Ribosomal profiling and secretome analysis identify that interleukin-1b driven cytokine/chemokine release from chondrocytic cells is underpinned by differential translation

**Purpose**

Mediators such as interleukin-1β (IL-1β) are increasingly thought to modulate chondrocyte function in the inflamed osteoarthritic joint. The response of chondrocytes to a number of cytokines has been well characterised, with prolonged stimulation leading to increases in catabolic factors. The early responses of chondrocytes to cytokine stimulation are not as well understood although it is clear that rapid cell signalling occurs. In this study, we have examined the early secretory response of SW1353 chondrosarcoma cells to IL-1β stimulation. We have combined ribosome profile data analysis with proteome and secretome measurements.

**Methods**

SW1353 cells were treated with 10ng/ml IL-1β for 3-hours or 24-hours under serum free conditions. Ribosome-protected and total RNA was isolated from 3 hour cultures. RNA samples were analysed using RNA Seq. Secreted proteins in the media were examined at 24-hours. Differential translation was assessed from the RNA-Seq datasets using the riboseqR package through the RIboGalaxy web interface. Secretome analysis was carried out using Progenesis software.

**Results**

When differential translation was examined 3-hours after IL-1β stimulation we observed regulation of two major subsets of mRNAs encoding ribosomal proteins and inflammatory proteins. Notably there was differential translation of a suite of chemokines and cytokines, alongside known cytokine-associated signalling molecules. Secretome analysis after 24 hours IL-1β treatment also identified increased accumulation of these cytokine/chemokines in the cells’ media.

**Conclusions**

SW1353 cells represent a common model system to investigate chondrocyte responses to cytokines and in this study offered the cell numbers required to perform the ribosomal profiling technique. The study has shown that IL-1β stimulation the release of a suite of cytokines and chemokines, many of which can be attributed to rapid alterations in translational efficiency. Further clarification of altered translation is required in primary cells using targeted approaches. An increased inflammatory environment is now considered to be a key influence on osteoarthritis pathology and understanding the responses of joint cells to inflammatory stimuli are of critical importance. The extent of how a chondrocyte secretory response, suggested by our data, might propagate further inflammatory responses within the joint is not clear and warrants further investigation.