最新研究揭示人类早期胚胎发育染色质状态重编程规律

Recent Research Reveals the Reprogramming of Chromatin Status in Human Early Embryo Development

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5 月 2 日，清华大学生命科学学院颉伟研究组、医学院那洁研究组与郑州大学第一附属医院孙莹璞研究组紧密合作，在 Nature 杂志发表最新研究论文，揭示了人类早期胚胎发育各阶段染色质重编程变化规律。

这一重要发现不仅有助于我们进一步理解人类胚胎发育过程中染色质调控机制，也为研究体外受精、试管婴儿等相关应用和胚胎发育相关疾病提供了理论基础。

人类的个体生命起源于受精卵，受精卵在胚胎发育早期经历了一系列剧烈的染色体重编程事件。以小鼠为模式生物的研究表明：胚胎染色体的重编程过程中，来源父本、母本染色体的开放状态、高级结构以及其携带的表观遗传信息都发生了剧烈的改变。这些改变能够帮助介导胚胎基因组转录的启动，重塑崭新的全能性胚胎，并为后期胚胎发育和细胞分化奠定基础。之前的研究发现，基因转录的关键调控元件通常坐落在染色质开放区域。这些调控元件与细胞特异的转录因子共同调控了细胞命运决定和个体的发育。

在最新的研究中，清华大学颉伟组优化了现有的细胞染色质开放区域定位技术(ATAC-seq)，实现了在极少量细胞（20）水平上进行开放染色质区域的检测，进而与郑州大学第一附属医院孙莹璞研究组紧密合作，揭示了人类早期胚胎发育过程中开放染色质的调控规律。最后通过与清华大学医学院那洁实验室合作进行小鼠胚胎相关实验，发现染色质调控规律在人和小鼠胚胎发育过程中同时存在保守性和物种特异性。

该研究揭示了人类胚胎早期发育过程染色质状态和基因表达调控模式，首次揭示人类胚胎 ZGA 前存在广泛的染色质开放区域，并阐明其在胚胎发育过程的重编程模式，阐述了胚胎基因组转录激活对于开放染色质区域重编程的必要性。研究成果为深入理解人类胚胎早期发育表观遗传调控提供了理论基础，将对辅助生殖技术临床产生深远影响，对提高辅助生殖成功率以及发育相关出生缺陷防控具有重大意义。

Chromatin analysis in human early development reveals epigenetic transition during ZGA

人早期胚胎染色质研究揭示基因组激活前后表观遗传转换规律

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Upon fertilization, drastic chromatin reorganization occurs during preimplantation development1. However, the global chromatin landscape and its molecular dynamics in this period remain largely unexplored in humans. Here we investigate chromatin states in human preimplantation development using an improved assay for transposase-accessible chromatin with high-throughput sequencing (ATAC-seq)2. We find widespread accessible chromatin regions in early human embryos that overlap extensively with putative cis-regulatory sequences and transposable elements. Integrative analyses show both conservation and divergence in regulatory circuitry between human and mouse early development, and between human pluripotency in vivo and human embryonic stem cells. In addition, we find widespread open chromatin regions before zygotic genome activation (ZGA). The accessible chromatin loci are readily found at CpG-rich promoters. Unexpectedly, many others reside in distal regions that overlap with DNA hypomethylated domains in human oocytes and are enriched for transcription factor-binding sites. A large portion of these regions then become inaccessible after ZGA in a transcription-dependent manner. Notably, such extensive chromatin reorganization during ZGA is conserved in mice and correlates with the reprogramming of the non-canonical histone mark H3K4me3, which is uniquely linked to genome silencing3,4,5. Taken together, these data not only reveal a conserved principle that underlies the chromatin transition during mammalian ZGA, but also help to advance our understanding of epigenetic reprogramming during human early development and in vitro fertilization.