**The structural property and pro-inflammatory function of cytosolic IgG antibodies**

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**Part I: Distinct folding and assembly properties of IgGs expressed in the cytosol**

Intrabodies have capacity for functional intervention or imaging of intracellular molecules, giving them the potential to be research tools for biotechnology and medicine. However, the expression of intrabodies workable in the reducing cytosol is still a major challenge. It is because intrabodies have failed in the functional assembly and folding into an intact antibody due to the reducing environment of the cytosol. However, it has yet to be proven that not only the failure in the functional assembly of IgG intrabodies in the cytosol is a generalizable event, but also the disulfide bond formation can be formed in the H and L chains of IgG intrabodies in mammalian cells. We addressed these issues with a systematic investigation using four chimeric IgG1s, of which variable (V) domains are distinct but constant (C) domains are identical.

**Part II: Production of the inflammatory cytokines by internalizing free IgG to the cytosol**

A subset of anti-DNA autoantibodies (called self-internalizing antibodies) is able to enter the living cells and reach the cytosol. Anti-DNA autoantibodies are the hallmark of SLE and titers of anti-DNA antibody correlates with the disease activity of SLE, although not how anti-DNA antibodies exert their pathogenic potential is clearly defined. We investigated what happens to the cells if free IgG spontaneously enters the cell and localizes the cytosol, without formatting immune complexes that activate TRIM21 immune signaling, using 3D8 IgG anti-DNA monoclonal antibody that localizes to the cytosol after internalization. Our study shows that the cytosolic internalization of free antibody can induce an immune signaling in human monocytes (THP-1 cell line and primary monocytes).