

The impact of *Fasciola hepatica* excretory-secretory products on human macrophage polarization

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Helminths are considered as masters of immunoregulation due to their ability to modulate the host immune response and escape its defense mechanisms, ultimately allowing their long-term survival and establishment of chronic infections. Recently, several studies have shown that parasite-derived molecules could reduce the severity of various immune-related diseases. This effect may be due to the immunomodulatory properties of specific parasite proteins, at least in part through their direct influence on macrophage polarization. Altogether, parasite-derived molecules may be a great source of unique molecules for manipulating immune processes or inducing tissue-specific beneficial immune responses. In the present study, our aim was to investigate the effects of the F. hepatica adult parasite excretory-secretory products (ESA) on macrophage polarization using primary human monocyte derived macrophages.

For this purpose, monocytes were isolated from human blood and differentiated to macrophages with human recombinant M-CSF. The differentiated cells were polarized towards M0, M2 and M1- like macrophages and next treated with ESA for 48h. The secreted cytokines profile was determined using proteome profiler antibodies arrays and ELISA.

We found that ESA reduced the secretion of various prototypical inflammatory cytokines (e.g. TNF-α and IFN-γ) both in M0 and M1 macrophages. Similarly secretion of chemokines (e.g. CCL20, CXCL1, CXCL5 and CXCL11) was decreased in both types of macrophages. Interestingly we could observe induction of growth factors secretion (e.g. FGF-19 and GDF-15) in M0 and M1 ESA treated macrophages what characterise M2 macrophage polarization. Moreover, inhibitory effect for some of the cytokines and chemokines was dose dependent and induced by enzymatic activity of ESA as heat inactivation reduced inhibitory activity of parasite products. Altogether, our preliminary data suggest that ESA might trigger macrophage repolarization from pro-inflammatory (M1-like) towards an anti-inflammatory (M2-like) phenotype. Further studies are required to explore the exact underlying mechanisms and to identify molecule/s that induces this effect.

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