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Neural crest- and primary mesoderm-derived morphogenetic-like fields in the nasal septum of the human embryo: implications for engineering of the articular cartilage

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The cartilage of the adult human nasal septum has recently been found as a source of neuroectodermal-derived chondrocytes exhibiting capacity to regenerate the articular cartilage [1,2]. To shed light on the key cellular players of this differentiation, we studied the contribution of neural crest (NC)- and primary mesoderm (Mes)-derived stem cells to the development of the nasal septum in the human embryo. Ninety-nine sagittal and horizontal, paraffin-embedded and formaldehyde-fixed sections of 8 human embryos (CRL 11, 19, 20, 24, 30) from the collection of the Museum and Historical Library of Biomedicine (BIOMED) of the University of Parma were used. After dewaxing and rehydration, tissue epitope retrieval was achieved soaking sections in boiling citrate buffer pH 6.0 for 20 min, followed by immunocytochemical labelling with primary antibodies to Wnt1, Notch1, Msi1, Nestin, Sox10, and Chromogranin A (Chrom A) as NC markers, and Brachyury (T) as Mes marker. Immunoreactive (IR) material was detected using either the peroxidase or alkaline phosphatase - ABC techniques, and DAB or Vector Red as chromogens, respectively and analyzed with light microscopy. A topographical arrangement was apparent for both Mes- and NC-derived stem cells: vertical stripes of Wnt1-IR cells segmented the lateral aspects of the septal primordium, moving from a posterior to an anterior direction. These cell fields alternated with either Notch1-IR, T-IR, or Nestin-IR cell columns / groups, the latter two diffusing also into the medial aspects of the septum. In contrast, Sox10-IR, T-IR, Chrom A-IR, and Msi1-IR cell groups contributed to the most anterior portion of the lateral aspects of the septal cartilage, giving rise to a caudally- to cranially- oriented pile of individual stem cell fields. These results raise the possibility that development of the human nasal septum is driven by a place-dependent, morphogenetic code provided by both NC- and Mes-derived stem cells. In addition, it suggests that different areas of the adult nasal septum may provide different types of stem cells, whose differentiation potential could be selectively exploited in bioengineering of cartilaginous grafts for the repair of a variety of mesodermal tissues including the articular and intervertebral disk cartilages.

References

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[2] Mumme et al. (2016), Lancet 388:1985-1994

Key words

Stem cells, neural crest, nasal septum, cartilage.