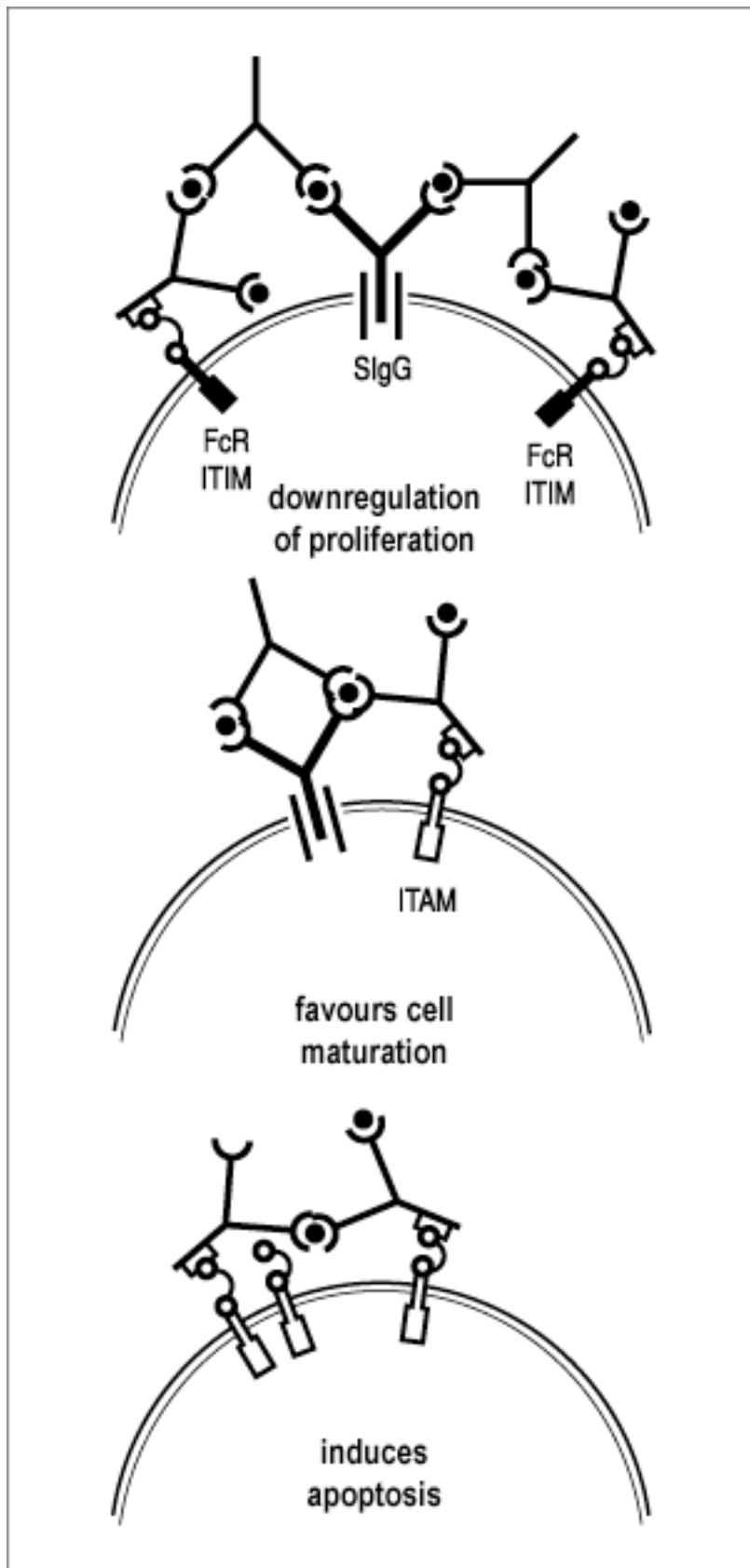


Phagozytose

The fact that soluble proteins find structures on cell surfaces, receptors, to which they specifically bind as ligands is known long ago. Distribution of such receptors is two sided: (i) one given cell can exhibit receptors of more than one specificity and (ii) one given receptor specificity might be found on several cell types. Most cell biologists include effector function triggering by ligand into the definition of a receptor: effector function proceeds, most often through tyrosine-kinase phosphorylation, the universal currency of effector pathway triggering in our body. In the mid-1990ies, the then well known phagocytes were identified as Fc-receptor carrying cells hence to which immune complexes will belay. Whichever antigen the immune complex is carrying, it will thus be presented to the phagocyte and eventually phagocytosed. Immune complexes do exhibit several types of potential ligands (see website tag: physiology/antibody). By occupation of several receptors and crosslinking the cells become strongly activated such that they can fire their cell specific effector function. Where and how this happens decisively depends on receptor location on particular cell types. Chemokine release and anaphylatoxin production join into a targeted inflammatory reaction to destroy invaders, or into a general disorder making patients sick. People like Ruddy, Fearon and Nicholson Weller asked themselves during the 1970ies, how our cells protect themselves from continuous presence of active complement and the answer came with research conducted on red blood cells of patients with paroxistic nocturnal hemoglobinuria. These red cells get lysed easily by complement because they lack protecting proteins, again a type of complement receptors, which inhibit complement as soon as it is assembled on the red cell surface – during nighttime, when pH in kidneys slightly drops, they become a victim of complement. One later found, that CR1 (see transport tag) forms part of these protecting proteins. In summary, immune complexes interact with two larger groups of receptors: the receptors specific for Immunoglobulin Fc-fragments and those for complement. Binding of immune complexes to these cells essentially are the following: (i) transport from one location to the other, (ii) endocytosis/phagocytosis and (iii) induction of specific effector functions. The adjacent figure displays schematically the most important receptors: like the handshake between antigen and antibody, the interaction of ligand with receptor is not subject to covalent chemical bonding but depends on affinity, the strength of which one can measure using Scatchard plots. In fact ligand can escape from receptor binding the striking example holding over its anchor being immune complex release from red blood cells in the destined harbour. The principle of control over excessive activation by downregulating mechanisms in nature is again obvious from the figure which distinguishes cell activating (ITAM) from inhibiting (ITIM) receptors in the neighbourhood of cell surface bound monomeric IgG (sIgG). Therefore three major consequences are possible from immune complex-cell interaction: reduced proliferation, enhanced maturation/proliferation and apoptosis induction.



Three situations are depicted: ITIM: inhibitory receptor, ITAM: activating receptors, and ITAM induced apoptosis.