**CORRIGENDUM**

# FcγRIIB in autoimmunity and infection: evolutionary and therapeutic implications

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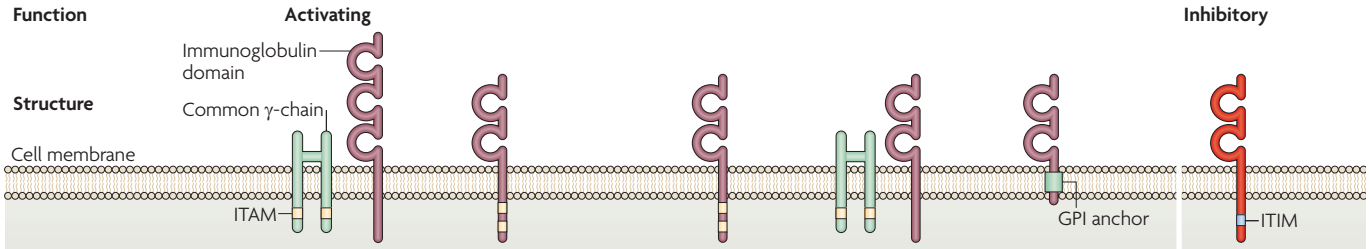
The authors unintentionally overlooked a recent publication that provides a detailed analysis of the affinity of the receptors for the Fc region of IgG (FcγRs) for different IgG isotypes, based on data from both surface plasmon resonance and binding to the surface of transfected cells[1]. The key finding of this paper was to accurately determine the high affinity of IgG3 for FcγRIIIA and FcγRIIIB, which is underestimated by surface plasmon resonance experiments owing to the long hinge region that influences accessibility of IgG3. This finding underpins the strong activating effect of IgG3, particularly on myeloid cells (for example, see REF. 2). A modified version of FIG. 1 is shown below to reflect these findings. The authors would like to thank G. Vidarsson of the Department of Experimental Immunohematology, Sanquin Research, and Landsteiner Laboratory, Academic Medical Center, University of Amsterdam, The Netherlands, for bringing this to their attention.




| Name | | FcγRI | FcγRIIA | FcγRIIC | FcγRIIIA | FcγRIIIB | FcγRIIB |
|---|---|---|---|---|---|---|---|
| Expression | Lymphoid | Not expressed | Not expressed | NK cell | NK cell | Not expressed | B cell and plasma cell |
| | Myeloid | Monocyte, DC and macrophage | Monocyte, DC, platelet and macrophage | Not expressed | Monocyte, DC and macrophage | Not expressed | Monocyte, DC and macrophage |
| | Granulocyte | Neutrophil and eosinophil | Neutrophil | Not expressed | Not expressed | Neutrophil, mast cell and eosinophil | Neutrophil, basophil and mast cell |
| IgG binding affinity (to cell surface FcγRs) | | IgG3>IgG1> IgG4>>IgG2 | Variant H131*: IgG3>IgG1> IgG2>>IgG4<br>Variant R131*: IgG3>IgG1>> IgG2 and IgG4 | IgG3>IgG1 and IgG4; does not bind IgG2 | Variant V158‡: IgG3>IgG1>>> IgG2 and IgG4<br>Variant F158‡: IgG3>>>IgG1; does not bind IgG2 and IgG4 | IgG3>>IgG1; does not bind IgG2 and IgG4 | IgG3>IgG1 and IgG4; does not bind IgG2 |

Figure 1 | **Structure, cellular distribution and IgG isotype-binding affinity of human activating and inhibitory FcγRs.** Human Fc receptors for IgG (FcγRs) differ in function, affinity for the Fc fragment of antibody and in cellular distribution. There are five activating FcγRs: the high-affinity receptor FcγRI, which can bind monomeric IgG, and four low-affinity receptors (FcγRIIA, FcγRIIC, FcγRIIIA and FcγRIIIB), which bind only immune-complexed IgG. Cross-linking of activating FcγRs by immune complexes results in the phosphorylation of immunoreceptor tyrosine-based activating motifs (ITAMs) that are present either in the cytoplasmic domain of the receptor (FcγRIIA and FcγRIIC), or in the associated FcR common γ-chain (FcγRI and FcγRIIIA), resulting in an activating signalling cascade. FcγRIIIB is a glycosylphosphatidylinositol (GPI)-linked receptor that has no cytoplasmic domain. FcγRIIB is the only inhibitory FcγR. It is a low affinity receptor that binds immune-complexed IgG and contains an immunoreceptor tyrosine-based inhibitory motif (ITIM) in its cytoplasmic domain. FcγRIIB cross-linking by immune complexes results in ITIM phosphorylation and inhibition of the activating signalling cascade. FcγRs differ in their cellular expression; myeloid cells express FcγRI, FcγRIIA and FcγRIIIA, whereas granulocytes express FcγRI, FcγRIIA and FcγRIIIB. In such cells, immune complex-mediated activation of these receptors is negatively regulated by FcγRIIB. FcγRIIB is the only FcγR expressed by B cells and negatively regulates B cell receptor activation by immune-complexed antigen. FcγRs bind different IgG subtypes with differing affinity. For example, in the case of FcγRIIB, binding affinity is highest for IgG3, followed by IgG1 and IgG4. The ratio of binding of an IgG subtype to activating FcγRs and inhibitory FcγRIIB is known as the A/I ratio, and it determines the activation threshold of the cell. *The gene encoding human FcγRIIA generates two variants differing at position 131 (H131 and R131). ‡The gene encoding human FcγRIIIA generates two variants differing at position 158 (V158 and F158). DC, dendritic cell; NK, natural killer.

1. Bruhns, P. *et al.* Specificity and affinity of human Fcγ receptors and their polymorphic variants for human IgG subclasses. *Blood* **113**, 3716–3725 (2009).
2. Vidarsson, G. *et al.* Activity of human IgG and IgA subclasses in immune defense against *Neisseria meningitidis* serogroup B. *J. Immunol.* **166**, 6250–6256 (2001).