroneously increasing H3K4me3 levels and activating transcription of these genes. Together, these results implicate EMBOW as a regulator of WDR5 that regulates its interactions and prevents its off-target binding in multiple contexts.

Key words: WDR5, chromatin, spindle assembly, unannotated microprotein

m6A regulates pericentric heterochromatin

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Constitutive heterochromatin, formed in compact and transcriptionally inert chromatin state, comprises the significant portions of eukaryotic genomes and plays vital roles in chromosome dynamics and genome integrity. The majority of constitutive heterochromatin is concentrated at pericentromeric and telomeric regions. Gene-poor and repeat-rich pericentromeric heterochromatin (PCH) is not evolutionally conserved in different species, which is also greatly variable among individuals. In mice, it consists of tandem noncoding major satellite repeats (MSR). Aberrant expression of PCH provokes genome instability and defective heterochromatin establishment in mouse early embryos. However, the regulation of these highly repetitive sequences remains poorly understood. Our previous data showed that RNA m6A reader YTHDC1 silences retrotransposons especially for IAP, ERVK and

LINE1 elements. Mechanistically, m6A modification of chromatin-associated transposable elements RNAs targets YTHDC1 to chromatin, followed by the recruitment of SETDB1-mediated H3K9me3 on retrotransposons. The depletion of YTHDC1 in mouse embryonic stem cells triggers ectopic expression of these repressed retrotransposons and initiates the transition to 2cell-like state. Recently, we find that the removal of YTHDC1 also activates the expression of major satellite repeats, which suggests that RNA m6A modification may also participate in the modulation of pericentromeric heterochromatin.

Reorganization of chromatin during fertilization and blastocyst formation in mice

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Chromatin remodeling is essential for epigenome reprogramming after fertilization, as well as the cell fate determination in early embryo. However, the underlying mechanisms of chromatin remodeling remain to be explored. Here, we investigated the dynamic changes in nucleosome occupancy and positioning in pronucleus-stage zygotes using ultra low-input MNase-seq. We observed distinct features of inheritance and reconstruction of nucleosome position in both paternal and maternal genomes and predicted potential pioneer functions in ZGA based on the NDR establishment dynamics of their binding sites. Interestingly, we found establishment of nucleosome profiles around the CTCF motif sites shortly after fertilization, we therefore utilized CUT&RUN technology to investigate CTCF occupancy in mouse pre-implantation development. Our found CTCF begins binding to the genome prior to zygotic genome activation (ZGA), with a preference for CTCF anchored chromatin loops. Although the majority of CTCF occupancy is consistently maintained, a specific set of binding sites, which enriched in the mouse-specific short-interspersed element (SINE) family B2, are restricted to the cleavage stages. Our analysis explored an ADNP-dependent restriction of CTCF-binding during cell differentiation in pre-implantation embryos, which provided new insights into the regulation of transcription factor (TF) binding kinetics on exapted sites arising from transposable element (TE) expansions in early embryos.

Fluorogenic CRISPR for genomic DNA imaging in living human cells

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人类基因组 DNA 和染色体的功能与其细胞核内的定位相关。实时成像基因组 DNA 的动态和定位有助于时空研究染色体生物学功能，解析相关疾病的发生机制。

基于 CRISPR(Clustered Regularly Interspaced Short Palindromic Repeats)/dCas9 的 DNA 成像系统是最近广为使用的活细胞 DNA 标记工具。该工具利用 dCas9- 荧光蛋白作为探针，通过 sgRNA 标记和成像染色体和基因组 DNA。但是，dCas9- 荧光蛋白在不结合 DNA 时也会产生荧光，导致 CRISPR/dCas9 示踪技术产生高背景噪音问题，不利于实际应用 DNA 追踪。

为了解决 CRISPR/dCas9 示踪技术的背景噪音问题，我们构建了低背景、荧光响应的 CRISPR（fluorogenic CRISPR, fCRISPR）成像体系。在 fCRISPR 体系，我们将“荧光蛋白”改造成“荧光响应蛋白”。fCRISPR 只有在结合到 DNA 靶标时，“荧光响应蛋白”才会发出荧光，在未结合到靶标时“荧光响应蛋白”会被细胞蛋白酶体降解从而不发荧光。因此 fCRISPR 能够低背景、高信噪比和高灵敏地追踪活细胞中基因组 DNA 位点。

基于 fCRISPR 成像体系，我们追踪到各类人源活细胞的染色体，以及不同低拷贝的基因组 DNA 位点。此外，fCRISPR 应用于多条染色体的正交成像，实时追踪染色体动力学，监测和对比癌变细胞端粒长度。最后，我们深入研究了染色体双链断裂（DSBs）及修复的过程，观察到染色体的重复切割与修复、同源重组修复等事件，时空研究了染色体 DNA 损伤及其修复后的生命活动。

综上所述，fCRISPR 为活细胞基因组 DNA 和染色体动态成像提供了一个高信噪比、高灵敏的成像工具。

关键词：DNA 标记；荧光响应蛋白；CRISPR-Cas9；活细胞染色体成像

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Systematic characterization of the CHD4 enhancers reveals cooperative functions among the homotypic ZNF410 clustered motifs

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Transcription factors often regulate numerous target genes. However, ZNF410 controls only a single gene CHD4 in human erythroid cells by its highly restricted chromatin occupancy to the CHD4 locus via two clusters of ZNF410 binding motifs. Here, we uncover that ZNF410 controls chromatin accessibility and activity of the two CHD4 enhancer regions. Combining CRISPR/Cas9 genomic deletion with CRISPRi approaches, we demonstrate that both enhancer regions contribute to CHD4 gene expression in an additive manner. Mutations of the di-adenine nucleotides within the ZNF410 binding motif fully disrupt ZNF410-DNA interaction. In vitro luciferase assays, ChIP-seq and ATAC-seq studies reveal that the homotypic clustered motifs are recognized by ZNF410 in a collaborative fashion. Together, our findings expose a complex functional hierarchy of motifs, where clustered motifs bound by the same transcription factor cooperate to fine-tune the expression of target gene.

JMJD2/KDM4 Is the Epigenetic Stabilizer of the Phase Separation at Enhancer-Promoter Loops for Pluripotency and Totipotency

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Enhancer-promoter (E-P) loops regulate gene transcription for cell fate determination. The E-P loops are modulated by phase separation, although the regulatory mechanisms remain elusive. We developed a chromatin structure-based proteomics approach, LoopID, to identify the proteins of phase separation at specific E-P loop, which we termed as looposome. The JMJD2/KDM4 family of histone demethylases can stabilize the looposome dependent on the form of biomolecular condensates. Additionally, JMJD2/KDM4 condensates induce E-P loops of totipotency and enhance the totipotent-like molecular features of 2-cell-like cells. Furthermore, we developed a system to engineer totipotency-specific E-P loops by establishing JMJD2/KDM4 condensates at the specific genomic loci, which further promote the transition from pluri-to-totipotent-like stem cells. Our findings provide insights into the mechanisms underlying the regulation of chromatin structures through the non-canonical role of biomolecular condensates of histone demethylase, and present a novel strategy for regulating cell fate determinations.

Key words: Enhancer-Promoter loop, phase separation, JMJD2/KDM4, totipotency, epigenetic regulators.

Epigenetic regulation of lymphocyte differentiation and function

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Regulation of the chromatin state is critical to cell fate determination and functioning. Our research focus on how chromatin regulators, including Histone modifying enzymes and chromatin

remodelers, play essential roles in lineage commitment, differentiation, and proper functioning of T and NK cells. For example, we found that specific deletion of histone demethylase Lsd1 in thymocytes caused significant thymic atrophy and reduced peripheral T cell populations with impaired proliferation capacity. Single-cell RNA sequencing combined with strand-specific total RNA-seq and ChIP-seq analysis revealed that ablation of Lsd1 led to the aberrant derepression of endogenous retrovirus (ERV) elements, which resulted in a viral mimicry state and activated the interferon pathway. Furthermore, the deletion of Lsd1 blocked the programmed sequential down-regulation of CD8 expression at the DP→CD4+ CD8lo stage and induced an innate memory phenotype in both thymic and peripheral T cells. Single cell TCR sequencing revealed the kinetics of TCR recombination in the mouse thymus. However, the preactivation state after Lsd1 deletion neither disturbed the timeline of TCR rearrangement nor reshaped the TCR repertoire of SP cells. Overall, our study provides new insight into the function of Lsd1 as an important maintainer of endogenous retroelement homeostasis in early T-cell development.

Nuclear Condensation of KDM2B promotes transcription elongation for Treg activation

Xudong Wu

Regulatory T cells (Treg) are activated in response to environmental cues for its immunosuppressive functions. We sought to elucidate the connections between Treg activation and adaptive mechanisms of stimulation-induced transcription elongation. Here we found that KDM2B, which is widely present at CpG island (CGI) promoters, is crucial for transcription activation of genes associated with active Treg and consequently Treg activation and immunosuppressive functions. Through its N-terminal intrinsically disorder region, KDM2B facilitates formation of transcriptional condensates, in which KAP1 is phosphorylated at serine 824 (KAP1S824ph) and therefore promotes signal-dependent transcription elongation. Consistently, either KDM2B or KAP1S824 phosphorylation is indispensable for the transcription elongation of genes associated with in vitro Treg activation. Using a mouse melanoma model, we demonstrate that Treg-specific inactivation of KDM2B enhances anti-tumor immune responses and increases anti-PD-L1 therapeutic efficacy. Therefore, our study has provided novel mechanistic insights into transcription elongation from CGI-promoters and highlighted its functional significance in Treg activation and controlling context-dependent immunosuppression.

R-loop-dependent promoter-proximal termination ensures genome stability

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The proper regulation of transcription is essential for maintaining genome integrity and executing other downstream cellular functions. Here we identify a stable association between the genome-stability regulator sensor of single-stranded DNA (SOSS) and the transcription regulator integrator-PP2A (INTAC). Through SSB1-mediated recognition of single-stranded DNA, SOSS–INTAC stimulates promoter-proximal termination of transcription and attenuates R-loops associated with paused RNA polymerase II to prevent R-loop-induced genome instability. SOSSINTAC-dependent attenuation of R-loops is enhanced by the ability of SSB1 to form liquid-like condensates. Deletion of NABP2 (encoding SSB1), or introduction of cancer-associated mutations into its intrinsically disordered region, leads to a pervasive accumulation of R-loops, highlighting a genome surveillance function of SOSS–INTAC that enables timely termination of transcription at promoters to constrain R-loop accumulation to ensure genome stability.

Molecular mechanism of human Trmt13 in tRNA modification and translational regulation

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Modification at the acceptor stem of tRNAs is rare, but 2'-O-methylation at the 4th position (Nm4) is conserved in eukaryotes. In yeast, a special RNA methyltransferase Trm13p, which has no sequence similarity with other known methyltransferases, was identified as the modifying enzyme for Nm4 of tRNA (Wilkinson et al, 2007). Recently, we identified Trmt13 as the human homolog of Trm13p that catalyzes Nm4 formation on tRNAGly and tRNAPro and regulates protein translation (Li et al, 2022). On the other hand, Trmt13 directly binds DNA as a transcriptional co-activator of key epithelial-

mesenchymal transition factors, thereby promoting cell migration independent of tRNA-modification activity (Li et al, 2022). So far, the molecular basis of the Trm13/Trmt13 as a tRNA methyltransferase or a transcriptional co-activator remains elusive. Here, we used Cryo-Electron Microscopy to determine a high-resolution structure of human Trmt13 in complex with SAM and tRNA substrates, providing insights into the molecular mechanisms of Trmt13 binding and catalyzing tRNA. Human Trmt13 contains a main methyltransferase domain, two zinc fingers that are involved in tRNA binding, and a coil-coiled domain that links them. Although Trmt13 has no sequence similarity to other known methyltransferases, its methyltransferase domain presents as a classical Rossman fold, as seen in other RNA methyltransferases. Combining with more biochemical assays, we revealed how Trmt13 binds with tRNA or DNA using the specific Zinc-finger domain. Our work provides a molecular basis to understand the dual function of Trmt13 in tRNA methylation and transcriptional regulation.

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Multilevel regulation of NF-κB signaling by NSD2 suppresses Kras-driven pancreatic tumorigenesis

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Pancreatic ductal adenocarcinoma (PDAC) is a clinically challenging cancer with a dismal overall prognosis. NSD2 is an H3K36-specific di-methyltransferase which has been reported to play a crucial role in promoting tumorigenesis. Here, we demonstrate that NSD2 acts as a putative tumor suppressor in Kras-driven pancreatic tumorigenesis. Low level of NSD2 indicates aggressive feature of

PDAC. NSD2 restrains the mice from inflammation and Kras-induced ductal metaplasia, while NSD2 loss facilitates pancreatic tumorigenesis. Mechanistically, NSD2-mediated H3K36me2 promotes the expression of IκBα, which inhibits the phosphorylation of p65 and NF-κB nuclear translocation. More importantly, NSD2 interacts with the DNA binding domain of p65, attenuating NF-κB transcriptional activity. Furthermore, inhibition of NF-κB signaling relieves the symptoms of Nsd2-deficient mice. Together, our study reveals the important tumor suppressor role of NSD2 and multiple mechanisms by which NSD2 suppresses both p65 phosphorylation and downstream transcriptional activity during pancreatic tumorigenesis. This study contributes to understanding the pathogenesis of pancreatic tumorigenesis and identifies a novel negative regulator of NF-κB signaling.

Key words: multilevel regulation; NSD2; NF-κB signaling; p65; PDAC; H3K36me2; Kras

Loss-of-function Variants in Human C12orf40 Cause Male Infertility by Destabilizing mRNAs Required for Meiotic Progression

Lantao Gou

Non-obstructive azoospermia (NOA) stands for a major cause of male infertility. In clinics, the connections between various gene mutations/variants and sterility have been widely observed in NOA patients. However, it remains poorly understood which are authentic disease-causing genes and how these gene mutations lead to male infertility. Here, we report the homozygous mutations of a previously uncharacterized gene C12orf40 identified in NOA patients, and further establish the causal role of such loss-of-function mutations in male infertility by demonstrating the requirement of the orthologous protein CN725425 for mouse spermatogenesis. Interestingly, in accordance with the patients we identified, the germ cell development of CN725425-null mice is arrested at meiosis, deficient XY chromosome pairing and crossover formation failures are found in the resulted spermatocytes. Remarkably, transcriptome analysis suggests that CN725425 orchestrate meiotic progression by protecting essential mRNAs from the programmed degradation during zygotene-to-pachytene transition in meiosis. Collectively, our findings establish C12orf40 as a factor in human infertility and unveil its crucial role in stabilizing abundant mRNAs during meiosis.

Understanding the RNA dysregulation in Rett syndrome

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Rett syndrome (RTT) is a severe neurological disorder in young females, which is mainly caused by mutations found in the X-linked MeCP2 gene. Despite extensive studies, the mechanisms of MeCP2 dysfunction in RTT are still poorly understood. We have reported MeCP2 as a new subunit of a higher-order multiunit protein complex Rbfox/LASR, which is composed of several splicing regulators. Defective MeCP2 in RTT mouse models disrupts the assembly of the MeCP2/Rbfox/LASR complex, leading to aberrant splicing of Nrxns and Nlgn1 critical for synaptic plasticity. These results thus have linked RTT to an impaired function of MeCP2 in splicing control through its role in nucleating Rbfox/LASR macromolecule assembly. In my talk, I will present our recent studies on understanding the mechanisms and functions of MeCP2 in maintaining R-loop homeostasis and discuss the roles of its aberrant regulation underlying RTT pathogenesis.

KEOPS—tRNA 复合体在生长发育过程中的功能机制

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进化上保守的 KEOPS 复合体是一个由 Kae1、Bud32、Cgi121、Pcc1 和 Gon7 组成的多功能分子机器，参与 tRNA t6A 转录后修饰、端粒复制、转录调控及 DNA 修复等多个生物学过程。KEOPS 蛋白质的突变和缺失会导致细胞内蛋白质翻译紊乱，严重影响细胞生命和个体组织器官的发育。临床测序显示 Galloway-Mowat 综合征患者含有大量 KEOPS 复合体编码基因突变，但二者之间的因果关系尚不明确，究其根本原因是目前并不完全清楚 KEOPS 复合体分子机器的工作机制和调控机理。我们课题组长聚焦研究 KEOPS 复合体与 Sua5/YRDC 蛋白质偶联催化 tRNA t6A 生物合成的分子机制，在其酶催化功能、三维结构和分子机制等方面取得了一系列研究成果。我将在本次报告中系统介绍 KEOPS 复合体的结构与功能关系，并首次报告秀丽隐杆线虫 KEOPS 复合体的完整三维结构以及 KEOPS-tRNA t6A 通路对于线虫生长和发育的调控的最新研究结果，期望能和与会专家们针对相关问题进行深入探讨。

Determination of RNA Three-Dimensional Structures by Cryo-Electron Microscopy

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RNAs play different functional roles in human biology and disease dysfunction. For the vast majority of RNA molecules, a complex high-level structure is a prerequisite for their function. Obtaining the three-dimensional (3D) structures of non-coding RNAs is essential for the discovery of their functions, pathogenic mechanisms, and targeted drugs. However, due to their inherent flexibilities, few RNA 3D structures have been determined experimentally. Cryo-electron microscopy (cryo-EM) has stood out among other structural analysis methods in recent years thanks to the rapid development of detector technology and software algorithms and is not constrained by the requirements of NMR for small molecular weights and X-ray crystallography for crystallization. Here we provide an overview of the latest advancements made in the field of analyzing 3D structures of RNAs, primarily utilizing cryo-electron microscopy as the core technique, with the Tetrahymena ribozyme at near-atomic resolution serving as an exemplified example.

Molecular mechanism and regulation of RNA N6-methylasdenosine modification

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N6-methyladenosine (m6A) is the most abundant ribonucleotide modification among eukaryotic messenger and non-coding RNAs. The m6A “writer” consists of the catalytic subunit m6A-METTL complex (MAC) and the regulatory subunit m6A-METTL associated complex (MACOM), the latter being essential for enzymatic activity. Recently, we reported the cryo-electron microscopy (cryo-EM) structures of MACOM at a 3.0-Å resolution, uncovering that WTAP and VIRMA form the core structure of MACOM and that ZC3H13 stretches the conformation by binding VIRMA. Furthermore, based on the 4.4-Å resolution cryo-EM map of the MACOM–MAC complex, in combination with crosslinking mass spectrometry and GST pull-down analysis, we proposed a plausible model of the m6A writer complex, in which MACOM and MAC assemble mainly through interactions between

WTAP and METTL3 and bind RNA substrate simultaneously. In addition, we solved the crystal structure of METTL4 which also belong to MT-A70 family as METTL3 and METTL14, in complex with RNA substrate, illuminating the conserved catalytic mechanism of N6-methyladenosine modification. Finally, our efforts at the structural and biochemical studies of RBM15, a key component of MACOM, would shed light on its molecular mechanism of the role in the regulation of RNA m6A modification.

Structure-based investigations of the working mechanisms underlying some specific non-coding RNA molecules

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Riboswitches are conserved non-coding RNA domains that play a crucial role in gene regulation. These regulatory elements are primarily found in the 5' untranslated region of bacterial genes. Riboswitches consist of two main components: a sensing domain and an expression platform. Through the specific recognition of corresponding ligands, riboswitches undergo conformational changes, thereby modulating gene expression at the transcription or translation level.

Our research focuses on riboswitches that specifically sense enzyme co-factors such as S-adenosyl-L-methionine (SAM) and Nicotinamide adenine dinucleotide (NAD+)[1-3]. Through the determination of the tertiary structure of these riboswitches and employing techniques such as isothermal titration calorimetry and fluorescence spectroscopy, we investigate the binding thermodynamics and kinetics involved in the ligand recognition process. These experiments allow us to elucidate the structural basis for the specific recognition of co-factor ligands by riboswitches.

By analyzing the recognition modules of the ligands and conducting related biochemical experiments, we have established a comprehensive model for the regulation of gene expression by these riboswitches. This model integrates our findings on the structural features of the riboswitches, their ligand binding properties, and the downstream effects on gene expression. Through this research, we aim to deepen our understanding of riboswitch-mediated gene regulation and contribute to the broader field of RNA-based regulatory mechanisms.

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C-to-G editing generates double-strand breaks causing deletion, transversion, and translocation

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Base editors (BEs) introduce base substitutions without double-strand DNA cleavage. Besides the precise substitutions, BEs generate low-frequency "stochastic" byproducts through unclear mechanisms. Here, we applied in-depth outcome profiling and genetic screening to show that C-to-G BEs (CGBEs) generate substantial amounts of intermediate double-strand breaks (DSBs), which are at the center of several byproducts. Imperfect end-joining leads to small deletions via end-resection, templated insertions or aberrant transversions during end fill-in. Chromosomal translocations between the CGBE editing target and off-targets of Cas9/deaminase-origin were also detected. Outcome-screening of DNA repair factors revealed a central role of abasic site processing in DSB formation, and the shielding of abasic sites by the suicide-enzyme HMCES reduced CGBE-initiated DSBs, providing an effective way to minimize DSB-triggered events without affecting substitutions. This work demonstrates that CGBEs can initiate deleterious intermediate DSBs and therefore require careful consideration for therapeutic applications, and that the HMCES-aided CGBEs are potentially safer tools.

染色质重塑因子 CHD7 突变导致大脑早期发育异常的机制和干预

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染色质重塑因子 CHD7 (Chromo-Helicase-DNA binding protein 7) 的突变导致一种严重的发育性疾病 CHARGE 综合征，累及大脑、眼、耳和性腺等多个器官。我们利用人大脑类器官模型发现 CHD7 突变可导致神经干细胞增殖降低以及 PAX6 等转录因子表达缺失。而在小鼠胚胎神经上皮细胞里特异敲除 Chd7 则导致神经干细胞增殖分化障碍、凋亡增加，并最终表现出小头症和嗅球发育不全等表型。分子机制研究发现在 CHD7 缺失神经细胞内 PAX6 等基因的调控区域的染色质可及性和 H3K4me3 水平下降，而 H3K27me3 水平则上升。在 CHD7 突变类脑中的表观药物筛选发现 EZH2 抑制剂能够有效回补表型。而在小鼠胚胎发育中 EZH2 抑制剂处理能够回补嗅球发育不全等表型。这些数据揭示了 CHD7 在早期大脑神经发育中的新功能和机制，并为 CHD7 突变的干预提供了新的线索。

新型非编码 RNA 报告基因的开发与应用

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传统的报告基因一般在启动子下游敲入一个荧光蛋白，一般只能用于监测表达水平高的基因，并且有可能因为插入的序列对研究对象造成干扰；特别是对于非编码 RNA，一段编码蛋白质序列的插入极有可能会改变其定位与功能。因此，亟需开发对研究对象影响较小、且灵敏度高的报告基因。我们基于 CRISPR-Cas9 系统以及 RNA 编辑系统，开发了多种新型 RNA 报告基因，这些报告基因灵敏度高，且不干扰研究对象的活性与表达。利用这些新方法，我们构建了蛋白质基因和非编码 RNA 的报告基因体系，并用于研究细胞命运和状态的变化。我们将详

细汇报这一方向所取得的进展。

关键词： Reporter; CRISPR; RNA editing; Noncoding RNAs

DisP-seq reveals the genome-wide functional organization of DNA-associated disordered proteins

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Intrinsically disordered regions (IDRs) in DNA-associated proteins are known to influence gene regulation, but their distribution and cooperative functions in genome-wide regulatory programs remain poorly understood. Here we describe DisP-seq (disordered protein precipitation followed by DNA sequencing), an antibody-independent chemical precipitation assay that can simultaneously map endogenous DNA-associated disordered proteins genome-wide through a combination of biotinylated isoxazole precipitation and next-generation sequencing. DisP-seq profiles are composed of thousands of peaks that are associated with diverse chromatin states, are enriched for disordered transcription factors (TFs) and are often arranged in large lineage-specific clusters with high local concentrations of disordered proteins and different combinations of histone modifications linked to regulatory potential. We use DisP-seq to analyze cancer cells and reveal how disordered protein-associated islands enable IDR-dependent mechanisms that control the binding and function of disordered TFs, including oncogene-dependent sequestration of TFs through long-range interactions and the reactivation of differentiation pathways upon loss of oncogenic stimuli in Ewing sarcoma.

The epigenetic reader ENL controls oncogenic transcription driven by super-enhancer and represents a synergistic vulnerability for BET inhibition

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The accurate interpretation of epigenetic codes at cis-regulatory elements (CREs) fine-tunes proper transcriptional output under various biological contexts. However, how epigenetic reader interacts with oncogenic CREs and cooperates with other chromatin regulators to drive oncogene transcription largely remain elusive. Here, we reported that the YEATS domain-containing histone acetylation reader ENL (eleven-nineteen leukemia) acted as a key regulator of super-enhancers (SEs), which are highly active distal CREs. ENL occupied the majority of SEs with much higher preference over typical-enhancers across different cancer types, and the enrichment of ENL at SEs depended on its ability to bind acetylated histone. Rapid depletion of ENL protein by auxin-inducible degron tagging severely repressed the transcription of SE-controlled oncogenes such as MYC through inducing the decommissioning of their SEs. Importantly, restoring ENL protein expression mostly reversed these effects. In addition, ENL was indispensable for the rapid activation of SE-regulated immediate early genes in response to growth factor stimulation. Furthermore, ENL interacted with the histone chaperone FACT complex and was indispensable for the proper deposition of FACT over CREs for nucleosome reorganization required in transcription initiation and elongation. ENL was overexpressed in colorectal cancer (CRC) and functionally contributed to CRC growth and metastasis. Remarkably, ENL degradation or inhibition synergized with BET inhibitors that target BRD histone readers in restraining CRC progression. These findings established the essential role of epigenetic reader ENL in governing SE-driven oncogenic transcription and uncovered a synergistic vulnerability for BET inhibition.

Key words: ENL; super-enhancer; epigenetic reader; BET inhibition; colorectal cancer

Dscam 可变剪接多样性的调控机制和生物学功能研究

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高等真核生物前体 mRNA 的可变剪接是一种重要的机制来扩增蛋白质和 mRNA 的多样性，具有重要的生理调控功能，可变剪接异常可能与疾病发生密切相关。一个最极端的例子是

黑腹果蝇的唐氏综合征粘附因子（Dscam1）基因，它可以通过互斥可变剪接编码产生 38,016 种 mRNA 和蛋白亚型，在许多中外教课书中作为经典案例予以描述。但是对 Dscam1 可变剪接机制和功能远没有了解清楚。我们揭示竞争性 RNA 二级结构在 Dscam1 互斥可变剪接中的重要作用，建立 Dscam1 互斥可变剪接的机制框架。为进一步系统研究 Dscam1 可变剪接亚型多样性的生物学功能，分别对 Dscam 基因可变外显子簇进行不同程度地靶向敲除，结果表明 Dscam1 亚型多样性与树突分支神经元树突的自我识别、蘑菇体轴突形态等表型缺陷呈负相关性，但是同时具有可变外显子和结构域的特异性。此外，我们还在鳖肢动物中发现了一类“截短”的 Dscam 基因（命名为 sDscam），与脊椎动物 cPcdh 基因类似，该 sDscam 基因通过选择性启动子及可变剪接相结合方式产生异构体多样性。这些 sDscam 亚型介导细胞黏附，具有严格的嗜同型特异性。

关键词：Dscam；可变剪接；RNA 二级结构；调控机制；生物学功能

Structural Insights into H2B Ubiquitination-Dependent H3K4 Methylation by the human SET1B Complex

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The methylation of histone H3K4 is mediated by H3K4 methyltransferases, which play pivotal roles in the epigenetic regulation of gene expression and regulate many cellular processes. In mammals, there are six MLL (Mixed-Lineage Leukemia) family H3K4 methyltransferase complexes (MLL1, MLL2, MLL3, MLL4, SET1A, and SET1B). In contrast to other histone methyltransferase, the intrinsic catalytic activities of MLL SET domains are relatively low. The highly conserved C-terminal catalytic SET domains need to bind four conserved regulatory subunits, WDR5, RBBP5, ASH2L, and DPY30, to form the pentameric complex MLL-WDR5-RBBP5-ASH2L-DPY30 (referred to as MWRAD) and achieve the optimal methyltransferase activity on nucleosome substrate. However, current studies have predominantly focused on the more conserved carboxyl-termini of MLL. The roles of other regions of MLL and specific binding subunits (such as CFP1 and WDR82) in activity regulation remain poorly understood. Furthermore, the methyltransferase activity of MLL family proteins can be modulated by the trans-histone ubiquitin mark on H2B (H2Bub). Although structural insights have elucidated the molecular mechanism through which H2Bub activates the methylation activity of MLL1/MLL3

complexes, how SET1A/B complexes respond to H2B ubiquitination modifications still warrants further investigation. Here, we elucidated the structures of the SET1B complex bound to nucleosomes with different modification states. It has shed light on the roles of multiple regulatory subunits in complex assembly and activity regulation. Furthermore, it has unveiled the molecular mechanism by which H2B ubiquitination regulates SET1B methylation activity. These findings provide a foundation for a deeper understanding of the precise regulation of H3K4 methyltransferase activity in mammals.

⊙其它投稿摘要

The epigenetic reader ENL controls oncogenic transcription driven by super-enhancer and represents a synergistic vulnerability for BET inhibition

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The accurate interpretation of epigenetic codes at cis-regulatory elements (CREs) fine-tunes proper transcriptional output under various biological contexts. However, how epigenetic reader interacts with oncogenic CREs and cooperates with other chromatin regulators to drive oncogene transcription largely remain elusive. Here, we reported that the YEATS domain-containing histone acetylation reader ENL (eleven-nineteen leukemia) acted as a key regulator of super-enhancers (SEs), which are highly active distal CREs. ENL occupied the majority of SEs with much higher preference over typical-enhancers across different cancer types, and the enrichment of ENL at SEs depended on its ability to bind acetylated histone. Rapid depletion of ENL protein by auxin-inducible degron tagging severely repressed the transcription of SE-controlled oncogenes such as MYC through inducing the decommissioning of their SEs. Importantly, restoring ENL protein expression mostly reversed these effects. In addition, ENL was indispensable for the rapid activation of SE-regulated immediate early genes in response to growth factor stimulation. Furthermore, ENL interacted with the histone chaperone FACT complex and was indispensable for the proper deposition of FACT over CREs for nucleosome reorganization required in transcription initiation and elongation. ENL was overexpressed in colorectal cancer (CRC) and functionally contributed to CRC growth and metastasis. Remarkably, ENL degradation or inhibition synergized with BET inhibitors that target BRD histone readers in restraining CRC progression. These findings established the essential role of epigenetic reader ENL in governing SE-driven oncogenic transcription and uncovered a synergistic vulnerability for BET inhibition.

Key words: ENL; super-enhancer; epigenetic reader; BET inhibition; colorectal cancer

Structures and function of the yeast SIN3 histone deacetylase complexes

Chengcheng Wang, Zhouyan Guo, Chen Chu, and Xiechao Zhan (Westlake University)

SIN3 histone deacetylase (HDAC) complexes have important roles in facilitating local histone deacetylation to regulate chromatin accessibility and gene expression. Two major types of SIN3-HDAC complexes (named SIN3L and SIN3S) are wildly existing in eukaryotes and targeting different chromatin regions. We recently determined the atomic structures of the SIN3L and SIN3S complexes from budding yeast Saccharomyces cerevisiae and fission yeast Schizosaccharomyces pombe, revealing two distinct representative organization mechanisms of the SIN3-HDAC family. Furthermore, we successfully assembled the budding yeast SIN3S complex with endogenous nucleosomes and resolved the cryo-EM structures in three distinct mononucleosome-bound states. The rigid core of SIN3S exhibits three distinct orientations relative to the nucleosome, assisting the deacetylase to locate above the SHL5-6, SHL0-1, or SHL2-3, respectively. The potential deacetylation sites in each state have been scrutinized through elaborate structural analysis. This work provides a structural framework that reveals a dynamic working model for the SIN3S complex to engage diverse deacetylation sites.

Post abstract

Siyuan Xu

Transcription factors often regulate numerous target genes. However, ZNF410 controls only a single gene CHD4 in human erythroid cells by its highly restricted chromatin occupancy to the CHD4 locus via two clusters of ZNF410 binding motifs. Here, we uncover that ZNF410 controls chromatin accessibility and activity of the two CHD4 enhancer regions. Combining CRISPR/Cas9 genomic deletion with CRISPRi approaches, we demonstrate that both enhancer regions additively contribute to CHD4 gene expression. Moreover, mutations of the di-adenine nucleotides within the ZNF410 binding motif fully disrupt ZNF410-DNA interaction. In vitro luciferase assays, ChIP-seq and ATAC-seq studies reveal that the homotypic clustered motifs are recognized by ZNF410 in a collaborative fashion. Together, our findings expose a complex functional hierarchy of motifs, where clustered motifs bound by the same transcription factor cooperate to fine-tune the expression of target gene.

The multi-faceted roles of ATRX in chromatin remodeling

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Alpha Thalassemia/Mental developmental retardation, X-linked (ATRX) protein is an SNF2-like ATP-dependent enzyme that regulates chromatin remodeling process. ATRX can interact with DAXX (Death domain-associated protein 6) to form a stable complex, promoting the deposition of H3.3 at heterochromatin. ATRX is a major etiological factor for ATRX syndrome, and somatic mutations are also frequently found in various ALT (alternative lengthening of telomeres) pathway positive cancers. However, the structure of ATRX and the mechanism by which ATRX remodels chromatin remain elusive. Here we report the crystal structure of human ATRX ATPase domain (ATRXATPase) in the resting state and the cryo-EM structure of ATRXATPase bound with NCP (nucleosome core particle). ATRXATPase detaches one turn of DNA from histone octamer and mainly binds to the detached SHL+7 DNA, in a way distinct from other chromatin remodelers. A loop in ATRX, which is unstructured and invisible in the apo ATRXATPase crystal structure, becomes partial ordered and latches on the H3 and H2A core regions exposed by DNA detaching. ATRX binding with histone core regions causes the deformation of the histone octamer, suggesting a potential role of ATRX in disrupting nucleosome integrity. Biochemical assays confirm that ATRXATPase can disassemble NCPs in an ATP-dependent manner and this NCP-disassembly activity is not coupled with nucleosome sliding activity. Our findings reveal a new chromatin remodeling activity of ATRX and suggest the multi-faceted roles of ATRX in heterochromatin maintenance.

N^2-methylation on the spliceosome catalytic center of U6 snRNA regulates pre-mRNA splicing and retina degeneration

Wen-Qing Yang[1*], Jian-Yang Ge[1*], Xiaofeng Zhang[2], Lin Lin[1], Wen-Yu Zhu[1], Yigong Shi[3], Beisi Xu[4#] and Ru-Juan Liu[1#]

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How the relatively conserved spliceosome enables to manage the enormously expanded number of splicing events that occur in humans (~200,000 vs. ~400 reported for yeast) is not well understood. Here, we show deposition of one RNA modification-N2-methylguanosine (m2G)-on the G72 nucleoside of U6 snRNA (known to function as the catalytic center of the spliceosome) results in profoundly increased pre-mRNA splicing activity in human cells. We find this U6 m2G72 is conserved among vertebrates. Further, we demonstrate that THUMPD2 (THUMP domain-containing protein 2) is the methyltransferase responsible for U6 m2G72 by specifically recognizing U6-specific sequences and structural elements. THUMPD2 KO eliminates U6 m2G72 and impairs the pre-mRNA splicing efficiency of the major spliceosome, yielding thousands of changed alternative splicing events of endogenous pre-mRNAs. Notably, the aberrantly spliced pre-mRNA population elicits the nonsense-mediated mRNA decay (NMD) pathway. We also show that THUMPD2 is associated with age-related macular degeneration (AMD) and retinal function. Our study thus demonstrates how an RNA epigenetic modification of the major spliceosome regulates global pre-mRNA splicing and impacts physiology and disease.

Molecular mechanism of human Trmt13 in tRNA modification and translational regulation

Hao Li, Pei-Yu, Tian Hui-Min Zhao Di-Jun Du & Ru-Juan Liu*

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Modification at the acceptor stem of tRNAs is rare, but 2'-O-methylation at the 4th position (Nm4) is conserved in eukaryotes. In yeast, a special RNA methyltransferase Trm13p, which has no sequence similarity with other known methyltransferases, was identified as the modifying enzyme for Nm4 of tRNA (Wilkinson et al, 2007). Recently, we identified Trmt13 as the human homolog of Trm13p that catalyzes Nm4 formation on tRNAGly and tRNAPro and regulates protein translation (Li et al, 2022).

On the other hand, Trmt13 directly binds DNA as a transcriptional co- activator of key epithelial-mesenchymal transition factors, thereby promoting cell migration independent of tRNA-modification activity (Li et al, 2022). So far, the molecular basis of the Trm13/Trmt13 as a tRNA methyltransferase or a transcriptional co-activator remains elusive. Here, we used Cryo-Electron Microscopy to determine a high-resolution structure of human Trmt13 in complex with SAM and tRNA substrates, providing insights into the molecular mechanisms of Trmt13 binding and catalyzing tRNA. Human Trmt13 contains a main methyltransferase domain, two zinc fingers that are involved in tRNA binding, and a coil-coiled domain that links them. Although Trmt13 has no sequence similarity to other known methyltransferases, its methyltransferase domain presents as a classical Rossman fold, as seen in other RNA methyltransferases. Combining with more biochemical assays, we revealed how Trmt13 binds with tRNA or DNA using the specific Zinc-finger domain. Our work provides a molecular basis to understand the dual function of Trmt13 in tRNA methylation and transcriptional regulation.

References

Wilkinson ML, Crary SM, Jackman JE, Grayhack EJ, Phizicky EM (2007) The 2'-O-methyltransferase responsible for modification of yeast tRNA at position 4. RNA 13: 404-413

Li H, Dong H, Xu BS, Xiong QP, Li CT, Yang WQ, Li j, Huang ZX, Wang ED, Liu RJ (2022) A dual role of human tRNA methyltransferase hTrmt13 in regulating translation and transcription. EMBO J 41(6):e108544

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References

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Multilevel regulation of NF-κB signaling by NSD2 suppresses Kras-driven pancreatic tumorigenesis

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Pancreatic ductal adenocarcinoma (PDAC) is a clinically challenging cancer with a dismal overall prognosis. NSD2 is an H3K36-specific di-methyltransferase which has been reported to play a crucial role in promoting tumorigenesis. Here, we demonstrate that NSD2 acts as a putative tumor suppressor in Kras-driven pancreatic tumorigenesis. Low level of NSD2 indicates aggressive feature of PDAC. NSD2 restrains the mice from inflammation and Kras-induced ductal metaplasia, while NSD2 loss facilitates pancreatic tumorigenesis. Mechanistically, NSD2-mediated H3K36me2 promotes the expression of IκBα, which inhibits the phosphorylation of p65 and NF-κB nuclear translocation. More

importantly, NSD2 interacts with the DNA binding domain of p65, attenuating NF-κB transcriptional activity. Furthermore, inhibition of NF-κB signaling relieves the symptoms of Nsd2-deficient mice. Together, our study reveals the important tumor suppressor role of NSD2 and multiple mechanisms by which NSD2 suppresses both p65 phosphorylation and downstream transcriptional activity during pancreatic tumorigenesis. This study contributes to understanding the pathogenesis of pancreatic tumorigenesis and identifies a novel negative regulator of NF-κB signaling.

Highlights

NSD2 overexpression restrains and NSD2 loss facilitates the Kras-induced ductal metaplasia in mice.

NSD2-mediated H3K36me2 promotes the expression of IκBα, which inhibits the phosphorylation of p65 and NF-κB nuclear translocation.

NSD2 interacts with the DNA binding domain of p65 and inhibits NF-κB transcriptional activity in the nucleus.

Inhibition of NF-κB signaling relieves the symptom of Nsd2-deficient mice.

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10月15日	
时间	事项
10:00-20:00	注册，签到领取材料
15:00-17:30	**推荐：屯溪老街自由活动**

10月16日	
时间	事项
9:00-9:10	**开幕致辞**
Session 1： DNA甲基化和染色质调控	
9:10-9:26	翁杰敏（华师大） **DNA甲基化调控与功能**
9:26-9:42	吴薇（生化细胞所） Active DNA demethylation promotes cell fate specification and the DNA damage response
9:42-9:58	吴强（上海交大） Outward-oriented sites within clustered CTCF boundaries are key for intraTAD chromatin interactions and gene regulation
9:58-10:14	史竹兵（西湖大学） Mechanistic insights into chromosome folding by cohesin
10:14-10:30	王海峰（清华大学） CRISPR tools for studying chromatin organization in living cells
10:30-10:50	茶歇
10:50-11:06	李兵（上海交大） RNA exporting factor Yra1 connecting DNA replication and histone deposition
11:06-11:22	何向伟（浙大） Centromere Weakening Drives Efficient Chromosome Fusion in S. pombe
11:22-11:38	陈勇（生化细胞所） The nucleosome-independent role of histones
12:00-13:30	午餐
Session 2： 表观，转录和新机制	
13:30-13:46	蓝斐(复旦大学) Heterochromatin senses nuclear mechanical force
13:46-14:02	陈飞（复旦大学） How does Pol2 decide where to stop？
14:02-14:18	林承棋（东南大学） LINE-1 5’ UTRs function as enhancers to regulate naïve pluripotency
14:18-14:34	俞洋（生物物理所） Pcf11 condensates facilitate piRNA-guided transposon cotranscriptional silencing via inducing Pol II pausing
14:34-14:50	李俊（武汉大学） **H3.3磷酸化调控异染色质建立和固化**
14:50-15:20	茶歇
15:20-15:36	陆发隆（遗传发育所） Epigenetic regulation through poly(A) tails
15:36-15:52	杨娜 （南开大学） Mechanism of the allosteric activation of deacetylase SIRT1
15:52-16:08	王露（生化细胞所） Evolutionarily conserved function of polycomb in suppressing mobile genetic elements through licensing Histone expression
16:08-16:24	陈浩（南科大） Dinoflagellate: extraordinary chromatin features and gene expression regulation
16:24-16:40	宋晓元（中国科学技术大学） **同一个长链非编码RNA的多重功能**

16:40-16:56	李斌（广州医科大学） Lysine 2-hydroxyisobutyrylation of NAT10 promotes cancer metastasis in an ac4C-dependent manner
16:56-17:12	曹雄文（华东师范大学） Unannotated microprotein EMBOW regulates the interactome and chromatin and mitotic functions of WDR5
17:30-19:00	自助晚餐
19:00-19:40	石雨江（复旦大学） **表观调控与衰老研究：** Epigenetic regulation of four-stranded DNA secondary structure I-MOTIF
19:40-20:20	徐彦辉（复旦大学） Visualization of Transcription Initiation
20:20-21:30	墙报交流

10月17日	
时间	**事项**
Session 3： 分化发育，生理病理	
9:00-9:16	高亚威 （同济大学） Reorganization of chromatin during fertilization and blastocyst formation in mice
9:16-9:32	陈捷凯 (广州生物医药与健康研究院) m6A regulates pericentric heterochromatin
9:32-9:48	丰伟军（复旦大学） **染色质重塑因子CHD7突变导致大脑早期发育异常的机制和干预**
9:48-10:04	蓝贤江（复旦大学） Systematic characterization of the CHD4 enhancers reveals cooperative functions among the homotypic ZNF410 clustered motifs
10:04-10:20	丁俊军（中山大学） Non-enzymatic KDM control promoter-enhance interaction
10:20-10:40	茶歇
10:40-10:56	李寅青（清华大学） **ES分化中dual TF的基因活化规律**
10:56-11:12	王玺（首都医科大学） **免疫细胞谱系分化发育以及功能的表观遗传调控**
11:12-11:28	吴旭东（天津医科大学） **时空特异的表观遗传信息动态调控**
11:28-11:40	徐从玲（同济大学） R-loop-dependent promoter-proximal termination ensures genome stability
11:40-11:52	邢晟晖（复旦大学） **肿瘤中新型甲基化开关**
11:52-12:04	李浩（上海科技大学） Molecular mechanism of human Trmt13 in tRNA modification and translational regulation
12:04-12:16	冯文心（上海交大） Multilevel regulation of NF-κB signaling by NSD2 suppresses Kras-driven pancreatic tumorigenesis
12:30-13:00	中国生物化学与分子生物学会基因专业分会 会场：206多功能厅
12:30-14:00	午餐
14:30-16:30	游览【唐模】，14:30 酒店大堂集合准时出发
17:00-18:00	墙报交流
18:00-20:30	晚宴

10月18日	
时间	事项
Session 4： RNA	
9:00-9:16	苟兰涛（生化细胞所） Loss-of-function Variants in Human C12orf40 Cause Male Infertility by Destabilizing mRNAs Required for Meiotic Progression
9:16-9:32	惠静毅 (生化细胞所) Understanding the RNA dysregulation in Rett syndrome
9:32-9:48	张文华（兰州大学） KEOPS—tRNA复合体在生长发育过程中的功能机制
9:48-10:04	张凯铭 (中国科学技术大学) Determination of RNA Three-Dimensional Structures by Cryo-Electron Microscopy
10:04-10:20	麻锦彪 (复旦大学) Molecular mechanism and regulation of RNA N6-methylasdenosine modification
10:20-10:40	茶歇
10:40-10:56	任艾明 (浙江大学) Structure-based investigations of the working mechanisms underlying some specific non-coding RNA molecules
10:56-11:12	孟飞龙（生化细胞所） 碱基编辑工具与DNA双链损伤
11:12-11:28	李幸 (中国科学院北京生命科学研究院) RNA imaging with fluorogenic RNA aptamer and small fluorophores
11:28-11:44	汪阳明 (北京大学) 新型非编码RNA报告基因的开发和应用
11:44-12:00	邢宇航（中国科学技术大学） DisP-seq reveals the genome-wide functional organization of DNA-associated disordered proteins
12:00-12:15	闭幕式&颁奖
12:15-14:00	午餐