Antibodies Against Fcrn And Use Thereof

RELATED APPLICATIONS

This application claims the benefit under 35 U.S.C. § 119(e) of U.S. provisional application 61/048,152, filed April 25, 2008, and U.S. provisional application 61/048,500, filed April 28, 2008, the entire disclosures of which are incorporated herein by reference in their entirety.

BACKGROUND

The most abundant antibody isotype in the serum is IgG and it has a critical role in mediating protection against pathogens as well as in mediating allergic and inflammatory responses that hasten recruitment of immune system components to the tissues, mucosae, and dermal surfaces (Junghans, Immunologic Research 16(1):29 (1997)). Moreover, it is also a key component of a variety of autoimmune diseases. Under normal conditions, the halflife of IgG in the serum is in the range of 5-7 days in mice and 22-23 days in humans, which is a prolonged period, relative to the serum half life of other plasma proteins. In part, this occurs because the neonatal FcRn receptor (FcRn) rescues pinocytosed IgG from degradative lysosomes and recycles it back to the extracellular compartment (Junghans and Anderson, Proc. Natl. Acad. Sci. USA 93:5512 (1996), Roopenian et al. J. Immunology 170:3528 (2003)).

FcRn binds to the the Fc portion of IgG. The interaction between the IgG Fc region and FcRn is pH-dependent. Upon entry into cells by fluid phase endocytosis, IgG is sequestered into endosomes and binds to FcRn with high affinity at acidic pH (6~6.5); when the IgG-FcRn complex cycles to the plasma membrane, IgG dissociates rapidly from FcRn in the bloodstream at slightly basic pH (~7.4). By this receptor-mediated recycling mechanism, FcRn effectively rescues the IgG from degradation in lysosomes, thereby prolonging the half-life of circulating IgG.