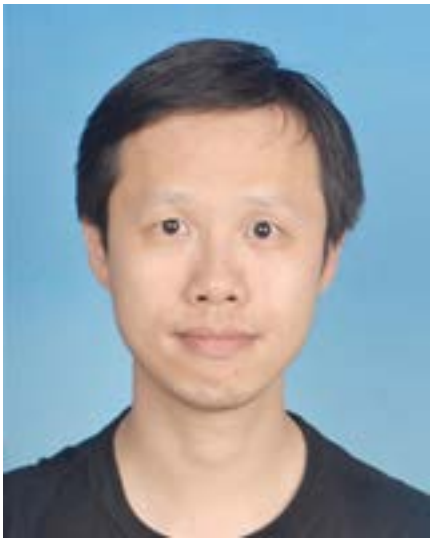
复旦大学发表原位捕捉染色质互作网络相关新成果

Fudan University Has Published the New Achievements of In Situ Capture of Chromatin Interactions

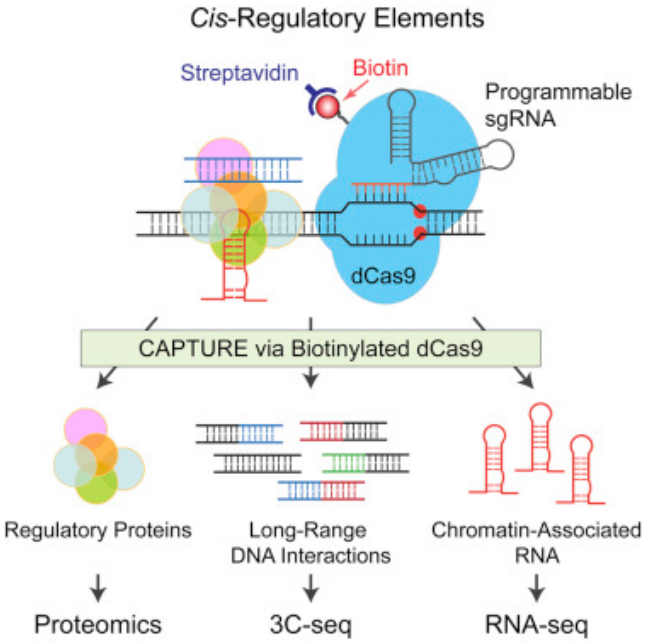


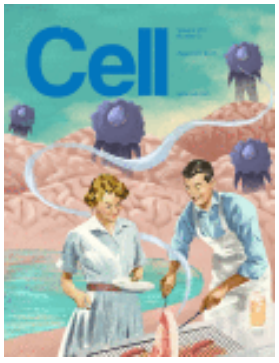
周峰研究员

【Cell 系列】德克萨斯州西南医学中心的徐剑教授课题组与复旦大学附属中山医院及生物医学研究院（IBS）周峰研究员课题组合作，首次利用了“biotinylated dCAS9”的方法建立了高分辨率、位点特异原位 DNA-蛋白质以及其他元件的互作网络 。8 月 24 日，相关研究成果在国际顶级学术期刊 Cell 杂志上发表。

随着功能基因组学的飞速发展，对调控基因表达的顺式（cis-）和反式(trans-)作用元件进行系统研究成为当前急需填补的领域空白。此前也有利用 3D 基因组图谱的方法来研究染色质结构的组学技术。染色质免疫沉淀技术 CHIA-PET 能够鉴定到全基因组范围内的染色质互作水平。此外，最近几年发展起来的 Hi-C 技术可以在更大范围内捕获包含各种拓补结构在内的与染色体相关的互作关联信息。但遗憾的是，目前为止，这些技术都无法得到与基因位点特异性相关的互作图谱，同时也缺乏反式作用原件(trans-)参与介导的互作图谱信息。

这项新研究中建立的“CAPTURE 方法”可以针对感兴趣的基因位点进行全面的挖掘，在原位发现对 DNA 的转录起到重要调控作用的蛋白质及其他元件。这种 3D 互作组学手段有助于科研人员今后就调控元件与疾病和发育的关系作进一步深入研究。





In Situ capture of chromatin interactions by biotinylated dCAS9
通过生物素化的 dcas9 原位捕捉染色质相互作用网络

复旦大学附属中山医院及生物医学研究院 周峰

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Cis-regulatory elements (CREs) are commonly recognized by correlative chromatin features, yet the molecular composition of the vast majority of CREs in chromatin remains unknown. Here, we describe a CRISPR affinity purification in situ of regulatory elements (CAPTURE) approach to unbiasedly identify locus-specific chromatin-regulating protein complexes and long-range DNA interactions. Using an in vivo biotinylated nuclease-deficient Cas9 protein and sequence-specific guide RNAs, we show high-resolution and selective isolation of chromatin interactions at a single-copy genomic locus. Purification of human telomeres using CAPTURE identifies known and new telomeric factors. In situ capture of individual constituents of the enhancer cluster controlling human β-globin genes establishes evidence for composition-based hierarchical organization. Furthermore, unbiased analysis of chromatin interactions at disease-associated cis-elements and developmentally regulated super-enhancers reveals spatial features that causally control gene transcription. Thus, comprehensive and unbiased analysis of locus-specific regulatory composition provides mechanistic insight into genome structure and function in development and disease.