two Fabs are almost collinear; thus, there is an approximate long axis running through the entire Fab assembly. The angle between the Fabs is $170 \pm 2^\circ$, and the Fab axes are offset by 9° ; (5) Fab1 has an elbow angle of 159° , and Fab2 has an elbow of 143° . These elbow angles are near the middle of the range of values observed for other Fabs¹; (6) the constant domains of Fab1 and Fab2 are related by a near exact dyad axis of symmetry. The variable domains are not so related because of the difference in elbow angles of the Fabs; (7) the dyad of the Fc is at an angle of about 120° with that dyad relating constant Fab domains; (8) the Fc 2-fold axis does not intersect the dyad relating the constant domains of the Fabs, nor does it intersect the approximate long axis of the Fabs; (9) in the crystal, all segments share extensive interfaces which severely restrict the dispositions of neighbours. The contacts, illustrated in Fig. 3, presumably stabilize this particular conformation.

The asymmetric conformation, observed in these crystals of the antitumour antibody, should probably not be considered as a static structure which is maintained in solution. The structure probably represents only one of many possible transient conformations. The unique structure is a product of the intrinsic flexibility of the antibody and the lattice interactions that stabilize this particular distribution of domains. Indeed, electron microscopy²⁰⁻²³, fluorescence polarization^{24,25} and previous X-ray crystallographic studies^{5,26,27} have provided extensive evidence for a wide range of conformations based on segmental flexibility.

The structure we present is instructive in that it illustrates the nature and extent of this structural variability, or dynamic range, which is inherent in the antibody. The Fabs are loosely tethered to a mobile Fc. Each Fab can assume its own elbow angle as its environment or function requires. Somewhat unexpected is the fact that, were the elbow angles the same, the Fabs would be related by an almost exact 2-fold axis that is quite independent of the Fc. It is the disposition of the Fc that disrupts the overall symmetry of the molecule. This is in keeping with the disorder, or multiple orientations of the Fc, observed in the Kol antibody structure^{7,8}.

The hinge polypeptides are not really hinges, but rather they are tethers that allow the Fab components to drift from the Fc to bind antigen or potentially allow the Fc to move in such a way to trigger effector functions, such as the activation of complement^{25,28}. The connecting polypeptides give the Fabs the freedom to move and twist so as to align hypervariable regions with antigenic sites on large, immobile carriers, in this case tumour cells. The crystal structure visually demonstrates that the antibody is an assembly of units possessing a high degree of flexibility, a molecule suited to the task of scavenging foreign objects or activating a cell lysis system. □

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RETRACTION

Identification by anti-idiotypic antibodies of an intracellular membrane protein that recognizes a mammalian endoplasmic reticulum retention signal

D. Vaux, J. Tooze & S. Fuller

Nature **345**, 495-502 (1990)

OUR further characterization of the M_r 72,000 (72K) protein has shown that the data in Fig. 2 of our paper are erroneous and not repeatable. We retract the statement that the 72K protein is an integral membrane protein. The present evidence is consistent with this protein being associated with the intermediate compartment. We also withdraw our speculation concerning its function. □

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