**Altered Acute Phase Response (APR) signalling following cartilage harvest can be identified in the plasma of ‘non-Responder’ Patients to Autologous Chondrocyte Implantation**

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**Purpose**

Stratification is required to ensure that only patients likely to benefit, receive Autologous Chondrocyte Implantation (ACI). At Stage I (SI), healthy cartilage is harvested from the joint and chondrocytes culture expanded before being implanted into a chondral/osteochondral defect at Stage II (SII). In ACI non-responders, there is a marked shift in the profile and abundance of proteins detectable in the synovial fluid (SF) at SII, many being associated with an acute phase response (APR)1. However, clinical biomarkers are easier to measure in blood than SF, so we have now performed this investigation in plasma.

**Methods**

Isobaric tag for relative and absolute quantitation mass-spectrometry was used to assess the proteome in plasma pooled from ACI responders (mean Lysholm improvement of 33, n=10) or non-responders (mean: -13 points, n=10), collected at SI or SII surgeries. Interactome networks were generated using STRING. Plasma proteome data were compared to matched SF data, previously analysed, to identify any proteins that changed across the fluids. Clusterin concentration was quantitated (ELISA; Biotechne).

**Results**

The most pronounced plasma proteome shift was seen in response to SI surgery in ACI non-responders (50 proteins; ±2.0FC; p<0.05). An interactome network was generated based on these proteins. Functions associated with this network included complement and coagulation cascade (FDR= 5.99x10-25). Sixteen matched proteins were differentially abundant between SI and SII in both the SF and plasma, 75% of which were APR associated proteins. These included clusterin, which was confirmed by ELISA (p=0.001).

**Conclusions**

Changes in APR signalling between SI and SII surgeries in non-responders to ACI can be identified in plasma and SF. The APR is the body’s first systemic response to trauma and surgery. Our data indicate that ACI non-responders may have a greater innate response to initial surgery, which is detectable in both their SF and plasma.