

## **A Multimeric Variant Of The Human Contraception Antibody (HCA) Demonstrates Enhanced Contraceptive Activity**

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HCA is an IgG1 monoclonal antibody (mAb) that potently agglutinates sperm through binding of its Fab regions to the target antigen, CD52g, on the surface of sperm. HCA was also recently shown to block sperm migration through cervical mucus in vitro and in vivo through two Fc-mediated functions: complement-dependent sperm immobilization and mucus trapping. We have engineered a hexameric version of HCA comprised of 6 IgG1 antibodies linked together using the IgM tailpiece (IgGt). Multimerization of IgG antibodies confers exponentially stronger avidity due to combined binding strength of multiple binding domains. In this study, we compared the activity of the parent IgG1 HCA to the hexameric variant in three assays of contraceptive function: sperm agglutination, sperm immobilization and cervical mucus trapping. As reported previously, IgG1 HCA agglutinated 100% of sperm in less than 30 seconds at low ug/ml concentrations. In contrast, the hexameric IgGt achieved the same effect at 10-100-fold enhanced potency. Similarly, the IgGt variant had greatly enhanced complement-mediated immobilization activity. Hexameric HCA more effectively trapped sperm in midcycle cervical mucus than the IgG1 HCA. These results indicate that HCA-IgGt is a promising second generation contraceptive antibody candidate due to its enhanced contraceptive capabilities.