FASSBERG SEMINAR SERIES

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special date & time

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Unleashing the developmental potential of induced pluripotent stem cells (iPSCs)

A current aim in cell and developmental biology is to program cells at will. One way towards converting a given cell type into another one is achieved via a pluripotent stem cell state that resembles that of embryonic stem cells (ESCs). In most cases, somatic cells are pushed into a pluripotent state by the introduction of exogenous factors, mostly transcription factors. Reprogramming of somatic cells into pluripotent stem cells designated as induced pluripotent stem cells (iPSCs) was first described in 2006. Fibroblasts were used and initially required introduction of the virally expressed transcription factor quartet Oct4, Sox2, Klf4, and c-Myc (OSKM). We previously reported that Oct4 alone is sufficient for directly reprogramming adult mouse and human fetal neural stem cells into iPSCs, thus highlighting the crucial role played by Oct4 in the process. As we now show the combination of SKM is sufficient for reprogramming mouse somatic cells into iPSCs. Actually, SKM even activates the pluripotency network in Oct4-knockout fibroblasts. Retroviral silencing requires the simultaneous expression of Sox2 and c-Myc, perhaps accounting for the discrepancy with respect to previous studies that used retroviral vectors to generate iPSCs without Oct4. Reprogramming in the absence of exogenous Oct4 results in iPSCs that are characterized by more faithful gene expression and greatly improved developmental potential. Our data suggests that expression of exogenous Oct4 during reprogramming leads to off-target gene activation, thereby worsening the quality of the generated iPSCs with major implications for further development and application of iPSC technology.

Host: Patrick Cramer

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