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Author(s)	Wong, MK; Li, M; Chan, YS; Shum, DKY
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70 Role of BMP/Smad signaling in cerebellum neurogenesis

Ma Tsz Ching (CUHK)
(Supervisor: Dr. Kwan Kin Ming, CUHK)

Cerebellum neurogenesis is tightly regulated by transcription factors and signaling molecules that specific types of neurons are produced sequentially from two germinal matrices, ventricular zone and anterior rhombic lip. Although both germinal matrices are equally important to cerebellum formation, our understanding on the maintenance and specification of multipotent neural stem cells in ventricular zone is far uncomparable to that in anterior rhombic lip. Bone morphogenetic proteins (BMPs) are signaling molecules crucial to the maintenance of stem cell identity. We previously demonstrated that Smad1/5 is critical to granule cell production by governing proliferation and specification of neural progenitor cells in anterior rhombic lip. Because BMPs are secreted from rhombomere 1 roof plate during cerebellum development, we proposed that canonical BMP/Smad signaling is involved in neurogenesis within ventricular zone as well. Our En1-cre driven Smad1/5 double conditional knockout mice displayed an enlarged Purkinje cell population at E11.5, implying abnormal neurogenesis from ventricular zone. However, because of the observation of thinner PCNA-positive domain in mutant cerebellum, enhanced Purkinje cell neurogenesis in Smad1/5-null cerebellum is unlikely attributed by an expanded progenitor cell pool. Taken together, our data suggest canonical BMP/Smad signaling regulates the balance between stem cell renewal and specification to Purkinje cells in ventricular zone.

71 Expression of Chondroitin Sulfotransferase in Cranial Motor Neurons for Cell Migration in Rat Embryonic Hindbrain

M. K. Wong¹, M. Li¹, Y. S. Chan^{2,3} and D. K. Y. Shum^{1,3}

Departments of ¹Biochemistry and ²Physiology, ³Research Centre of Heart, Brain Hormone & Healthy Aging, Faculty of Medicine, The University of Hong Kong, Hong Kong

Neuronal migration allows the proper positioning of neurons for establishing functional connectivity of defined neural circuits. We and others reported the restrictive role of Chondroitin sulfate (CS) moieties in axonal fasciculation. CS moieties of proteoglycans are therefore hypothesized to control the timely orchestration of cranial motor neuron migration during hindbrain development by the varying sulfation patterns of the chondroitins between the migrating and ready-to-migrate neurons. Hindbrain explants of E11.5 Sprague Dawley rats were maintained in culture for time lapse video recording of individual neuronal somal movements. In control cultures, we observed the advancement of neuronal somata in the direction of the leading process away from the explant core. In test cultures treated with chondroitinase ABC, the neuronal cell bodies lost the direction movement but remained motile. Immunocytochemistry confirmed the presence of CS56 epitopes among Tuj-1-positive neurons not only in the explant core and those advancing beyond the core, but also in the vicinity of the migrating neuronal somata. In situ hybridization revealed chondroitin-4-sulfotransferase 2 (C4ST2) mRNA expression among cells heading away from the core whereas chondroitin-4-sulfotransferase 1 (C4ST1) mRNA was found essentially in the core of the explant. Thus far, the results suggest differential sulfation of chondroitins on proteoglycans expressed by neurons in determining the migratory phenotype.