**Proteomic Identification of Predictive Autologous Chondrocyte Implantation Biomarkers in Plasma**

Objectives

Stratification is required to ensure that only those patients likely to benefit, receive Autologous Chondrocyte Implantation (ACI); ideally by assessing a biomarker in the blood. This study aimed to assess differences in the plasma proteome of individuals who respond well or poorly to ACI.

Methods

Isobaric tag for relative and absolute quantitation (ITRAQ) mass spectrometry and label-free proteomics analyses were performed in tandem as described previously by our group (Hulme et al., 2017; 2018; 2021) using plasma collected from ACI responders (n=10) compared with non-responders (n=10) at each stage of surgery (Stage I, cartilage harvest and Stage II, cell implantation).

Results

iTRAQ using pooled plasma detected 16 proteins that were differentially abundant at baseline in ACI responders compared with non-responders (n=10) (≥±2.0 fold; p<0.05). Responders demonstrated a mean Lysholm (patient reported functional score from 0-100) improvement of 33±13 and non-responders a mean worsening of -13±13 points. The most pronounced plasma proteome shift was seen in response to Stage I surgery in ACI non-responders, with 48 proteins being differentially abundant between the two surgical procedures. We have previously noted this marked shift in response to initial surgery in the SF of ACI non-responders, several of these proteins were associated with the Acute Phase Response. One of these proteins, clusterin, could be confirmed in patients’ plasma using an independent immunoassay using individual samples. Label-free proteomic data from individual samples identified only cartilage acidic protein (known to associate with osteoarthritis progression) to be significantly more abundant at Stage I in the plasma of non-responders.

Conclusions

This study indicates that proteins can be identified within the plasma that have potential use in ACI patient stratification. Further work is required to validate the findings of this discovery-phase work in larger ACI cohorts.