利用高通量单细胞RNA测序解析人类多能干细胞的分化通路 Genome Biology

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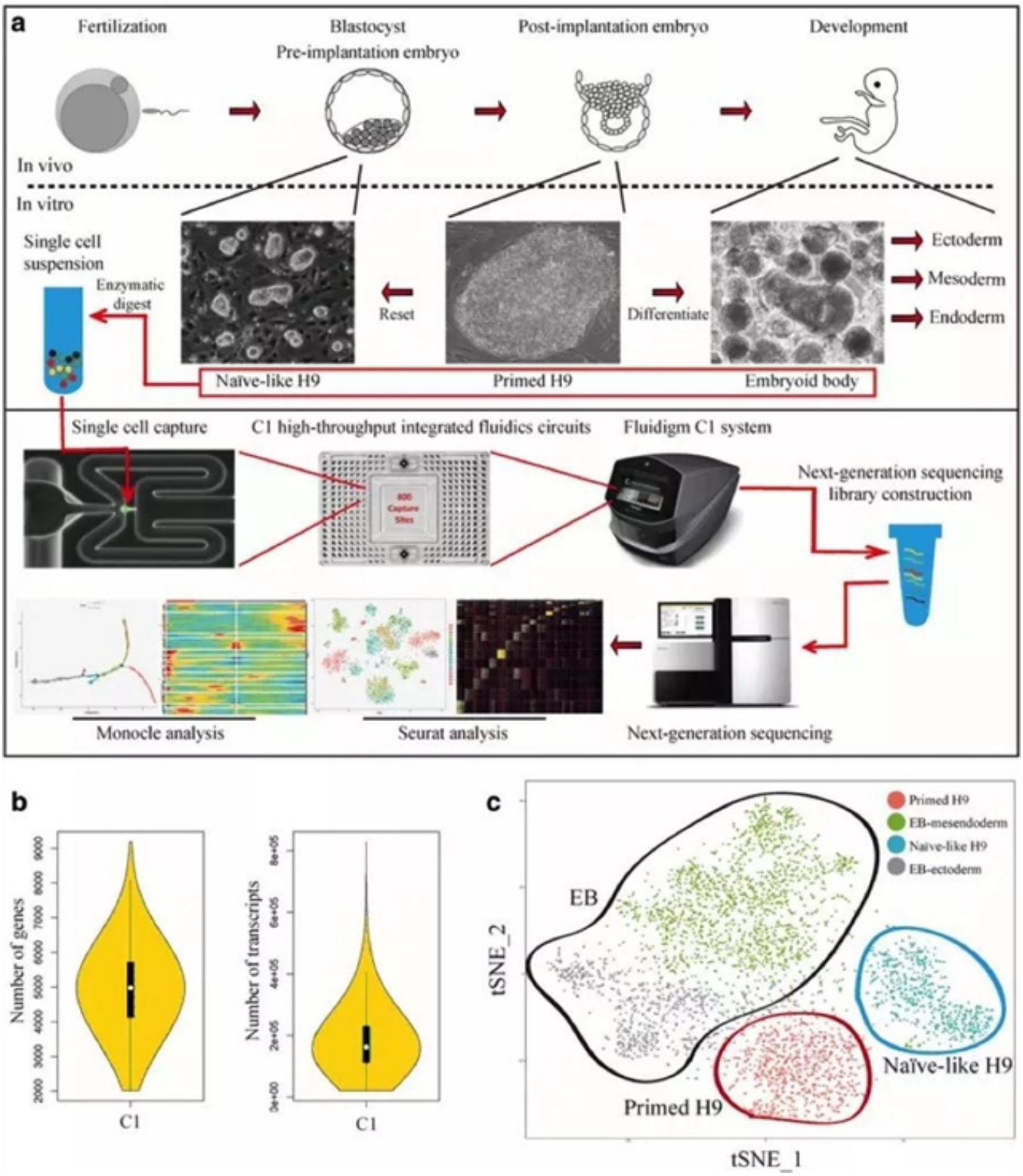
利用高通量单细胞RNA测序解析人类多能干细胞的分化通路 Genome Biology。人类多能干细胞(Human pluripotent stem cells, hPSCs)是用于细胞分化研究的重要模型，为再生医学提供了无限的细胞来源。然而，目前仍未建立全面的hPSCs单细胞水平分化图谱。

在发表于Genome Biology上的Mapping human pluripotent stem cell differentiation pathways using high throughput single-cell RNA-sequencing文章中，来自浙江大学的Haide Chen、Guoji Guo及其研究团队使用高通量单细胞RNA测序法(scRNA-seq)，在优化的微流体环路基础上分析了人胚胎体系中的早期分化谱系。



图：高通量单细胞RNA测序法(scRNA-seq)分析hPSC的早期分化

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该研究展示了涵盖多种细胞谱系的hPSC早期分化的细胞状况，其中包括神经细胞、肌肉细胞、内皮细胞、基质细胞、肝脏细胞和上皮细胞。通过拟时间分析法，研究者们构建了这些祖细胞的

发育轨迹，并揭示了细胞分化过程中的基因表达动态。他们还将始发态H9细胞(primed H9 cells)重新编程为原始态H9细胞(na ï ve-like H9 cells)，用于研究细胞态的转换过程。研究者发现在原始态H9细胞中富含血源性内皮发育相关基因。在功能上，原始态H9细胞分化成造血细胞的潜力比始发态细胞更高。

该单细胞分析揭示了hPSC早期分化的细胞状况，并提出了有关优化分化方案的新见解。

摘要：

Background

Human pluripotent stem cells (hPSCs) provide powerful models for studying cellular differentiations and unlimited sources of cells for regenerative medicine. However, a comprehensive single-cell level differentiation roadmap for hPSCs has not been achieved.

Results

We use high throughput single-cell RNA-sequencing (scRNA-seq), based on optimized microfluidic circuits, to profile early differentiation lineages in the human embryoid body system. We present a cellular-state landscape for hPSC early differentiation that covers multiple cellular lineages, including neural, muscle, endothelial, stromal, liver, and epithelial cells. Through pseudotime analysis, we construct the developmental trajectories of these progenitor cells and reveal the gene expression dynamics in the process of cell differentiation. We further reprogram primed H9 cells into na ï ve-like H9 cells to study the cellular-state transition process. We find that genes related to hemogenic endothelium development are enriched in na ï ve-like H9. Functionally, na ï ve-like H9 show higher potency for differentiation into hematopoietic lineages than primed cells.

Conclusions

Our single-cell analysis reveals the cellular-state landscape of hPSC early differentiation, offering new insights that can be harnessed for optimization of differentiation protocols.

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期刊介绍:

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