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Mechanical limitations of cells under direct neuronal reprogramming

Abstract

The traditional strategies to impose cell reprogramming are mainly focus in generate changes at the level of gene expression. However, at the same time cells will experience dramatic morphological changes that also have an impact at transcriptional levels. In our model, primary astrocytes undergo direct reprogramming to induce neurons (iN) that presents a radical reduction of the nuclear volume (approx. 4 times). In order to understand the relevance of the nuclear shrinkage during reprograming we altered its nuclear volume reduction by pharmacological and external mechanical stimuli. We found that impairing nuclear shrinkage decrease the presence of cytoplasmic reprogrammed proteins but it kept similar transcriptional levels of mRNA. Also, we demonstrated that nuclear shrinkage must escort the reprogramming process during at least 3 days for a successful occurrence. Nevertheless, a lethargy of the nuclear compaction phase can put the cells at the brink of cell death. Our results, shed light on what cell morphological changes could mechanically impact at transcriptional levels and cell viability determining the cell limits and possibilities of being reprogrammed.

Publications

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Biography

Marcelo Salierno is a senior associate research at the Centre for Developmental Neurobiology at King's College London. His current work focuses on the development of biomaterial to study neuronal migration and glial reprogramming and their impact on brain development and associated diseases. Early in his career he was advocated to design photolabile compounds applied to opto-biology. As a postdoc at the Max Planck institute for Polymers, he designed photoactivatable systems using mimetic cell-adhesive molecules to promote cell migration in a variety of conditions. More recently, their engineered materials were able to stimulate stem cells to a neuronal fate and to generate single cell migration of new-born neurons. He has over 30 publications that have been cited over 1000 times, and his H-index is 16 and has been serving as an editorial member of journals such as Biomaterials and Scientific Report among others.

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