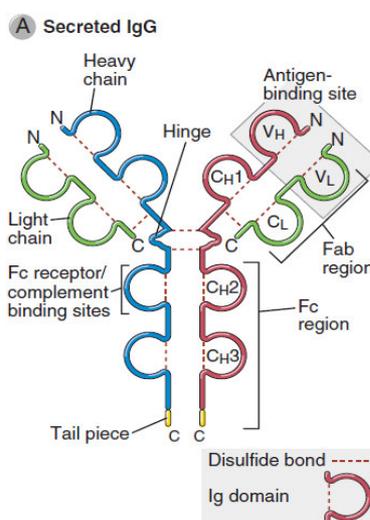


Nano-Immunology

Molecular recognition and nano-mechanical properties of antibodies

The medical application of nanotechnology, i.e. nanomedicine, has enormous potential to improve health care. Aided by nanomedicine, pathomechanisms of disease are being discovered and molecular diagnostics refined. Antibodies, as superior natural nanomedicines with their high specificity for cognate antigens, constitute a paradigm for molecular recognition. They play a key role in opsonization of pathogens by assembling into clusters that attract phagocytes and thus promote binding of the complement system, resulting in clearance of the invader. It is essential to fundamentally advance our understanding of the nanomechanical properties of IgG molecules in the process of antigen recognition.



Atomic force microscopy is the method of choice for such measurements under physiological conditions with respect to the strength of antibody-antigen bonds and other nanomechanical properties of antibodies at the single-molecule level. The goal is to investigate the binding capability, energetics and dynamics of a set of human IgG antibodies by atomic force microscopy (AFM) – based single molecule force spectroscopy (SMFS).

Figure 1 - Structure of IgG molecule

IgG molecules consist of one Fc region and two light and heavy chains, of which the ends form the antigen-binding sites.

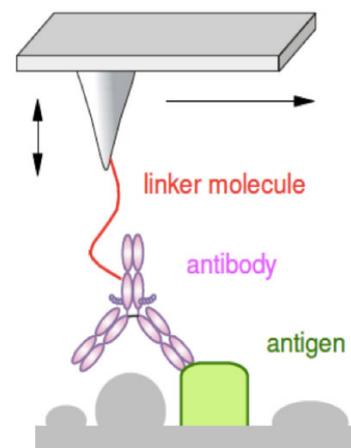
Differences in the IgG subtypes (e.g. IgG1, IgG2 or IgG4) were found to be in the inter-chain bridges: They differ in the amino acid composition and the structure of the hinge region, which determines the flexibility of the molecule.

Tasks performed by the student:

- Tip-Chemistry: Functionalization of tips and surfaces with IgG antibodies and PNAG or CD40 molecules, respectively, for SMFS experiments
- Force Spectroscopy: Single Molecule Force Spectroscopy (SMFS) Experiments
- Data Evaluation and Binding Models

Figure 1 – SMFS experiment with antibodies

The IgG antibody is immobilized via a linker molecule to the AFM tip, brought to the antigen, and finally pulled away to disrupt the bond.



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