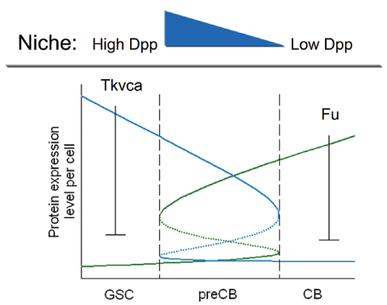
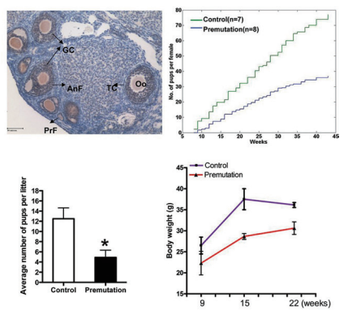
Chen Dahua, Institute of Zoology, Chinese Academy of Sciences

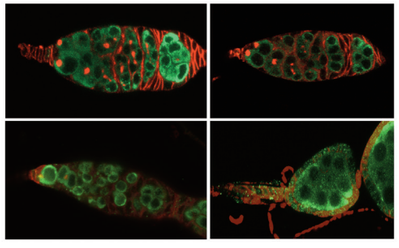
Over the last ten years, the research team led by Professor Dahua Chen has been using *Drosophila* and mouse as model organisms to study the molecular mechanisms that control asymmetric division of germline stem cells (GSCs), cell lineage development and epigenetic regulation, and has made great contributions to the field of developmental biology. His works clearly elucidate the molecular basis of how a GSC and its differentiating daughter (CB) differentially respond to niche BMP signal, thus forming a steep gradient of BMP signaling response that controls the GSC fate. Moreover, Dahua Chen and his colleague (Yi Tao) performed mathematic modeling analyses and revealed a bistable behavior of the feedback-loop system in controlling fate determination of GSCs. In studying mechanism of how the Hh signaling regulates cell lineage development, they uncovered a bidirectional control mechanism that is important for signal-receiving cells to precisely interpret external signals, thus maintaining reliability of signaling transduction during development. Recently, Dahua Chen and his colleague (Hailin Wang) identified a novel DNA modification (6mA) in *Drosophila* and proposed a potential role of the 6mA modification in controlling development in higher eukaryotes. This finding opens a new direction in the fields of developmental biology and epigenetic regulation.





数学模型研究表明，BMP响应梯度的形成受“双稳态调控”机制所控制，由此决定生殖干细胞的两个子细胞的不同命运，自我更新和分化

Mathematic modeling reveals a bistable behavior of the feedback-loop system in controlling the bam transcriptional on/off switch and determining GSC fate

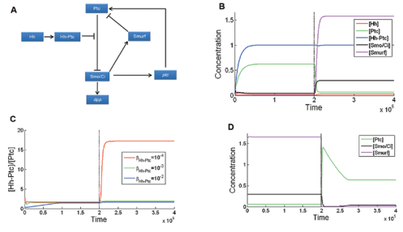


发现果蝇dfmr基因的缺失导致生殖干细胞维持功能的丧失，证明了FMRP参与生殖干细胞命运调控，阐明了FMRP在生殖细胞的作用机制

Fragile X mental retardation protein (dfmr) modulates the fate of germline stem cells in *Drosophila*, likely via the miRNA pathway. Our results provide the first evidence that FMRP might be involved in the regulation of adult stem cells

以携带人类FMR1前突变序列的转基因小鼠为研究对象，发现FMR1前突变导致卵巢早衰。研究结果表明FMR1前突变序列能够引起Akt/mTOR信号通路的改变

We characterize a mouse model carrying the human FMR1 premutation allele and show that FMR1 premutation RNA is sufficient to impair female fertility. The results show that the FMR1 premutation allele can lead to reduced phosphorylation of Akt and mTOR proteins



Smurf通过降解Ptc双向调控Hh信号途径。细胞发育过程中系统稳定性维持的重要机制（双向调控与基因网络的鲁棒性）。进一步数学模型分析表明Smo对于Smurf在降解ligand-unbound Ptc方面起促进作用。这一机制有利于生物体内信号受体细胞对外源Hh信号进行有效的解读，并在维持Hh信号的稳定传递上起重要作用

Smurf controls Hh signaling transduction by targeting the receptor Ptc, and dynamic assays revealed that a bidirectional control of activation of Smo involving Smurf and Patched is important for maintaining Hh signaling reliability. The further mathematic modeling analysis reveals that a bidirectional control of activation of Smo involving Smurf and Patched is important for signal-receiving cells to precisely interpret external signals, thereby maintaining Hedgehog signaling reliability

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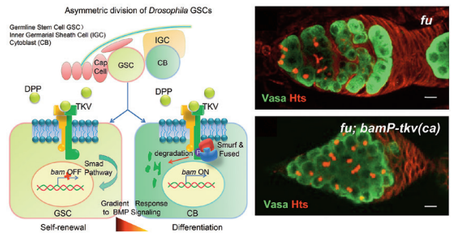
主要科技贡献：

陈大华研究员长期以果蝇等模式生物为模型，在生殖干细胞不对称分裂、细胞发育动态调控和表观遗传研究中做出系统性和原创性工作。阐明了生殖干细胞命运决定过程中干细胞及其分化子细胞对微环境信号响应梯度形成机理。陈大华及其合作者（陶毅）提出了控制生殖干细胞不对称分裂的“双稳态调控”模型；揭示了细胞发育过程中系统稳定性维持的“双向调控”机制，为一些疾病发生和发病机理研究提供新线索。近年来，陈大华及其合作者（汪海林）在果蝇基因组中首次发现新型 DNA 修饰形式（6mA）及其动态调控机制，该研究揭示了高等真核生物中表观遗传调控的新途径，在基础研究中取得了原创性成果。为表观遗传学和发育生物学开辟了一个新的研究方向。

The Fused/Smurf Complex Controls the Fate of *Drosophila* Germline Stem Cells by Generating a Gradient BMP Response

Laixin Xia,[1,2,4] Shunji Jia,[3,4] Shoujun Huang,[1,4] Hailong Wang,[1] Yuanxiang Zhu,[1] Yanjun Mu,[1] Lijuan Kan,[1] Wenjing Zheng,[1] Di Wu,[3] Xiaoming Li,[3] Qinmiao Sun,[2] Anming Meng,[2,3] and Dahua Chen[1,*]

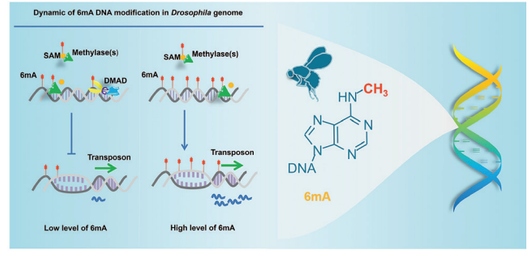


干细胞的分化子细胞通过Fused/Smurf复合体主动拮抗来自微环境的BMP信号，从而产生BMP响应梯度，进而促进干细胞不对称分裂

Fused (Fu)/Smurf complex regulates ubiquitination and proteolysis of the BMP receptor Thickveins in CBs. This regulation generates a steep gradient of BMP activity between GSCs and CBs, allowing for bam expression on CBs and concomitant differentiation

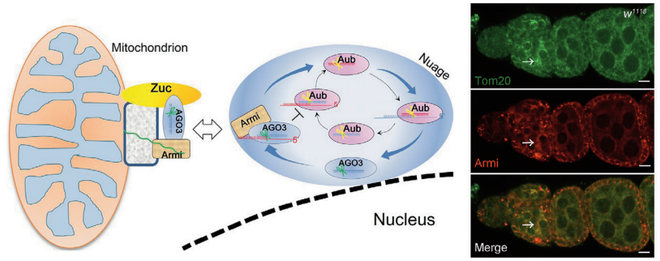
N^6-Methyladenine DNA Modification in *Drosophila*

Guoqiang Zhang,[1,5] Hua Huang,[2,5] Di Liu,[2,5] Ying Cheng,[1] Xiaoling Liu,[2] Wenxin Zhang,[1] Ruichuan Yin,[2] Dapeng Zhang,[2] Peng Zhang,[3] Jianzhao Liu,[4] Chaoyi Li,[1] Baodong Liu,[2] Yuewan Luo,[1] Yuanxiang Zhu,[1] Ning Zhang,[2] Shunmin He,[3] Chuan He,[4] Hailin Wang,[2,*] and Dahua Chen[1,*]



一种新的DNA修饰方式6mA在果蝇基因组中分布情况及其在果蝇发育过程中的动态变化

DNA N6-methyladenine (6mA) modification is present in the *Drosophila* genome. 6mA plays a potential role in controlling *Drosophila* development



RNA结合蛋白AGO3剪切酶活性对调控小分子RNA-piRNA生物合成起重要作用。研究证明AGO3与线粒体蛋白Zucchini存在相互作用调控AGO3/Armitage复合体在线粒体和Nuage两个细胞器之间动态地穿梭，由此调控piRNA的初级和次级生物合成

A proposed model describing that AGO3 Slicer functions in the Ping-Pong cycle and acts in concert with Zuc to regulate dynamic subcellular localization of the AGO3–Armi complex between mitochondrion and nuage that contributes to piRNA amplification