CD163

CD163 (Cluster of Differentiation 163) is a protein that in humans is encoded by the CD163 gene.

CD163 is the high affinity scavenger receptor for the hemoglobin-haptoglobin complex and in the absence of haptoglobin - with lower affinity - for hemoglobin alone.

Macrophage CD163 is a hemoglobin scavenger receptor involved in blood clearance after SAH.

It also is a marker of cells from the monocyte/macrophage lineage.

CD163 functions as innate immune sensor for gram-positive and gram-negative bacteria.

The receptor was discovered in 1987.

The molecular size is 130 kDa. The receptor belongs to the scavenger receptor cysteine rich family type B and consists of a 1048 amino acid residues extracellular domain, a single transmembrane segment and a cytoplasmic tail with several splice variants.

A soluble form of the receptor exists in plasma, and cerebrospinal fluid., commonly denoted sCD163. It is generated by ectodomain shedding of the membrane bound receptor, which may represent a form of modulation of CD163 function.

sCD163 shedding occurs as a result of enzymatic cleavage by ADAM17.

sCD163 is upregulated in a large range of inflammatory diseases including liver cirrhosis, type 2 diabetes, macrophage activation syndrome, Gaucher's disease, sepsis, HIV infection, rheumatoid arthritis and Hodgkin Lymphoma.

Differences between mouse and man in CD163 biology are important to note since preclinical studies are frequently conducted in mice. sCD163 shedding occurs in man but not mouse, due to the emergence of an Arg-Ser-Ser-Arg sequence in man, essential for enzymatic cleavage by ADAM17.

Human CD163, but mouse CD163, exhibits a strikingly higher affinity to hemoglobin-haptoglobin complex compared to hemoglobin alone.

Pigs with a section of the CD163 gene removed showed complete resistance to the virus that causes Porcine Reproductive and Respiratory Syndrome.

CD163 has been shown to interact with CSNK2B.

Thomas et al., from the Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, hypothesized that the modified Fisher scale is independently associated with cerebrospinal fluid (CSF) macrophage CD163 expression on postictal day 1, and that CSF macrophage CD163 expression is associated with 1-month neurological outcome.

CSF macrophages from 21 SAH and 28 unruptured aneurysm patients (control) were analyzed for CD163 expression using flow cytometry and confocal microscopy on postictal day 1. Significant associations with modified Fisher scale grades or modified Rankin Scale scores were determined using

linear regression and a matched case control study.

CSF macrophage CD163 expression was significantly increased in SAH patients compared with controls ($p < 0.001$). The modified Fisher scale (mF) grades ($\beta = 0.407$, $p = 0.005$) and CSF bilirubin concentrations ($\beta = 0.311$, $p = 0.015$) were positively and independently associated with CSF macrophage CD163 expression when the analysis was controlled for age and sex. CSF macrophages from an SAH patient with a high mF grade had increased co-localization of CD163 and glycophorin A (CD235a, an erythrocyte marker) compared with those from an SAH patient with a low mF grade. The controls had no co-localization. CSF macrophage CD163 expression ($p = 0.003$) was inversely associated with 1-month neurological outcome, when SAH patients were matched based on mF grade.

This early study suggests that CSF macrophage CD163 expression, as measured by flow cytometry, may have some neuroprotective function given its inverse association with outcome and provides unique insights into the neuroinflammatory process after SAH [1].

1)
Thomas AJ, Ogilvy CS, Griessenauer CJ, Hanafy KA. Macrophage CD163 expression in cerebrospinal fluid: association with subarachnoid hemorrhage outcome. J Neurosurg. 2018 Jul 20:1-7. doi: 10.3171/2018.2.JNS172828. [Epub ahead of print] PubMed PMID: 30028262.