Knee function and pain are associated with differences in the proteomic landscape of knee osteoarthritis

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Identifying knee osteoarthritis (KOA)-specific biomarkers may provide means for early interventions and for subtyping KOA to individualize treatments. This study examined associations between knee function, pain and KOA-specific biomarkers.

Thirteen individuals with KOA and eleven controls performed the 30s Single Leg Mini Squat (SLMS) test and Sit-to-Stand test with simultaneous recording of joint kinematics. Individuals with KOA completed the Forgotten Joint Score-12 (FJS), and Knee Injury and Osteoarthritis Outcome Score (KOOS). In blood plasma samples, SureQuant quantitative Mass Spectrometry (MS) was used to identify 500 differentially expressed proteins (DEPs). Principal component analysis (PCA), hierarchical cluster analysis (HCA), and Reactome enrichment analysis of the proteome were conducted to identify groups. Group comparisons were performed using Student t-test, and correlations between clinical measures and MS data using Spearman's Rho.

Individuals with KOA displayed poorer joint function than controls, with fewer SLMS (Figure 1A) and sit-to-stand repetitions. MS analysis identified 392 proteins across all participants; 25 up-regulated and 58 down-regulated DEPs in KOA. PCA displayed distinct features between KOA and controls (Figure 1B), similar to HCA. Twelve DEPs were associated with knee function, and seven with pain outcomes. SLMS knee kinematics was moderately associated with a bone resorption marker (CAH2) (Figure 1C), and FJS and KOOS-Pain correlated with markers of platelet degranulation and inflammation.

We identified specific proteins related to knee function and pain. Further exploration of protein characteristics and associations with clinical measures may contribute to a better understanding of the underlying disease mechanisms, and provide novel biomarkers for targeted treatment.