

Intramembranous Bone and the Role of Neural Crest in Building the Head Skeleton

Bones form in two major ways. In one way, mesenchyme becomes cartilage and the cartilage is replaced by bone; this is called endochondral ossification, which we will describe in detail in Chapter 12. The other type of bone formation, where mesenchyme forms bones directly, is called intramembranous ossification. Both mesodermal and ectodermal (i.e., neural crest-derived) mesenchyme undergo intramembranous ossification in forming the face and skull.

The pathway from neural crest to intramembranous bone begins when cranial neural crest cells, under the influence of BMPs from the head epidermis, proliferate and condense into compact nodules. High levels of BMPs induce these nodules to become cartilage, whereas lower levels of BMPs induce them to become pre-osteoblast progenitor cells that express the Runx2 transcription factor and the mRNA for collagens II and IX. Later, these cells downregulate Runx2 and begin expressing the *osteopontin* gene, giving them a phenotype similar to that of a developing chondrocyte (cartilage cell); thus, this stage is called a chondrocyte-like osteoblast. Under the influence of Indian hedgehog (which it secretes and probably receives in an autocrine fashion), the chondrocyte-like osteoblast becomes a mature osteoblast—a committed bone precursor cell (Abzhanov et al. 2007). The osteoblasts secrete a collagen-proteoglycan osteoid matrix that is able to bind calcium. Osteoblasts that are embedded in the calcified matrix become osteocytes (bone cells). As calcification proceeds, bony spicules radiate out from the region where ossification began. Furthermore, the entire region of calcified spicules becomes surrounded by compact mesenchymal cells that form the periosteum (a membrane of cells that surrounds bone). The cells on the inner surface of the periosteum also become osteoblasts and deposit matrix parallel to the existing spicules. In this manner, many layers of bone are formed.

Literature Cited

Abzhanov, A., S. J. Rodda, A. P. McMahon, C. J. Tabin. 2007. Regulation of skeletogenic differentiation in cranial dermal bone. *Development* 134(17): 3133-44.
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