



## Monoclonal Antibody Fragments for Targeting Therapeutics to Growth Plate Cartilage

### Summary (1024-character limit)

In collaboration with the National Cancer Institute (NCI), researchers at The Eunice Kennedy Shriver National Institute on Child Health and Human Development (NICHD) have discovered monoclonal antibodies that bind to matrilin-3, a protein specifically expressed in cartilage tissue, that could be used for treating or inhibiting growth plate disorders, such as a skeletal dysplasia or short stature. The monoclonal antibodies can also be used to target therapeutic agents, such as those for anti-arthritis, to cartilage tissue. NICHD seeks statements of capability or interest from parties interested in collaborative research to co-develop, evaluate, and/or commercialize treatment of skeletal disorders using targeting antibodies.

### NIH Reference Number

E-003-2014

### Product Type

- Therapeutics

### Keywords

- Growth plate, Human Growth Hormone, Skeletal Dysplasia,
- Short Stature, Anti-matrilin-3 Antibody, Monoclonal,
- Cartilage, Osteoarthritis, Arthritis
- Eunice Kennedy Shriver National Institute on Child Health and Human Development
- NICHD, Dimitrov, Baron

### Collaboration Opportunity

This invention is available for licensing and co-development.

### Contact

- John D. Hewes  
NCI - National Cancer Institute

240-276-5515

[John.Hewes@nih.gov](mailto:John.Hewes@nih.gov)

### Description of Technology

A child's growth is dependent on the proper functioning of the growth plate, a specialized cartilage structure located at the ends of long bones and within the vertebrae. The primary function of the growth plate is to generate new cartilage, which is then converted into bone tissue and results in the lengthening



of bones. Failure of the growth plate to function properly can result in short stature or sometimes a skeletal dysplasia, such as achondroplasia, in which the bones are not just short but also malformed. Current treatments for severe short stature and skeletal growth disorders are limited. Recombinant human growth hormone (GH) is typically used, but the results are often less than optimal and growth hormone has potential adverse effects.

Researchers at the [Eunice Kennedy Shriver National Institute on Child Health and Human Development \(NICHD\) Section on Growth and Development](#), collaborating with the [NCI Laboratory of Experimental Immunology](#), created human monoclonal antibody fragments that bind to matrilin-3, a protein specifically expressed in cartilage tissue. When injected intravenously in mice, these antibody fragments honed to cartilage and were not detectable in other tissues. Coupling these cartilage-binding antibodies to growth-stimulating endocrine factors, such as growth hormone and IGF-I, and paracrine factors, such as CNP, could allow therapy targeted specifically to growth plate, and also articular cartilage, thereby opening up broad new pharmacological approaches to treat skeletal dysplasias and short stature. The same approach could also be used in adults to treat articular cartilage diseases like osteoarthritis. The research is currently in preclinical development, with *in vitro* data and *in vivo* mouse model data demonstrating that these antibody fragments target cartilage *in vivo*.

The researchers are interested in licensing this technology or for a collaboration to explore applications of this new approach. For example, a collaborator could produce fusion proteins combining the antibody fragments with various chondrogenic proteins that enhance growth. The collaborator might produce and purify the fusion proteins, which could then be tested for therapeutic effects in mice by the NICHD investigators.

### Potential Commercial Applications

- A new treatment option for cartilage disorders, such as (1) skeletal dysplasias, (2) short stature, and (3) articular diseases like osteoarthritis

### Competitive Advantages

- Avoidance of the risks associated with systemic treatment using growth hormone, such as increased intracranial pressure, slipped capital femoral epiphysis, insulin resistance, and possibly type II diabetes

### Inventor(s)

[Jeffrey Baron \(NICHD\)](#), [Sao Fong \(Crystal\) Cheung \(NICHD\)](#), [Chun Kin Julian Lui \(NICHD\)](#), [Dimitar S. Dimitrov](#), [Zhongyu Zhu \(NCI\)](#)

### Development Stage

- Pre-clinical (in vivo)

### Publications

C.S. Cheung et al., Human monoclonal antibody fragments targeting matrilin-3 in growth plate cartilage.



[PMID 25690340]

Lui JC, et. al. Cartilage-Targeted IGF-1 Treatment to Promote Longitudinal Bone Growth. [PMID 30765323]

#### Patent Status

- **U.S. Provisional:** U.S. Provisional Patent Application Number 61/927,904, Filed 15 Jan 2014
- **PCT:** PCT Application Number PCT/US2015/011433, Filed 14 Jan 2015
- **U.S. Patent Issued:** U.S. Patent Number , Issued 18 Jun 2019
- **Foreign Filed:** EP (validated in France, Germany, and Great Britain) - Patent Application 15704405.8, Filed 14 Jan 2015
- **Foreign Filed:** Canadian - Patent Application 2931005, Filed 14 Jan 2015
- **Foreign Filed:** Australian - Patent Application 2015206515, Filed 14 Jan 2015
- **U.S. Patent Filed:** U.S. Patent Application Number 16/391,101, Filed 22 Apr 2019

#### Therapeutic Area

- Musculoskeletal