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(54) **Title**: MODULAR METHOD TO PREPARE TETRAMERIC CYTOKINES WITH IMPROVED PHARMACOKINETICS BY THE DOCK-AND-LOCK (DNL) TECHNOLOGY

(57) **Abstract**: The present invention concerns methods and compositions for forming cytokine-antibody complexes using dock-and-lock technology. In preferred embodiments, the cytokine-MAb DNL complex comprises an IgG antibody attached to two AD (anchor domain) moieties and four cytokines, each attached to a DDD (docking and dimerization domain) moiety. The DDD moieties form dimers that bind to the AD moieties, resulting in a 2:1 ratio of DDD to AD. The cytokine-MAb complex exhibits improved pharmacokinetics, with a significantly longer serum half-life than naked cytokine or PEGylated cytokine. The cytokine-MAb complex also exhibits significantly improved in vitro and in vivo efficacy compared to cytokine alone, antibody alone, unconjugated cytokine plus antibody or cytokine-MAb DNL complexes incorporating an irrelevant antibody. Most preferably, the complex comprises an anti-CD20 IgG antibody conjugated to four IFN-α2b moieties, although other antibodies and cytokines have been used to form DNL complexes.