TNF-α BASED PROTEIN NANOPARTICLES AND THEIR USE IN BIOMEDICAL APPLICATIONS

(Dr. Gorazd Hribar, KI)

Universal technology for protein nanoparticle (NP) formation was developed based on metal coordination of specifically designed protein analogs. TNF-α analogs with surface exposed clusters of histidines (LK801) or histidine tags attached to N-terminus (His10-TNF and H7dN6TNF) were designed as model proteins. Since TNF-α is a pleiotropic protein we prepared various TNF-α analog based NPs for different biomedical applications.

Different approaches were used to form protein NPs, either by binding of protein molecules to inorganic NPs or by self-assembly of NPs comprised of different polyfunctional biocompatible chelators or dendrimers with chelating function in combination with histidine rich TNF-α analogs and zinc ions.

NPs containing TNF-α analog LK801 were analyzed on mouse tumor model. Anti-tumor therapy was efficient due to slower release of protein molecules. Additionally, PEGylated analog LK801 was prepared with on-column PEGylation and tested on tumor bearing mice.

On the other hand, TNF-α NPs containing analog with reduced biological activity (H7dN6TNF) could be used for different application. As it is known, TNF-α plays a central role in chronic inflammatory diseases, therefore anti-TNF therapy is an effective way for tackling them. A principle of active immunization and formation of anti-TNF antibodies could serve as a good solution.