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Protein phosphatase/Smek complex negatively regulate Par3 and promote neuronal differentiation

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Neural progenitor cells (NPCs) are self-renewing multipotent cells that are capable of differentiating into neurons and glial cells. Mechanisms that control the fate decisions of NPCs are not well understood. SMEK homolog 1, suppressor of mek1 (Smek-1) is a regulatory subunit of the serine/threonine protein phosphatase PP4. We found that Smek-1 is expressed in NPCs promotes neuronal differentiation and suppresses the proliferation of NPCs. Mass spectrometry analysis identified one of Smek-1's binding partners, Par3. Par3, a cell polarity protein is a negative regulator of neuronal differentiation. We demonstrate that Par3 is a substrate of Smek-1 and Smek-1 can negatively regulate its activity in neurogenesis. Interestingly, Smek-1 is expressed mainly in the nucleus but is exclusively localized in the cytoplasm during mitosis. We show that the cytoplasmic Smek-1 can interact with cytoplasmic Par3 and thereby mediate de-phosphorylation by the catalytic subunit PP4C. Collectively, our results show that the PP4/Smek-1 complex is likely a key regulator of neurogenesis.

Biography

Vicky Yamamoto is a Cancer Scientist at Keck School of Medicine of USC in the Department of Head and Neck Surgery with more than 10 years of research experience ranging from developmental neurobiology and stem cell to molecular targeted therapy. Prior to joining Keck School of Medicine of USC, she worked at Mount St. Mary's College, The Scripps Research Institute, the Cedars-Sinai Medical Center and California Institute of Technology. She has received a PhD in Biochemistry and Molecular Biology from Keck School of Medicine of USC. She has significant teaching experience and mentored numerous students.

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