Selective RARγ Ligand-loaded Nanoparticles for Manipulation of Targeted Bone Growth

Summary

Imbalance in bone length, caused by congenital conditions or fractures, can result in progressive deformity and physical problems. To date, the only way to adjust these bone length problems are surgical procedures. UMB researchers have identified a nuclear retinoid receptor, RARγ, which controls the rate of transition from cartilage to bone and is therefore critical for longitudinal bone growth. They have developed a poly-L-lactide (PLLA)-based nanoparticle formulation for the targeted delivery and release of RARγ agonists and antagonists into the growth plate of specific bones. This represents a new method of treating abnormal bone growth by enhancing or blocking ossification.

Key Investigator
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Field
Orthopedics
Therapeutics
Drug Delivery System

Technology
Drug-targeting technology
Method of treatment for bone growth

Advantages
Pharmacological treatment can replace surgical standard of care

Regimen can be accompanied with other pharmacological treatments

Status
Available for licensing

UMB Docket Reference
MI-2017-124

External References

Technology

This technology allows the control of endochondral bone formation locally, anywhere in the body, through modulation of RARγ receptors. Delivery of a RARγ agonist via nanoparticles to one side of the growth plate, or systemically, induces early closure of the plate, which can be used to correct bone alignment in joints. Conversely, delivery of RARγ antagonists, systemically or via nanoparticles, can prevent the early closure of growth plates and promote cartilage growth, helping heal growth plate fractures by preventing bone-bridge formation. RARγ targeting can be combined with the delivery of bone morphogenetic protein (BMP), bone conducting grafting materials, and BMP/scaffold/skeletal progenitor cells to promote bone repair, heal fractures, and aid spinal fusion.

Market

Currently, surgery is the only mean to correct significant imbalance of bone length or malalignment of the bones. RARγ targeted therapies could replace these invasive growth-restriction and bone alignment surgeries. Only one FDA approved compound, BMP2, induces bone regeneration. It is typically used for spinal fusion surgery, fracture repair, amd bone distraction. However, a large dose of BMP can cause complications, including excessive ossification, local inflammation, loosening of fixative devices due to bone resorption, and is associated with an increase in cancer risk. Targeting of RARγ receptors combined with BMP therapy could decrease BMP-related complications and potentially decrease treatment costs.

Technology Status

Proof of concept experiments with RARγ agonist and antagonist nanoparticles have been performed in a tibia defect repair model in wild-type and R*ARγ*-null mice. These studies show bone repair is enhanced in *RARγ*-null mice, an effect mimicked by pharmacological isotype-specific antagonism of RARγ in a mouse ectopic bone model. In contrast, RARγ agonists inhibit chondrogenesis and reduce cartilage size.

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