Priority Statement Title: New funding mechanisms for long-term studies of chronic joint disease

Priority Statement Code: CJ2F

Domain: multi-domain

Priority Statement

Background and Relevance

There are many prevalent theories concerning the role of mechanical factors in the development of chronic musculoskeletal disorders, such as osteoarthritis (OA) and disc disease. The premise of these theories is that even subtle alterations in joint loading, e.g. from joint injury or musculoskeletal disorder, can have an adverse impact on joint tissue health. The affects of altered loading can accumulate over many years, gradually degrading joint tissues and eventually leading to potentially irreversible joint disease. Causal relationships require long-term, prospective studies, as cross-sectional designs cannot distinguish between biomechanical factors that drive disease development and those that have resulted from it.

Most chronic musculoskeletal diseases (such as OA) can take many years to develop. Direct evaluations of the links between altered mechanics and definitive disease have been very difficult to establish. Such links have been identified in animal models, but the mechanics and rate of disease progression in humans are dramatically different. Thus, how the mechanisms identified in animals are related to progressive joint disease in humans is unknown. Also, whether early changes that can be identified with existing technologies actually progress to full-blown disease remains an open and important question.

The absence of sensitive imaging or bio-markers for early disease states (in spite of much investment from NIH) has continued to impede progress in this area. Even biomarkers that have been linked to early disease development are relatively insensitive to short-term change, requiring large sample sizes to identify meaningful effects. Longer followup would greatly increase affect size, enabling smaller sample size and significantly reducing study cost (especially for complex biomechanical studies).

Clear relationships between mechanical alterations and joint disease are essential for developing preventive programs and optimal treatments for preventing the development and/or progression of chronic joint disease. The 5-year maximum length of the standard NIH funding cycle presents a significant obstacle for designing studies that can definitively establish these links. Breaking up studies into smaller intervals is problematic, since in many cases it is difficult to achieve meaningful aims (other than meeting recruitment goals and collecting baseline data) or address significant hypotheses during the first 5 years. Large-scale projects, such as the Osteoarthritis Initiative, can be highly effective for large-scale studies. However, without a mechanism for funding smaller, investigator-initiated projects, many innovative and potentially significant ideas will remain untested.

Objective

- To create a mechanism for supporting studies of diseases that cannot be completed within a 5-year interval.

  Such studies could have a major impact on our understanding of the development and progression of all diseases that significantly impair quality of life. Though applicable to a wide range of diseases (including those outside of the musculoskeletal domain), this would be especially valuable for improving diagnosis and treatment of slow-developing musculoskeletal disorders. These studies are difficult to fund in a 5-year

time frame, since meaningful hypothesis testing often cannot be competed before the end of the project period.

Recommended Action

- Encourage the NIH to establish funding mechanisms for studies requiring greater than 5 years to achieve meaningful objectives, based on the time frame for detectable disease progression. Such mechanisms would allow greater flexibility for the timing of expenses, without necessarily increasing overall project budget relative to existing funding options.

  There are many possible approaches for implementing this recommendation. Many of these studies have the greatest cost early (for recruitment and baseline measurements) and late (for collecting long-term follow-up data and analyzing results), with lower costs in middle years. Thus, one approach might be to stage the projects, and authorize funding for the long-term component based on successful completion of aims for subject recruitment and baseline testing.