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Subcellular localization of catenin-β1 instructs fate bias during neurogenesis

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Statement of the Problem: Neural self-organization refers to spontaneous evolution of global order from local interactions between neural progenitor cells during neurogenesis. However, the molecular basis for programming various aspects of neural self-organization including sub-lineage fate choice of the progenitor cells remains ambiguous. Here we report the role of Catenin-β1 in encoding the programmable dimension of neural self-organization based on subcellular localization of this protein.

Method: We used human neural progenitors with neuronal and glial differentiation capacities in the current study. Prior to neural induction, small molecule inhibitors were applied to program the subcellular localization of Catenin-β1. Subsequent to programming, the proliferation rate of the progenitors was assessed using live imaging phase contrast microscopy. Differentiation of the programmed cells into neuronal and glial elements was then investigated using a combination of immuno-histochemical staining and real-time PCR.

Findings: The application of IWR-1 resulted in depletion of cytoplasmic free Catenin-β1 by mobilization into junctional N-cadherin. The IWR-1+ cells also demonstrated increased nuclear notch-1 and down regulation of YAP-1. The application of ML-141, on the other hand, mobilized the junctional Catenin-β1 into the cytoplasmic pool and subsequently into the nucleus, increased activity of free Catenin-β1 lead to the depletion of antagonistic Notch-1 in these cells. While Catenin-β1+/Notch-1- neural progenitors adopted a neuronal fate, the Catenin-β1-/Notch-1+ cells mainly differentiated into glial elements.

Conclusion: Subcellular localization of Catenin-β1 is a major determinant of neurogenic fate bias. Localization of this protein to junctional complexes anticipates a glial fate bias and mobilization into the cytoplasmic pool instructs a neuronal differentiation bias. These findings may be utilized to program the progenitor cells in guided tissue engineering.

Biography

Saba Rezaei-Lotfi has completed her MPhil in Faculty of Dentistry, Department of Life Sciences. Her thesis provided novel experimental evidence regarding the regulation of neurogenesis by microRNA signaling. She is currently a PhD student at the Faculty of Medicine and Health. Her research project focuses on investigating the role of Catenin-β1 in determining fate in neural differentiation.

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