Protein-stabilized nanomaterials as novel MRI contrast agents

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Protein-stabilized nanomaterials recently emerged as materials of interest in the biomedical field due to the biocompatibility, stability, and ease of preparation,[1] presenting advantages over currently available diagnostic and therapeutic agents. Engineered metal-coordinating proteins combine the safety/biocompatibility with the diverse functionality of metal nanoparticles. Consensus tetratricopeptide repeat (CTPR) proteins are particularly notable for the robustness and mutational permissibility, due to the repeat nature of the protein, allowing the introduction of metal coordination sites without substantial impact on the structure.[2]

In the current project, cysteine- and histidine-based metal-binding sites were introduced into CTPR proteins for the coordination of Gd and Fe. These proteins were then used to generate protein stabilized nanoparticles (Prot-NPs) with tailored relaxivity properties (Figure 1), thereby allowing their exploration as Magnetic Resonance Imaging (MRI) contrast agents. Moreover, two different strategies were explored to target the Prot-NPs to specific pathologies. In a first approach, Prot-GdNPs were developed as T1-contrast agents, with the Gd particles stabilized on a cysteine-based scaffold that also contained an Hsp90 binding module. This binding module allowed the targeting of a cellular chaperone protein, Hsp90, that is overexpressed in several pathologies, *e.g.,* fibrosis and certain cancers. Likewise, protein stabilized iron oxide nanoparticles (Prot-IONPs) were also developed as contrast agents. The Prot-IONPs were grown on a histidine-based scaffold that was subsequently modified with alendronate to target calcifications in atherosclerotic plaques. This work serves as a proof-of-concept revealing the versatility and potential of the Prot-NPs in biomedical applications through the development of MRI contrast agents with targeting ability.

References

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Figures

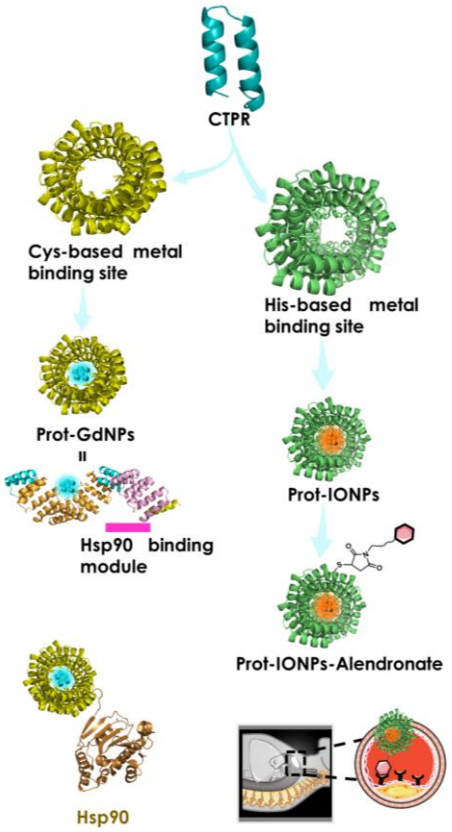

Figure 1. Designed CTPR proteins were used to generate custom Prot-NPs with tunable properties for use as targeted MRI contrast.