NEONATAL FC RECEPTOR (FCRN) TRANSGENIC RABBITS SHOW IMPROVED ANTIBODY PRODUCTION AGAINST CHALLENGING ANTIGENS

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We previously reported that the genetically modified mice that overexpress the bovine (b)FcRn have augmented humoral immune response. FcRn is known to be involved in protecting and transporting IgG within and across the cells of diverse origin, and in doing so, it regulates IgG concentration. Higher than normal expression levels of FcRn reduce exogenous IgG catabolism in these transgenic (Tg) mice. We demonstrated that beyond these effects bFcRn overexpression enhances the expansion and diversity of antigen (Ag)-specific B cells and plasma cells in Tg mice which is due to augmented antigen presentation. Furthermore, we found that our Tg mice were able to mount robust humoral immune response against weakly immunogenic antigens and to improve hybridoma production efficiency.

Since rabbit is one of the most important sources of polyclonal, and recently also monoclonal antibodies for wide range of applications, we created Tg rabbits that overexpress this receptor, and analyzed their humoral immune response. Our data showed that FcRn overexpression enhances the rabbit humoral immune response (higher Ag-specific IgG titer and more Ag-specific antibody-producer B cells) similarly to what we observed in the immunized bFcRn Tg mice. The enhanced immune response in FcRn Tg rabbits was proven by demonstrating 4-fold higher level anti-thymocyte globulin (rATG) production, a well-established therapeutic tool for preventing host rejection of transplanted organs and by several, unique rabbit antibodies against highly challenging G-protein coupled receptors (GPCRs) such as CB1, GPR12 and GPR35.

All these data demonstrate the FcRn Tg rabbits are ideal tools to generate highly sensitive and specific antibodies even in case of challenging targets.

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