# 論　文　要　旨

## Expression of glycoprotein nonmetastatic melanoma protein B in macrophages infiltrating injured mucosa is associated with severity of experimental colitis in mice

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Glycoprotein nonmetastatic melanoma protein B (Gpnmb) is a transmembrane glycoprotein that negatively regulates the inflammatory responses of macrophages. The role of Gpnmb in intestinal macrophages, however, remains unclear. We investigated Gpnmb expression and its effects on colonic mucosal injuries associated with dextran sulfate sodium (DSS)-induced colitis in BALB/c mice, DBA/2J (D2) mice lacking Gpnmb, and Gpnmb-transgenic DBA/2J (D2-gpnmb+) mice. Colonic expression of Gpnmb increased with the severity of DSS-induced colitis in BALB/c mice, and macrophages infiltrating the inflamed mucosa expressed Gpnmb. Compared to D2-gpnmb+ mice, however, D2 mice lacking Gpnmb exhibited more severe DSS-induced colitis, accompanied by higher levels of proinflammatory cytokines such as interleukin (IL)-1β and IL-6. Following lipopolysaccharide stimulation, macrophages from D2 mice expressed higher levels of proinflammatory cytokines and lower levels of IL-10, than D2-gpnmb+mice. Additionally, in the RAW264.7 murine macrophage cell line, knockdown of Gpnmb by small interfering RNA was associated with higher production of proinflammatory cytokines which were potentially mediated by the extracellular signal-regulated kinase (ERK) and p38 signaling pathways. Our results indicate that macrophages infiltrating injured mucosa express Gpnmb, and Gpnmb-positive macrophages may ameliorate inflammation in the intestinal mucosa by decreasing proinflammatory cytokine production *via* the ERK and p38 signaling pathways.