

Department of Immunology

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"Scavenger receptors and macrophage activation phenotypes"

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Macrophages express various kinds of scavenger receptors. In the present talk, I will focus on two scavenger receptor molecules, CD204 (class A scavenger receptor) and CD163 (hemoglobin scavenger receptor).

CD204 is a macrophage-restricted multifunctional receptor which binds modified low density lipoproteins (LDLs) such as acetylated LDL and oxidized LDL, and a diverse array of other negatively charged macromolecules. It plays an important role in the pathological deposition of cholesterol in macrophage-derived foam cells during atherogenesis through receptor-mediated uptake of modified LDL. Targeted disruption of the CD204 gene resulted in a reduction in the size of atherosclerotic lesions in atherosclerosis model mice. It is also important in inflammation by optimizing the inflammatory response by modulating the activity of inflammatory cytokines. In the experimental myocardial infarction produced in CD204-deficient mice, exaggerated inflammation induced sudden death caused by cardiac rupture. Real-time RT-PCR showed increased expression of MMP-9 mRNA in the infarcted myocardium in knockout mice. Augmented expression of TNF-alpha and reduction of interleukin-10 were also observed.

CD163 is a member of the scavenger receptor cysteine-rich superfamily that recognizes haptoglobin-hemoglobin complexes (hemoglobin scavenger receptor). Since CD163 expression is induced by interleukin-10 and glucocorticoid but down regulated by lipopolysaccharide and interferon-gamma, it is thought to be one of the molecules associated with an anti-inflammatory macrophage phenotype as well as CD204.

Accumulated evidence indicates that M2 polarized anti-inflammatory tumor-associated macrophages (TAMs) contribute to tumor development and poor prognosis in various cancers. To evaluate the role of TAM in human cancer tissues we utilized CD163 and CD204 as a marker for M2 macrophages. By immunohistochemical staining of paraffin-embedded tissues of glioma and epithelial ovarian cancer, we found that the numbers of CD163- and CD204-positive macrophages are positively associated with the histological grade of malignancy. Intimate association between the density of CD163-positive TAMs and patient's poor prognosis was also observed in intrahepatic cholangiocarcinoma. These observations indicate that CD163 and CD204 are useful markers for evaluating M2-polarized TAMs in tissue sections and predicting the clinical prognosis of the patients bearing some types of cancers.