The regulation of chondrogenesis via Adiponectin receptors and the therapeutic agents for osteoarthritis

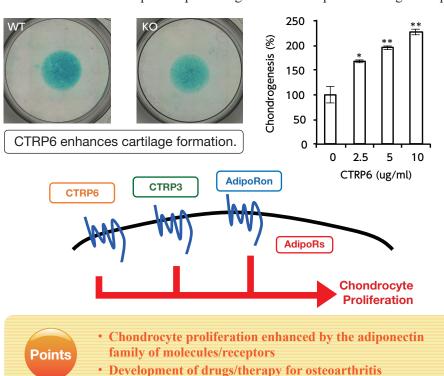
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Summary of Research

Osteoarthritis is a disease affecting many elderly people that is characterized by the deformity and degeneration of the articular cartilage, causing poor QOL and hindering the activities of daily life, substantially affecting healthy life expectancy. Osteoarthritis poses a great concern with the advent of the aging society because no radical treatment is available. In the present study, we have discovered that the adiponectin family of molecules and their receptors enhance the proliferation of chondrocytes. This finding is considered to be useful in developing new therapeutic agents for osteoarthritis.

Details of Research

No radical treatment is available for osteoarthritis. Regenerative medicine has received much attention recently, but there are still many problems that need to be worked out, and it will be some time before it can be used for practical applications. We found that a deficiency of CTRP6, a molecule in the adiponectin family of molecules, resulted in the spontaneous development of osteoarthritis and we analyzed its pathogenetic mechanism. As a result, we discovered that CTRP6 is a factor that enhances chondrocyte proliferation via adiponectin receptors. We also revealed that CTRP3 and AdipoRon, an adiponectin receptor agonist, have the same action. These findings strongly suggest that the drug discovery targeting the adiponectin family of molecules and their receptors is promising for the development of drugs/therapy for osteoarthritis.



Comparison with Conventional or Competitive Technologies

- Conservative therapy: Physical therapy, medication, and others
- Surgical therapy: Arthroscopic surgery, replacement arthroplasty, and others
 - → These are not radical treatments and impose a heavy burden.
- · Regenerative medicine: Stem cell therapy and others
 - → Stem cells derived from patients have a low proliferative capacity.

Expected Applications

- Direct application to the site of disease as a proliferation promoting agent for chondrocytes
- Proliferation promoting agents for chondrocytes derived from iPS cells and stem cells (improvement in quality of regenerative medicine)

Challenges in Implementation

- Investigation of the effects on chondrocytes derived from patients.
- Creation of a more specific agonist than ever before.

What We Expect from Companies

Osteoarthritis is one of the diseases requiring immediate action in association with the growing concern for the aging society. To solve this problem, we are willing to start a research collaboration program (basic/clinical research) to develop drugs/therapy.

Future Developments

Based on the findings obtained from the basic research to date, we wish to investigate the effects on chondrocytes derived from patients (including stem cells/iPS cells) with osteoarthritis and to conduct research and development aiming at clinical application.

- Intellectual Property: PCT Patent Application No. WO 2019/159925 "Proliferation promoting agents for chondrocytes, methods for enhancing chondrocyte proliferation, and screening methods for proliferation promoting agents for chondrocytes"
- Awards: Hideyo Noguchi Memorial Award for Medical Science (2015) Ando & Tajima Prize (2012)
 - Rheumatism Society Award (2009)
- Other: Mice with modified CTRP6 or CTRP3 genes, etc. can be



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