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# HCgp-39 positive monocytes in peripheral blood and synovium

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## Keywords

HCgp-39, rheumatoid arthritis

# Context

HCgp-39 is a candidate autoantigen in rheumatoid arthritis (RA). Although it remains unclear whether HCgp-39 is a protagonist in the pathogenesis of RA, over 50% of patients with RA, as well as some control subjects, mount secondary T cell proliferative responses to HCgp-39 peptides. HCgp-39 appears to be secreted in the inflamed joint since protein is present in the synovial fluid and mRNA has been detected in both cartilage and synovial tissue of RA patients. Recently, a new HCgp-39-induced murine model of inflammatory arthritis was described in BALB/c mice, suggesting that this glycoprotein might be an attractive target for immunotherapy. The localisation of HCgp-39 is not confined to the inflamed joint since it has been demonstrated at a number of sites of inflammation or involution, including cirrhotic liver, giant cell arteritis and post-lactational breast tissue. Therefore, although the function of HCgp-39 is unknown, a role in tissue remodelling has been proposed. To examine the cellular localisation of HCgp-39 within peripheral blood and synovial membrane and explore the correlation between the level of HCgp-39 expression and clinical features of RA.

# Significant findings

Immunohistochemistry demonstrated that the HCgp-39$^{+}$ cells were clustered in foci, sometimes even nodules, in the lining layer. Although they were not specific to RA, they occurred more frequently in RA than in the other arthritic patient groups. Furthermore, the number of serum HCgp-39$^{+}$, CD16$^{+}$ monocytes correlated significantly with serum HCgp-39 levels in 23 RA patients ($r = 0.52$; $P = 0.014$), and with C-reactive protein levels and erythrocyte sedimentation rate. There was a highly significant correlation between HCgp-39$^{+}$ cells in the synovial lining layer and the radiologic score ($r = 0.771$; $P < 0.001$).

# Comments

This paper indicates that the synovial autoantigen, human cartilage glycoprotein (HCgp)-39, is synthesised in synovial monocytes, although it is possible that these cells contain ingested HCgp-39. It appears to have been technically difficult to isolate human cartilage glycoprotein (HCgp)-$39^+$ cells from synovial samples in order to examine their phenotype. The correlation between the frequency of HCgp-$39^+$ cells in the synovium and markers of disease activity is interesting, irrespective of the cellular source of the HCgp-39. These data support the notion of an active role for HCgp-39 in inflammatory joint disease, although it remains unclear whether this protein contributes more to destruction or to reconstruction.

# Methods

Peripheral blood mononuclear cells (PBMCs) were obtained from patients with RA, spondyloarthropathy (SpA), osteoarthritis (OA) and liver cirrhosis as well as from healthy controls (n = 22). Cytospins and FACS analysis revealed that the percentage of HCgp-$39^+$ cells was higher in RA patients than healthy controls ($P < 0.00001$) and SpA patients ($P = 0.0022$) but similar to the percentage in patients with hepatic cirrhosis and OA. The HCgp-$39^+$cells all had a monocyte morphology and FACS analysis confirmed that they comprised a subset of monocytes, expressing CD68, CD15, CD16 and usually CD14, CD33 and HLA-DR. This phenotype was distinct from that of both classical monocytes and immature dendritic cells. Synovial membrane biopsies were taken from patients with RA, SpA and OA.

## References

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