



# Design and construction of new antibody derived molecules, "Pepbodies" and "Troybodies".

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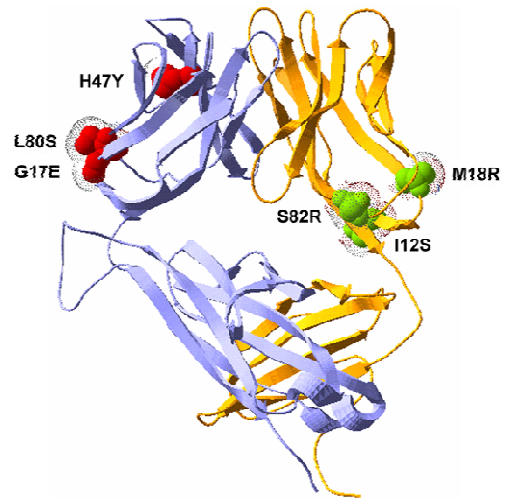
## **Abstract:**

A) Antibodies are complex molecules with the ability to interact with many different receptors via their constant regions. We try to construct small and simple molecules, so-called "Pepbodies", that harbor only one receptor binding ability, but mimic a complete antibody with regard to a separate function. The purpose of the project is to develop E. coli produced antibody fragments that may be used in vivo for therapeutic and diagnostic purposes.

The fragments will have a targeting portion derived from an antibody and in addition be genetically coupled to one or more peptides. Each peptide binds one of the molecules that normally bind to the constant region of antibodies. Examples are FcRn (Fc receptor responsible for the long serum half life of IgG and the transport of IgG from mother to fetus), C1q (complement protein), one of several FcγRs and poly Ig receptor (transports IgA and IgM to mucosae). A series of such peptides have been selected from phage display libraries, and will be discussed.

B) "Troybodies" are recombinant antibodies with specificity for APCs and with defined T cell epitopes genetically fused to the constant region. The goal is to design reagents that cause strong, specific immunomodulation. Notably, we use the T cell epitopes only, and not the whole antigen. A number of peptide sequences have successfully been incorporated as loops connecting beta strands of Ig C domains (similar to CDR loops of Ig V domains). The resulting Troybodies were tested in mice in vitro and in vivo and found to greatly increase specific CD4+T immune responses. We have made Troybodies with specificity for human MHC class II and FcγR1. In addition, several other specificities have been tested in Bjarne Bogens laboratory, with which we collaborate closely. Recent results from the project will be described. We have studied where peptides may be introduced in antibody molecules. We have observed that presentation efficiency varies and seems to depend on which loop structure holds the peptide. The results aim at the construction of a multivaccine reagent.

C) Finally, work in progress that aim at the construction of soluble T cell receptor will be described.



**Norwegian Society for Immunology (NSI)**