

DEC
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10AM CET
VIRTUAL

iPSZÜRICH

A Lecture Series Focused on Induced Pluripotent Stem Cells



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REPROGRAMMING FOR REJUVENATION AND STUDIES OF MITOCHONDRIAL FUNCTION

The process of organismal aging is both genetic and epigenetic. On the other hand, the process of reprogramming to pluripotency is primarily epigenetic, removing somatic cell identity. Reprogramming induces changes in genome methylation leading to cell proliferation and altered gene expression. Harnessing such positive changes has been considered as an approach to tissue rejuvenation. Yet, it is known that during the process of induced pluripotent stem (iPS) cell generation, clonal amplification of genetic mutations from donor somatic cells can occur. Similar to somatic mutations, mutations in mitochondrial DNA (mtDNA) are expected to accumulate with age yet are often overlooked as part of iPS cell quality control. We established a next generation sequencing protocol and bioinformatic pipeline for iPS cell mtDNA sequence analysis. We applied our method to classify mtDNA haplogroups and examine mtDNA heteroplasmy in a bank of iPS cells from diseased and healthy male and female Japanese donors of varying age. Combined with *in vitro* differentiation and mitochondrial respiration analysis, we aim to explain clonal variation of iPS cells and age-related phenotypes. These data are relevant to realize the potential of cellular programming for rejuvenation.

