Background: RA is a chronic inflammatory disease affecting 1% of the population. The aetiology of RA is unknown, although there are multiple postulated theories. In 1950, Philip Hench won the Nobel Prize for treating patients with RA with cortisone. He also treated 8 patients with adrenocorticotropic hormone (ACTH) with good results. ACTH is a melanocortin. The melanocortin system describes the five melanocortin receptors, their ligands, agonists and antagonists and the accessory proteins. The aim of this study was to explore the melanocortin receptors in RA synovium.

Methods: HA-tagged stable cell lines were created for MC1R, MC3R and MC5R. Multiple antibodies were tested for their utility using Western Blot, immunohistochemistry and flow cytometry. Samples of synovium from 28 patients with RA were tested using RTPCR for the presence of MC1R and MC3R. Gene expression was correlated with...
Results: The stable cell lines expressed MC1R, MC3R and MC5R respectively. Of the antibodies tested none were found to be of utility in detecting MC1R or MC3R. The MC1R RQ values in rheumatoid synovium appear to split into two groups, high and low. The medians of the two groups are significantly different ($P = 0.0005$). There is almost a 5 cycle, or 64 fold, difference in gene expression between the medians of the two groups (1.59 vs 6.23). Of note no MC3R positive samples were CD138 high (i.e. no MC3R positive samples had a significant plasma cell infiltrate) ($P = 0.006$). Categorical analysis using Fishers Exact test revealed an association between MC1R high samples and CD68 lining high scores (i.e. MC1R high samples also had a high macrophage score in the lining of the sample) ($P = 0.02$). MC1R low samples were associated with not being on combination therapy, this did not quite reach significance ($P = 0.07$). Linear regression analysis confirmed these associations for MC1R. PCA analysis did not show any grouping of samples according to any of the variables tested, likely due to sample size.

Conclusion: MC1R and MC3R are found in human synovium. Current commercial antibodies are not of utility in detecting MC1R or MC3R. Synovial samples can be split into high and low MC1R gene expression groups. MC3R was either present or absent. High expression of MC1R was associated with a high macrophage score and MC3R expression was associated with a low plasma cell score. MC1R and MC3R expression in RA synovium could be used as biomarkers of disease state or severity as well as a target for therapy.

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