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

Frank Beier
Western Bone & Joint Institute
fbeier@uwo.ca
@BeierLab
“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)
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
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
OA develops slowly over years or decades

→ Challenges to study early disease stages in human patients

→ Role of animal models
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
Hang & Beier *Nature Reviews Rheumatology* 2014
OA in a mouse knee joint

Normal knee joint  OA in control mouse  OA in mutant mouse

Ratneswaran et al. *Arthritis & Rheumatology* 2015
Gait analyses as functional outcome

Mutant

Control

WT
KO

Courtesy of Mike Pest
Tissue interactions in post-traumatic OA
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
Cartilage Response to Mechanical Loading

Moyer, Ratneswaran et al. Osteoarthritis & Cartilage 2014