

New zebrafish models will accelerate studies of the human skeleton and osteoporosis

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Although much scientific research has been done into the development of the skeleton, the underlying mechanisms that drive the formation and maintenance of bones are still not very well understood, and research into the development of bone remains of enormous importance. To date, 20 percent of women at the age of 65 years develop osteoporosis, and 40 percent of elderly men suffering a hip fracture die within the year during the recovery. Skeletal diseases are still among the most frequent syndromes in Western population that result in high mortality, urging scientists to research into better cures.



To gain more insight into these bone diseases, researchers at the Center for Medical Genetics Ghent (CMGG, Ghent University, www.cmgg.be) and the Ghent University hospital have developed a revolutionary zebrafish model that allows the detailed study of the build-up and breakdown of bone in the body. These two processes are balanced in a normal skeleton, but can become unbalanced in diseases such as osteoporosis, causing the loss of too much bone and making the skeleton prone to fractures. Zebrafish, a small tropical bony fish, is highly suitable for research into the skeleton, and can reveal the biological processes in the human skeleton. This has for long been a very controversial topic in the scientific world; zebrafish as a disease model for bone disorders was questioned in part due to the large genetic distance (400 million years) between humans and zebrafish. However, about 70 percent of the genes in humans are also present in zebrafish, and many parts of the skeleton are similar between both species, making zebrafish much more suitable for medical research than once thought, even to study the <u>skeleton</u>.

The researchers were able to introduce several genetic mutations in the zebrafish and modify genes that also have an important impact on bone quality and result in fragile bone diseases in humans. It now appears that these "mutated" zebrafish exhibit remarkably similar features as human patients, such as fractured ribs, bowed bones and facial deformities.

The importance of this finding is that it will provide researchers with new insights into how bone is produced and broken down, which can accelerate the development of new candidate drugs. An important advantage of these zebrafish models compared to laboratory mice is that they are much easier, much more efficient and much cheaper to work with. Zebrafish are also faster to breed and can produce up to 300 eggs in one breeding. These advantages, together with the study findings, can strongly reduce the number of experiments needed in mice, which is currently the main animal model for the study of skeletal development.



More information: Charlotte Gistelinck et al. Zebrafish type I collagen mutants faithfully recapitulate human type I collagenopathies, *Proceedings of the National Academy of Sciences* (2018). DOI: 10.1073/pnas.1722200115

Provided by Ghent University

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