

# Overcoming arthritis

Science offers hope for removing achy joints from the aging equation

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## ABOUT THE LECTURE

Working at the interface between basic and clinical research, Dr. Martin Lotz described the key molecular players involved in maintaining the health of our joints and how these may go awry as we age or suffer a physical injury. Lotz unveiled local injectable medicines, gene therapies and repurposed drugs currently in development to help transform quality of life for the millions of people globally affected by osteoarthritis.

## TOP TAKEAWAY POINTS

1. **Along with aging, mechanical stressors** (e.g. joint injury, overuse) **and certain diseases** (e.g. obesity, metabolic diseases) are clinical risk factors for osteoarthritis.
2. **Osteoarthritis is initiated by structural degeneration of cartilage**, the tissue that acts as a biomechanical shock absorber in our joints. As the disease progresses, all tissues in the joint, cartilage, bone, meniscus, ligaments or synovial fluid are affected, associated with inflammation, a main driver of joint pain and physical activity limitations.
3. **No successful drug therapies currently exist to manage or prevent osteoarthritis**, partly because the key drivers of tissue damage have been difficult to identify. The Lotz lab uses technologies that show precisely which of our genes control the development and health of our joints and how these genes are acting abnormally in patients with osteoarthritis.
4. **Scientists in his lab have homed in on relevant “transcription factors,”** specialized proteins that switch on the genes involved in instructing our body to make cartilage during development and maintain tissue health throughout life. Evidence suggests these transcription factors are not functioning properly during the development of osteoarthritis. This leads to the detrimental activation of disease-promoting genes and cartilage destruction.
5. **One class of transcription factors called FOXO are critical for cellular health and longevity.** Removing FOXO experimentally leads to severely damaged cartilage and the progression toward osteoarthritis. Screening the Scripps Research library of over 12,000 existing compounds, Lotz’s team has pinpointed a drug able to block cartilage destruction and reduce inflammation, both in isolated human cells and animal models of osteoarthritis.
6. **Scientists are also studying transcription factors at work in the meniscus**, which commonly degenerates with age, leading to increased risk of a painful tear. Using gene therapy to elevate the activity of a transcription factor called Mohawk, the Lotz lab has been able to promote repair in meniscus tissue and significantly reduce the risk for osteoarthritis onset and progression.

