Synthetic-biological Approaches to Osteoarthritis
The SJTU-BioX-Shanghai Team

Osteoarthritis, also called degenerative arthritis, is the most common arthritis and the leading cause of disability. OA is characterized by the cartilage matrix degradation and the remodeling of underlying bone, and these will cause the stiffness of joint and pain. Most of people with ages over 60 suffer from this disease, more or less. Its widespread influence and the fact that current treatments are focused on symptomatic relief but lack essential efficacy to control the progression of this disease have interested us to carry out a project aimed at curing it.

With the synthetic biology to be applied to many aspects of health and medicine, experts in this field are talking about extending the traditional prokaryotic synthetic biology into the eukaryotic field. We decided to carry out the whole project in two: directions: a eukaryotic approach which is similar but superior to gene therapy and a prokaryotic approach of traditional engineered E. coli, and we intend to explore their advantages and prospects in comparison with each other.

Design of our approaches to OA

In order to achieve artificial control of the expression of cartilage genes, we build a high-control system. There are two main factors: in the first one is blue-light activated calcium ion channel channelrhodopsin-2 (ChR2), and the second one is our synthetic promoter sensitive to the activation of calcium-dependent signaling pathways.

How do we achieve artificial control?

A population control and clean system based on common OP system and inducible promoters of our engineered E. coli ensure that the biotin density will not go too high and all engineered E. coli will be cleaned with induction of a certain external signal such as adenosine.

How can we detect OA?

We designed a detecting device that will start the transcription of downstream genes under OA-characteristic hypoxia and inflammatory factor nitrogen oxide (NO). P53 promoter senses hypoxia and SufB protein will form a complex with NO that activates PoxB promoter.

What is our treatment to OA?

The problem we met when using OisA and OisB as the curing genes in E. coli is that they need to be encoded out of the bacterial body or even enter chorionocytes to promote their expected function. We fused signal peptides OmpA and 11-Aarginine (11-R) protein transduction domains onto the original OisA and OisB proteins and solved the problem.

Outlook

Our designs are not limited to therapies to OA-MFs present two frameworks rather than two approaches. By changing components, they could realize different functions and they could be utilized in various disciplines.