Towards a Gold Nanoparticle-based Vaccine Directed against the Tumor Associated Mucin-1 Glycoprotein

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Mucin-1 (MUC1) has been identified as a top-priority cancer antigen for the development of therapeutic anticancer vaccines.[1] An effective strategy to enhance the immunogenicity of synthetic MUC1-derived glycopeptides and thus to obtain promising vaccine candidates is to couple these glycopeptides to a carrier protein,[2] to polymers[3] or self-assembling constructs[4] resulting in multivalent antigen presentation. We have developed PEGylated gold nanoparticles (AuNPs) which can be easily functionalized with a controllable number of peptides[5] and are expected to be ideally suited for the development of anticancer vaccines in view of their biocompatibility, simplicity of assembly and colloidal stability.
In this contribution we describe the preparation and characterization of glycopeptide-functionalized AuNPs and we show that they induce specific antibodies directed against the tumor-associated form of MUC1. In particular, we immobilized chimeric peptides, consisting of a glycopeptide sequence derived from MUC1 and the T-cell epitope P30 sequence, on PEGylated AuNPs. Analysis of the antisera of immunized mice indicates a significant MHC-II mediated immune response. Furthermore, the antisera recognize their target antigen on human MCF-7 breast cancer cells. We also show that MUC1-P30 chimeric peptides, not coupled to AuNPs, are less effective in stimulating antibody production underlying the importance of their presentation on AuNPs. These results indicate that PEGylated AuNPs functionalized with MUC1-derived glycopeptides are very promising conjugates for the development of anticancer vaccines.

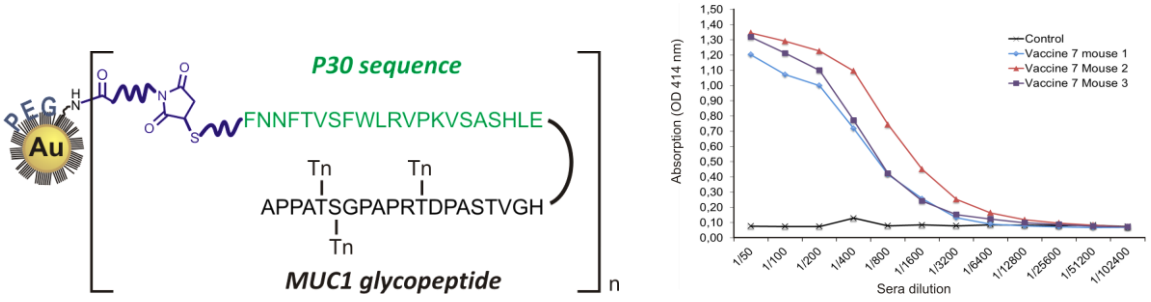

Figure 1. *Left:* Schematic structure of the immunized three-component AuNP-P30-MUC1 vaccine candidate with 3 Tn glycosylation sites. *Right:* Total antibody titers after the third bleed determined by ELISA.

References

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