

s8a.m9.p5 Chimeric Human-Simian Anti-CD4 Antibodies Form Crystalline High Symmetry Particles.

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A chimeric human simian IgG, antigen specific for CD4, when exposed to 0.5 M $\text{SO}_4^{=}$ containing 0.4 % polyethylene glycol or Jeffamine, self assembles into discreet, roughly spherical particles of 23 nm diameter. Increasing $\text{SO}_4^{=}$ to 1.55 M induces the IgG particles to crystallize in either a hexagonal or monoclinic form. From X-ray diffraction, the former crystal is of space group P622 with one IgG particle in the unit cell, thus the particle itself must have 622 point group symmetry. Both crystal forms have been imaged using atomic force microscopy. Detailed features of the duodecamer are evident, including the symmetry and a large solvent channel along the sixfold axis. The particles in some ways resemble the hexameric IgG aggregates believed to activate complement upon antigen binding and, therefore, may have physiological relevance. Investigation of seven other IgGs of diverse origins and subclasses indicates that many, if not most IgGs form similar particles. To our knowledge, this is the first observation of the assembly of IgG into high symmetry aggregates in the absence of antigen, or their crystallization.

s8a.m9.p6 The crystal structure of an anti-carbohydrate antibody directed against *Vibrio cholerae* in complex with antigen.

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Protective responses against microbial pathogens are frequently based on anti-carbohydrate antibodies produced against the cell surface polysaccharides of invading microorganisms. *Vibrio cholerae* strains can be divided into different serogroups based on their lipopolysaccharide structures. The serogroup O1, which is responsible for most cholera outbreaks, includes two major serotypes, Ogawa and Inaba. In order to understand *V. cholerae* serotype specificity and to gain further insight into the structural basis of carbohydrate recognition, we have undertaken crystallographic studies of protective anti-cholera antibodies in complex with antigen. We report here the crystallization and crystal structure determination of a murine Fab fragment specific for the Ogawa serotype in its unliganded form and in complex with synthetic fragments mimicking the *V. cholerae* O-specific polysaccharide. The 3D structure reveals that a complementary water-excluding hydrophobic interface and five antibody-antigen hydrogen bonds are crucial for carbohydrate recognition. The 3D structure explains the serotype specificity of anti-Ogawa antibodies and provides a rational basis towards the development of a synthetic carbohydrate-based anti-cholera vaccine.