INTRODUCTION

We developed a novel in vivo testing system that allows for quantification of joint, cartilage and chondrocyte loading and for analysis of changes in proteins contained in the synovial fluid of intact knees in live mice [1]. While loading mice knees with different knee extensor forces, we observed a discoloration of the synovial fluid suggesting that synovial fluid composition changes during knee loading. The purpose of this study was to test this hypothesis and determine if synovial fluid might be used to quantify joint loading and serve as a “biomarker” for positive-adaptive and negative-degenerative responses to exercise loading. Synovial fluid can be extracted easily from human joints, and thus might become a powerful tool for developing safe muscular exercise programs.

METHODS

The medial aspect of the mouse knee (n=9) was exposed with a 6mm incision (Fig 1a). A sequence of 15 repeat, isometric muscular contractions of “low” intensity (less than 40% of the maximal muscular force), moderate intensity (40-55% of maximal) and “high” intensity (>55% of maximal) were applied repeatedly (up to five times with a fifteen minute break) to the mouse knee (Fig 1b). Changes in total synovial fluid borne protein and proteoglycan 4 (PRG4, also known as lubricin) content for the different loading conditions were measured and compared to resting values.

RESULTS

Increased loading of knees was accompanied with increases in total protein (p<0.0001) and PRG4 content (Fig 2). Total protein and PRG4 contents decreased significantly with repeat “intense” loading (Fig 2). Following the addition of cell inhibitors (Brefedin A and MI-141) to the knee, PRG4 levels remained below the detection limit for all loading conditions (Fig 3).

DISCUSSION AND CONCLUSIONS

We developed an in vivo joint loading model that allows for quantifying changes in protein content in the synovial fluid. We found that muscular exercise caused cells to release PRG4 and that increased intensity of knee loading resulted in an increase of total protein and PRG4 content. Total protein and PRG4 content decreased with repeat “intense” loading conditions. These results suggest that synovial fluid protein content may be a potent indicator for the intensity and duration of acute joint loading, and might serve as a powerful clinical tool to assess the effectiveness of rehabilitation and prevention exercise programs.


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