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BONE

STATIN THERAPY FOR SKELETAL DYSPLASIA

A novel application for statins—the treatment of patients with skeletal dysplasia—has been revealed by new findings published in *Nature*.

Achondroplasia and thanatophoric dysplasia type 1 (TD1) are among a group of disorders characterized by mutations in the gene that encodes fibroblast growth factor receptor 3, *FGFR3*, and are a collectively known as FGFR3 chondrodysplasias. Previous studies have shown that these skeletal dysplasias are caused by gain-of-function mutations in *FGFR3*.

The team of researchers, led by Noriyuki Tsumaki from Kyoto University, Japan, developed an *in vitro* cell culture system using induced pluripotent stem (iPS) cells, in which they screened drugs that might be used to treat FGFR3 chondrodysplasias. Patient-specific iPS cells were generated from dermal fibroblasts of individuals with TD1 and achondroplasia, as well as from healthy controls. iPS cells were then differentiated into chondrocytes using cytokines. Differentiated TD1 iPS cells showed reduced proliferation and increased apoptosis (similar to chondrocytes from patients with FGFR3 chondrodysplasias) and decreased expression of chondrocyte markers compared with differentiated control iPS cells, as well as an inability to form cartilage.

Differentiated chondrocytes generated from cells of patients with TD1 and achondroplasia were treated with lovastatin (and other statins). This treatment rescued the cartilage formation phenotype of the cells, possibly via a mechanism that drives accelerated proteosomal degradation of mutant FGFR3 proteins.

In transgenic *Fgfr3*^{Ach} mice—a model for achondroplasia that is characterized by dwarfism, short limb bones and short snout—daily injections of rosuvastatin resulted in the elongation of skulls, ulnas, femurs and tibias. This finding suggests that statins have potential to be effective treatments for FGFR3 chondrodysplasias.

While these results are promising, Tsumaki does offer a word of caution. "As statins have been administered to large numbers of human patients for many years, there is abundant information on their safety, however, their effects on infants and juvenile patients are still largely unknown," he says.

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CORRECTION

Statin therapy for skeletal dysplasia

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In the version of this article originally published online and in print, the doi for the original article was cited incorrectly. The doi should have read 10.1038/nature13775 not 10.1038/nature13665. This has now been corrected online.