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Basic research in OA: Why is it important, and what have we learned

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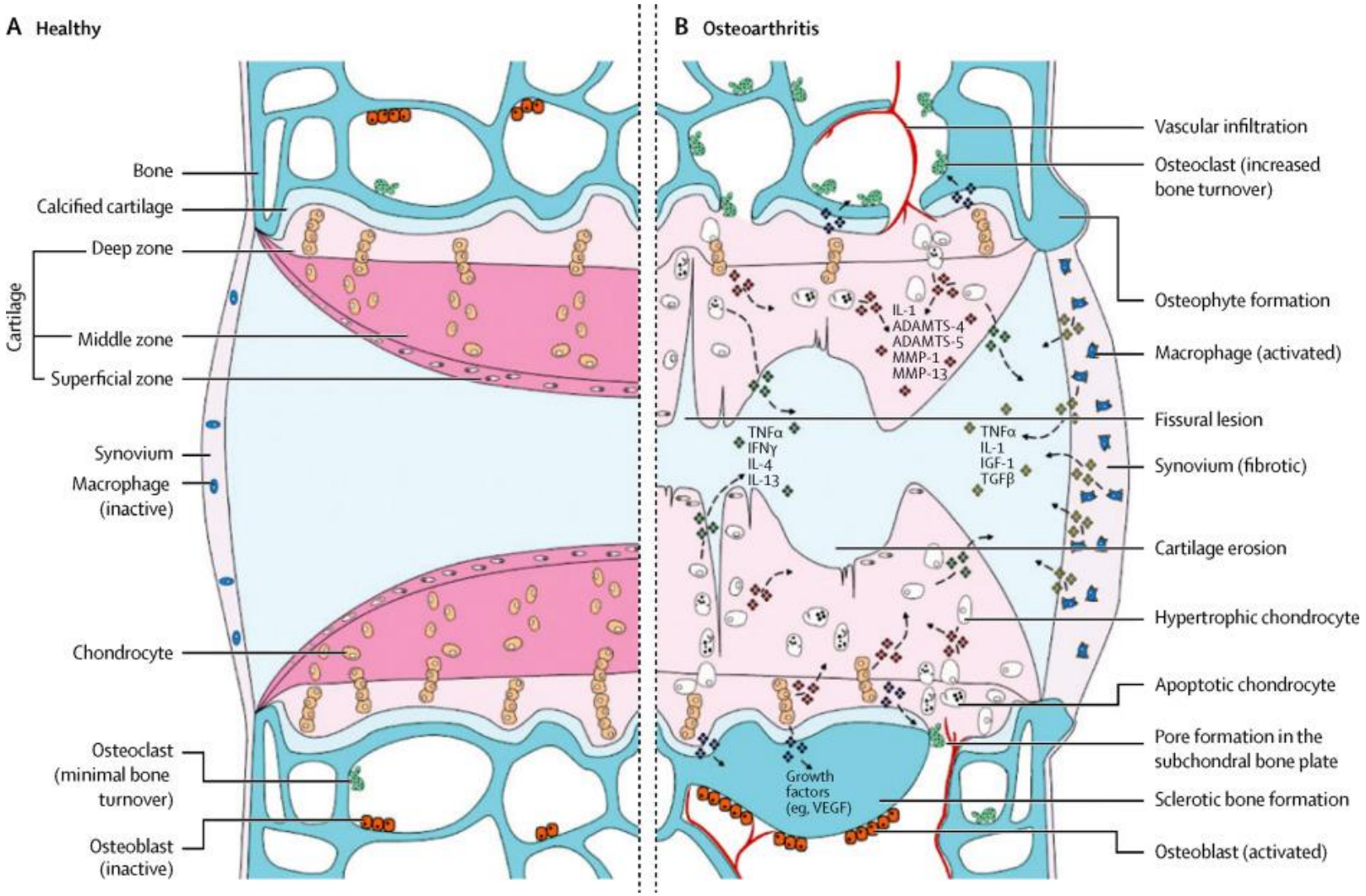

Glyn-Jones et al *Lancet* 2015

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"Basic research is systematic study directed toward greater knowledge or understanding of the fundamental aspects of phenomena and of observable facts without specific applications towards processes or products in mind. It includes all scientific study and experimentation directed toward increasing fundamental knowledge and understanding in those fields of the physical, engineering, environmental, and life sciences related to long-term national security needs. It is farsighted high payoff research that provides the basis for technological progress."

(Code of Federal Regulations of the United States)

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Basic research in OA:

- Trying to understand how the healthy joint works
- Identifying the causes and mechanisms of OA
- Biology, Chemistry, Mechanics, Epidemiology….
- Includes work with animal models and human samples

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Why is basic research in OA important ?

- No drugs that can slow, stop or reverse OA
- No diagnostic markers to detect OA early
- These deficiencies are due to our limited understanding of the causes and mechanisms
- Basic research is required to define them and to develop new treatments

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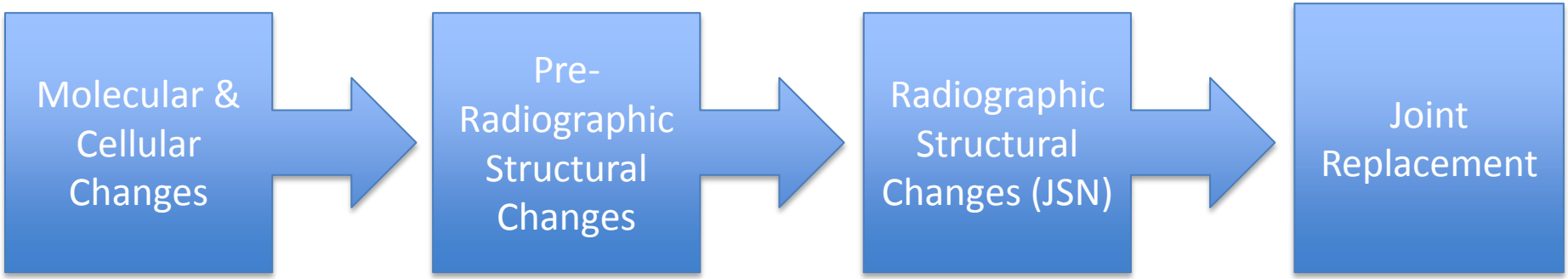
OA develops slowly over years or decades



→ Challenges to study early disease stages in human patients

→ Role of animal models

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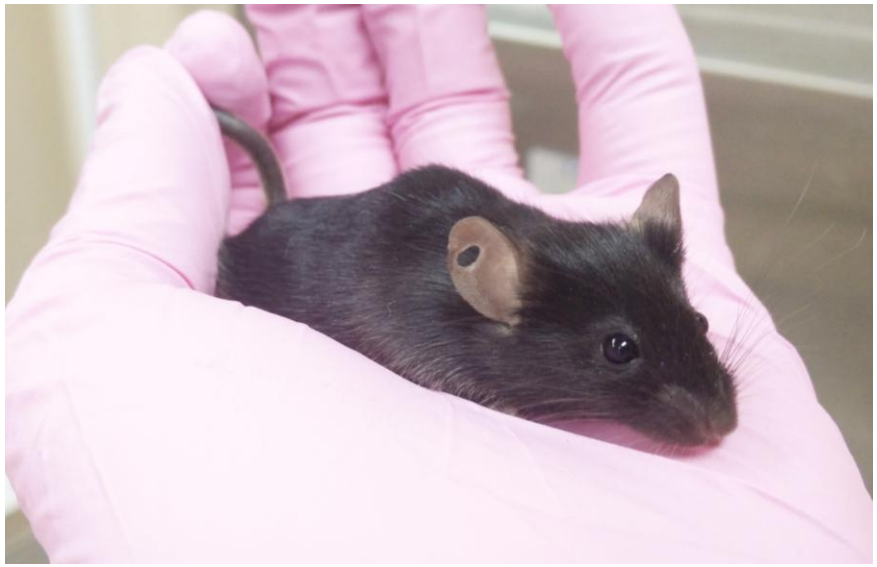
1. Emergence of the mouse as animal model of OA



- Biology of joint tissues is similar in human and mouse
- Mice provide un-matched tools for genetic manipulation

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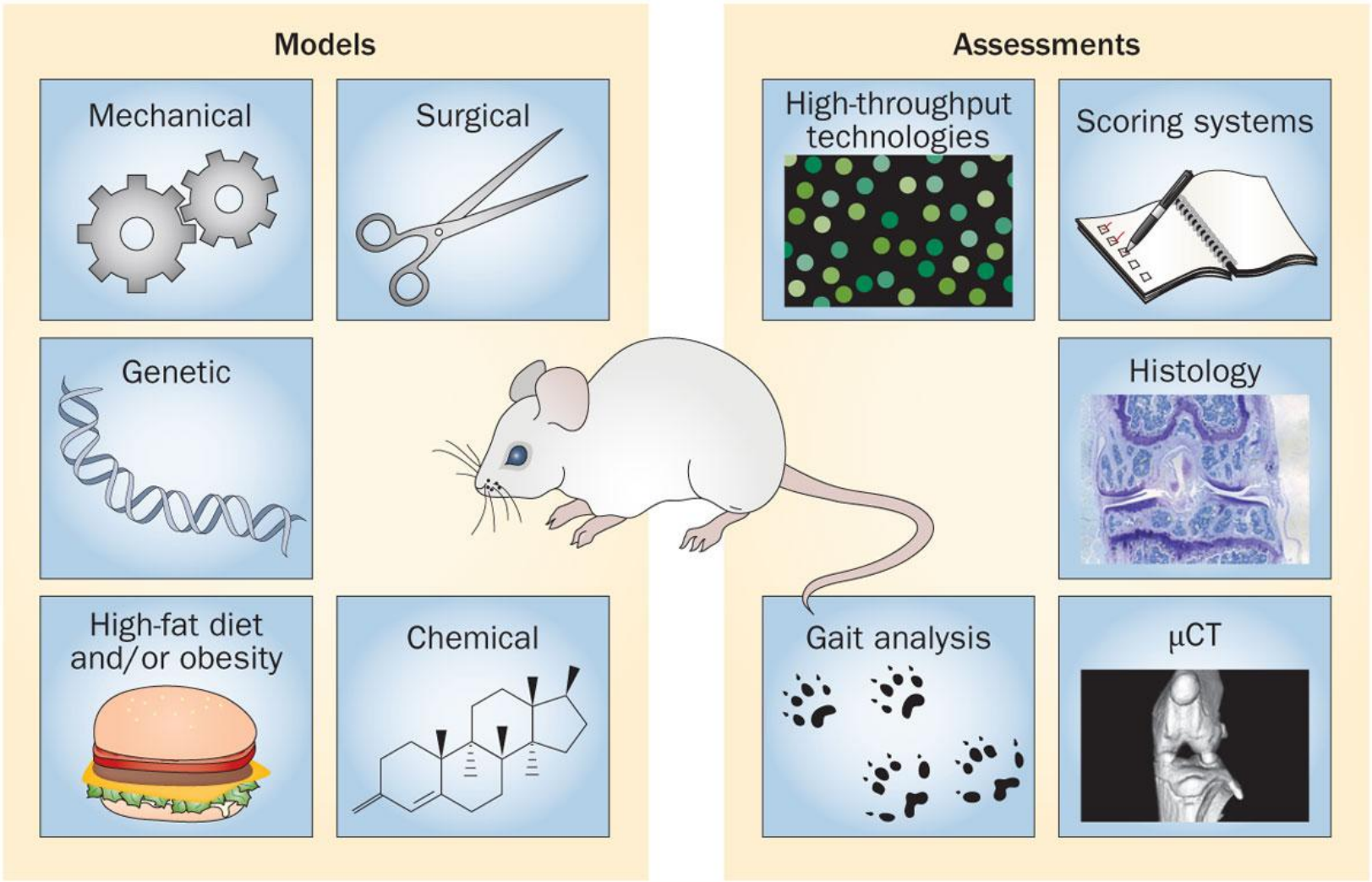

Hang & Beier *Nature Reviews Rheumatology* 2014

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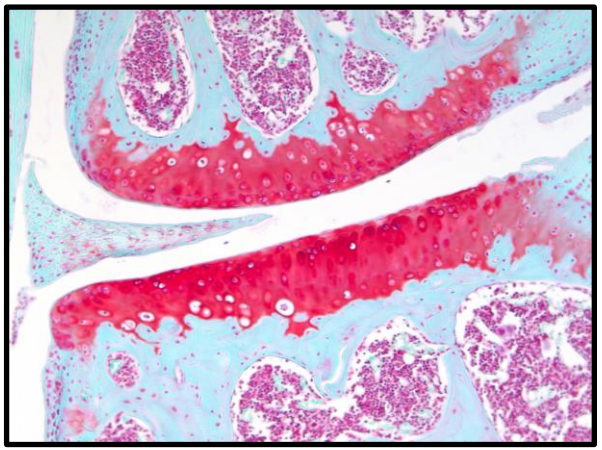
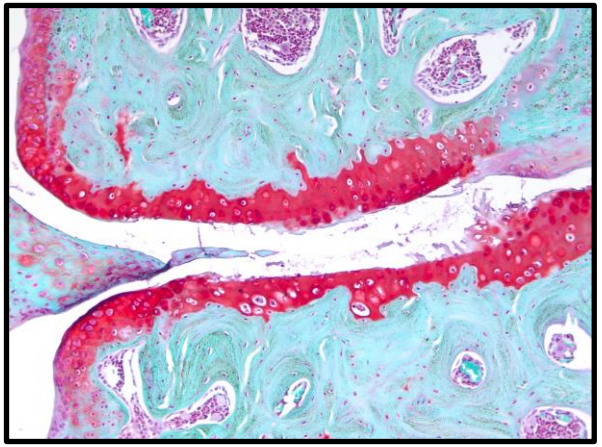
OA in a mouse knee joint

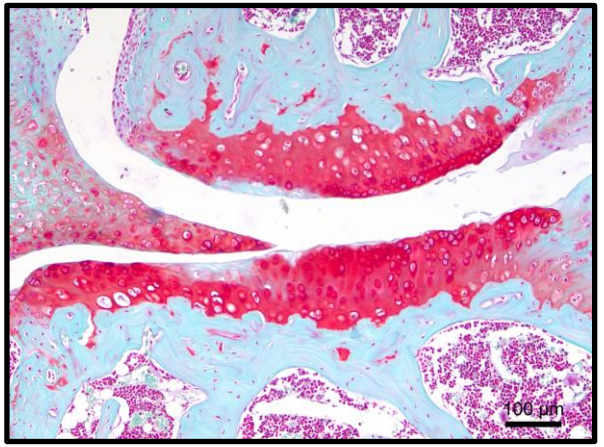
Normal knee joint



OA in control mouse



OA in mutant mouse



Ratneswaran et al. *Arthritis & Rheumatology* 2015

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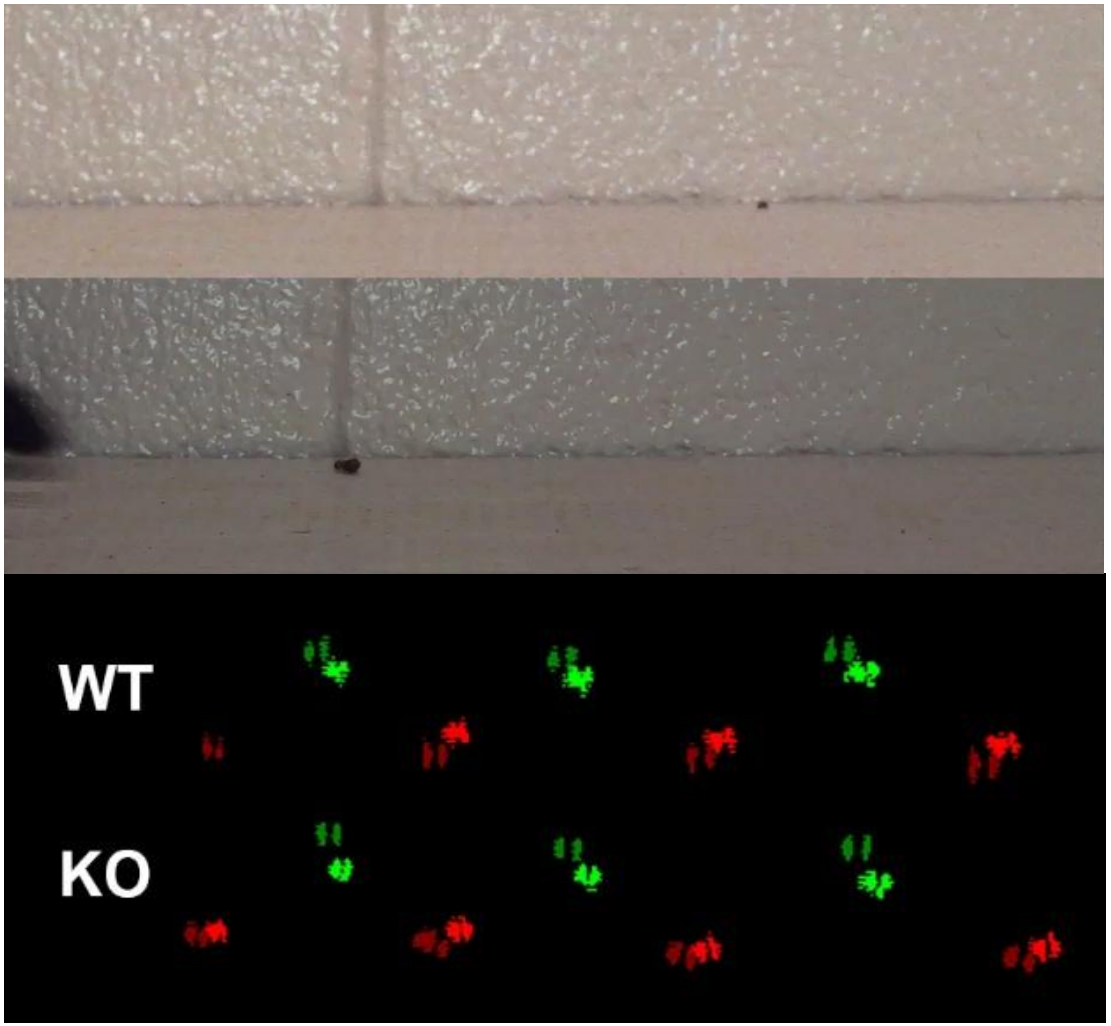
Gait analyses as functional outcome

Mutant

Control



Courtesy of Mike Pest

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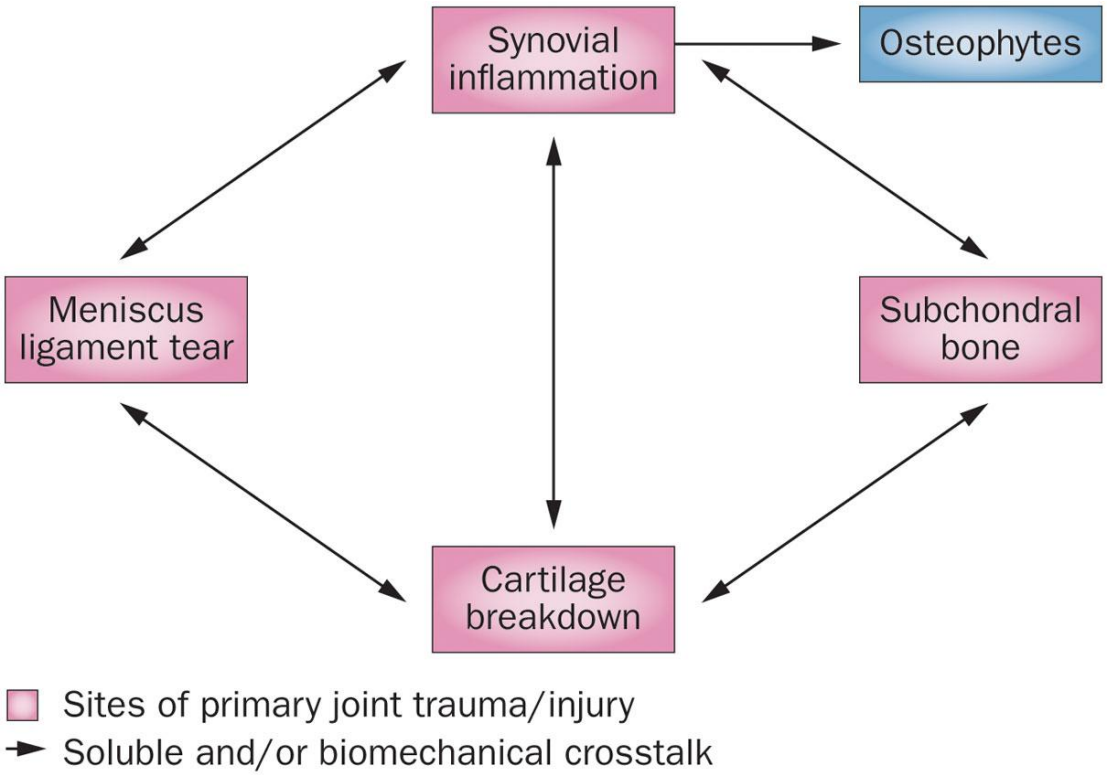
Tissue interactions in post-traumatic OA



Little & Hunter *Nature Reviews Rheumatology* 2013

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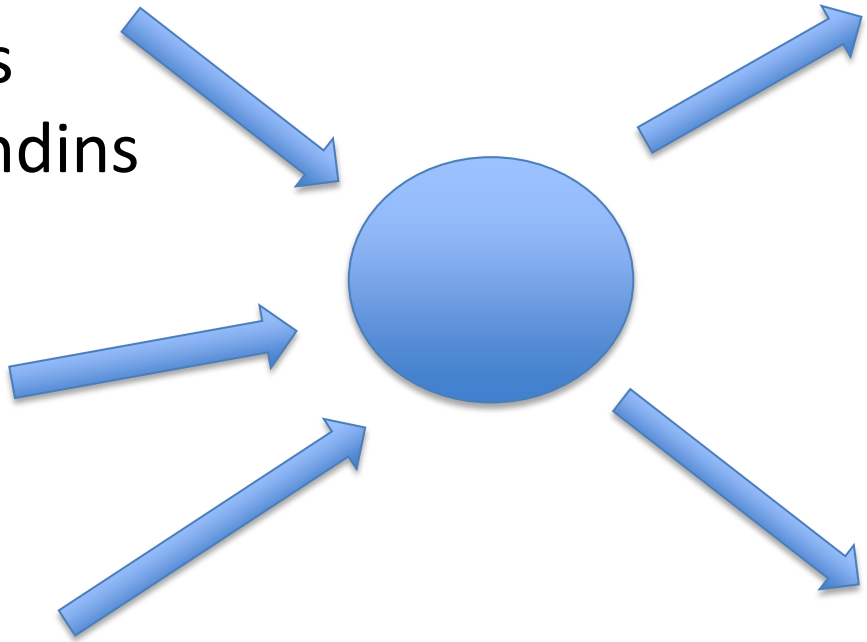
Chondrocyte behaviour is highly regulated

Growth factors
Cytokines
Hormones
Prostaglandins

Nutrients
Oxygen

ECM
Mechanical loading



Proliferation
Dedifferentiation
Hypertrophy
Autophagy
Senescence
Apoptosis

Gene expression
ECM remodeling

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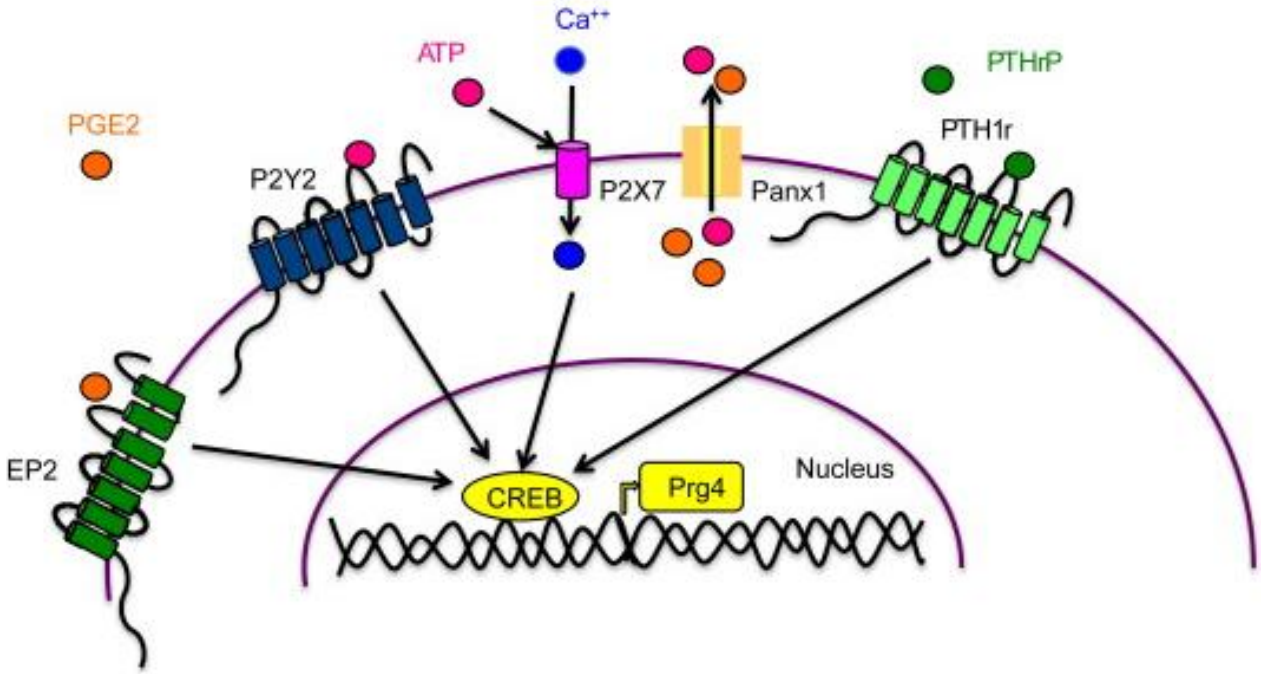
Cartilage Response to Mechanical Loading



Moyer, Ratneswaran et al. *Osteoarthritis & Cartilage* 2014