

**P2.2.20** A COMPARISON OF THE HYDRODYNAMIC PROPERTIES OF TWO NOVEL MONOCLONAL ANTIBODIES: B72.3 AND CHIMERIC B72.3. Olwyn Byron, Stephen Harding and Stephen Rhind, Department of Applied Biochemistry and Food Science, University of Nottingham, School of Agriculture, Sutton Bonington, LE12 5RD, UK.

B72.3 is a murine monoclonal antibody (IgG1) raised against a tumor-associated glycoprotein (TAG-72) found in colorectal, gastric and ovarian carcinomas. Prospects for its clinical effectiveness are overshadowed by some patients' immunological 'hammer' response to murine antibodies after a single administration. It has been reported that anti-B72.3 antibodies were found in over 50 % of patients involved in studies. Chimeric B72.3 (cB72.3), a combination of the variable regions of B72.3 and the constant regions of human IgG4, has greatly lessened this immunological rejection. Sedimentation velocity, sedimentation equilibrium and viscosity techniques have revealed significant differences in the hydrodynamic behaviour of the two molecules. B72.3 has a sedimentation coefficient ( $s_{20,w}^0$ ) of  $(6.51 \pm 0.04)$  Sv whilst that of cB72.3 is  $(6.89 \pm 0.04)$  Sv- markedly similar to the  $s_{20,w}^0$  value for human IgG4 of  $(6.75 \pm 0.05)$  Sv. The weight average molecular weights,  $M_r$ , of both antibodies were determined (via sedimentation equilibrium experiments) to be  $205,000 \pm 10,000$  for B72.3 and  $147,000 \pm 5,000$  for cB72.3 at pH 6.8, suggestive of some degree of association of native B72.3 but not cB72.3, as amino acid sequence analysis predicts that both antibodies have molecular weight values of approximately 148,000. Viscosity studies of both molecules are under way. The intrinsic viscosity values determined will subsequently be incorporated, together with sedimentation coefficients and radii of gyration, into hydrodynamic bead models of the two antibodies, giving insight into their actual solution conformations.

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