64] Cyp26b1 mediates differential regulation of RA signaling in neural progenitor populations along the anterior-posterior axis of the adult spinal cord

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Neural stem cells from the adult subventricular zone (SVZ) are highly heterogeneous, with their position of origin being a key factor in determining the neuronal subtype they can give rise to. Whether this diversity extends to other regions in the adult CNS has not been demonstrated. *In vitro* studies with directed neuronal differentiation of ES cells suggest that subtype specification may be regulated by the positional identity present in the ES-derived cell, since altering the positional identity leads to corresponding changes in motor neuron subtype. This limited plasticity suggests the position identity of the original stem cell source is a critical factor for the generation of the desired neuronal subtype. The adult spinal cord consists of endogenous stem/progenitor cells which are activated upon injury, with potential for repair in CNS diseases and spinal cord injury. However, our knowledge and understanding of these cells are limited. Our research is aimed at understanding the properties of endogenous progenitor cells in the adult spinal cord and how they can be utilized for neuronal regeneration. In this study, we identified multiple subpopulations of spinal cord progenitor cells (SCPCs) based on their position along the anterior/posterior (A/P) axis of the adult spinal cord. These subpopulations can be distinguished by the expression of distinct combinatorial *Hox* genes in a manner reminiscent of their expression in the developing neural tube. Moreover, different progenitor subpopulations display varying cellular properties, such as a higher neurogenic potential and higher neurosphere-forming ability observed in lumbar-derived progenitor cells.
We further demonstrate that axial-derived SCPCs are differentially responsive to the neurogenic agent retinoic acid (RA). In the presence of RA, neurogenesis was increased by two-fold during differentiation of cervical-derived spheres, while no increase was observed for lumbar-derived cells. Expression profile analysis of RA signaling components revealed that the RA degrading enzyme cyp26b1, absent in cervical SCPCs but highly expressed in lumbar SCPCs, is likely to regulate RA signaling in these SCPC populations. The heterogeneity in signaling factor regulation among adult A/P spinal cord progenitor cell populations suggests that different niche factor regimens are required for mobilizing endogenous SCPCs for site-specific neuronal regeneration from distinct spatial regions.