

Srini V. Kaveri, Gregg J. Silvermann and Jagadeesh Bayry (2012). Natural IgM in Immune Equilibrium and Harnessing Their Therapeutic Potential. *J Immunol* 188, 939-945.

Natural IgM Abs are the constitutively secreted products of B1 cells (CD5⁺ in mice and CD20⁺CD27⁺CD43⁺CD70⁻ in humans) that have important and diverse roles in health and disease. Whereas the role of natural IgM as the first line of defense for protection against invading microbes has been extensively investigated, more recent reports have highlighted their potential roles in the maintenance of tissue homeostasis via clearance of apoptotic and altered cells through complement-dependent mechanisms, inhibition of inflammation, removal of misfolded proteins, and regulation of pathogenic autoreactive IgG Abs and autoantibody-producing B cells. These observations have provided the theoretical underpinnings for efforts that currently seek to harness the untapped therapeutic potential of natural IgM either by boosting in vivo natural IgM production or via therapeutic infusions of monoclonal and polyclonal IgM preparations.