FACTORS THAT IMPACT SKELETAL DEVELOPMENT AND SKELETAL DEFORMITIES IN ZEBRAFISH AND OTHER TELEOST FISH THAT ARE USED AS MODELS IN BIOMEDICAL RESEARCH

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Skeletal tissues of vertebrates are lifelong subjected to reshaping, remodelling or even replacement/regeneration (teeth and antlers). The modes of changing the composition of the skeleton are (1) plasticity of skeletogenic cells (modulation), (2) transdifferentiation of skeletal tissues into other skeletal tissues (metaplasia) and (3) resorption of skeletal tissues and their replacement by another skeletal tissue type (remodeling). All three modes may occur lifelong in response to altered intrinsic and/or environmental conditions and therefore constitute the cellular equivalent of phenotypic plasticity. Comparing modes of development in extant (including in vitro studies) and extinct vertebrates suggests the early evolution of highly plastic skeletogenic cells. These cells can modulate their behaviour in response to intrinsic and environmental signals. Thus, skeletal tissues might best be understood by viewing them as dynamic rather than static entities. Much knowledge about intermediate skeletal tissues and about alternative pathways of skeletal development and remodeling derives from studies on teleost fish, especially zebrafish and medaka. Bone resorption in teleosts with acellular bone (bone that lacks osteocytes) by mononucleated osteoclasts is one example of an alternative pathway of skeletal remodelling. In mammals, mononucleated osteoclasts are generally viewed as osteoclast precursors and only multinucleated cells are considered to be capable of active bone resorption. The fact that bone resorption in teleosts with acellular bone can rely on mononucleated cells alone, sheds new light on often disregarded reports about mononucleated mammalian (human) osteoclasts and other "alternative" mechanisms of bone resorption, such as osteocytic osteolysis. Evolutionary conserved factors that affect bone remodelling, alterations of the skeleton and the development of skeletal malformations in fish are (a) the unlimited access to calcium through the gills, (b) a phosphate and not calcium driven bone mineral metabolism, (c) factual weightlessness, (d) infinite growth, (e) a lifelong capacity to resume skeletal development (as exemplified by continuous tooth replacement) and (f) the lack of hematopoietic tissue in the bone marrow. Considering conserved and advanced characters of teleost skeletal development is essential if zebrafish and medaka are used as models in biomedical research.