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Computational modeling of the FcαRI receptor binding in the Fcα domain of the human antibody IgA: Normal Modes Analysis (NMA) study MANORI JAYASINGHE, MONICA POSGAI, SAM TONDDAST-NAVAEI, University of Cincinnati, GEORGE IBRAHIM, University of Toronto, GEORGE STAN, ANDREW HERR, University of Cincinnati, GEORGE STAN GROUP COLLABORATION, HERR'S GROUP TEAM — FcαRI receptor binding in the Fcα domain of the antibody IgA triggers immune effector responses such as phagocytosis and antibody-dependent cell-mediated cytotoxicity in eukaryotic cells. Fcα is a dimer of heavy chains of the IgA antibody and each Fcα heavy chain which consisted of two immunoglobulin constant domains, C_H2 and C_H3, can bind one FcαRI molecule at the C_H2-C_H3 interface forming a 2:1 stoichiometry. Experimental evidences confirmed that FcαRI binding to the Fcα C_H2-C_H3 junction altered the kinetics of HAA lectin binding at the distant IgA1 hinge. Our focus in this research was to understand the conformational changes and the network of residues which co-ordinate the receptor binding dynamics of the Fcα dimer complex. Structure-based elastic network modeling was used to compute normal modes of distinct Fcα configurations. Asymmetric and un-liganded Fcα configurations were obtained from the high resolution crystal structure of Fcα-FcαRI 2:1 symmetric complex of PDB ID 1OW0. Our findings confirmed that FcαRI binding, either in asymmetric or symmetric complex with Fcα, propagated long-range conformational changes across the Fc domains, potentially also impacting the distant IgA1 hinge.

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