Multifunctional peptides for the synthesis of photothermally active gold nanoparticles

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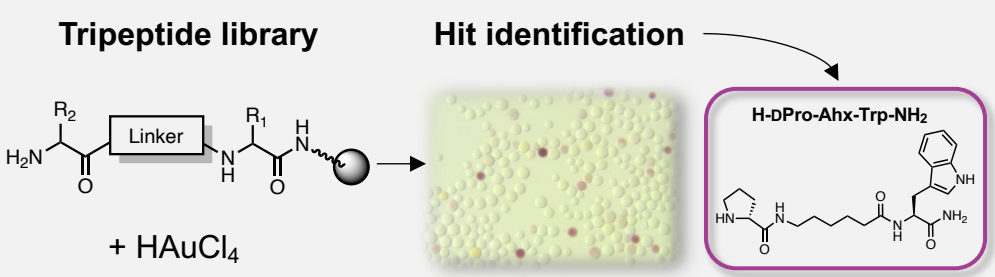
1 Introduction

Gold nanoparticles (AuNPs) have gained significant attention for therapy, imaging, and biosensing due to their unique properties that can be tailored by varying their size, shape, and coating.[1] Peptides offer multiple advantages for the formation and stabilization of AuNPs compared to traditional ligands.[2]

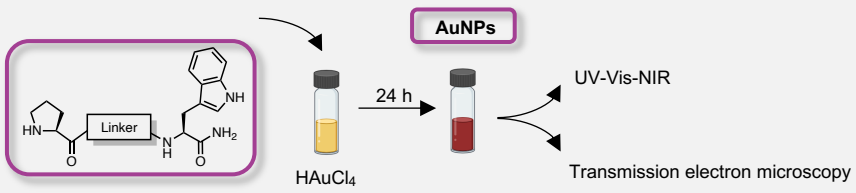
Here, we used a split-and-mix tripeptide library to identify peptides promoting AuNP formation without the need for external reducing agents. The lead peptide from our screening promoted the formation of stable anisotropic AuNPs with absorption in the near-infrared region. We envision that these peptide-coated AuNPs could become valuable tools for photothermal therapy.

2 Tripeptide library screening



3 Sequence optimization

- **Alanine scan** revealed that the C-terminal tryptophan is crucial for NP formation, and the N-terminal proline is essential for anisotropy.
- **Stereochemistry studies** showed that peptides with an N-terminal L-amino acid form AuNPs without aggregation and with optimal dispersity, in contrast to those with a D-amino acid.
- **Linker optimization**



- Hydrophobic or positively charged linker → anisotropic NPs
- Aromatic, negatively charged or no linker → isotropic NPs
- Lead: **H-Pro-Gly-Trp-NH$_2$** → best dispersity, long-term stability

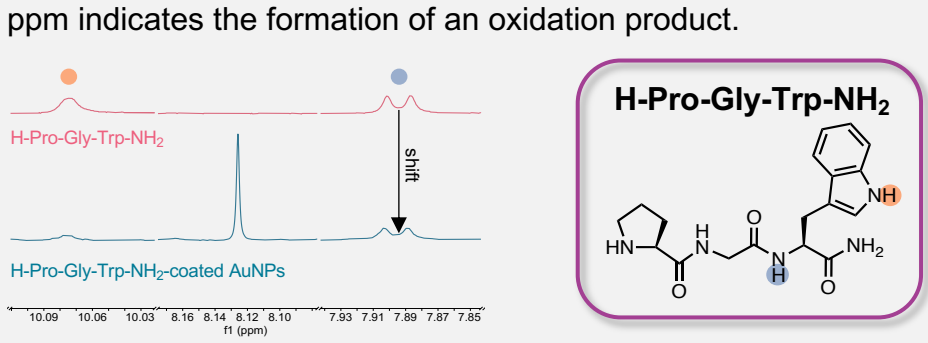
7 Conclusion

- **H-Pro-Gly-Trp-NH$_2$** is a reducing agent, stabilizer and a promoter of anisotropic AuNPs with NIR light absorption
- Potential photothermal agent
- Peptide modification for the formation of targeting AuNPs

Partner/Sponsor:

4 NMR studies

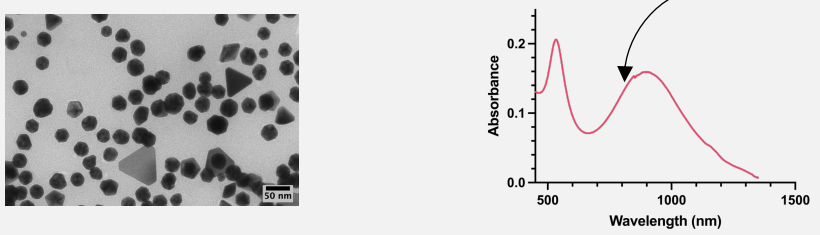
NMR studies revealed a decrease of the Trp N-H proton signal after AuNP formation, indicating that Trp is involved in $HAuCl_4$ reduction and is oxidized in the process. A new signal at 8.13 ppm indicates the formation of an oxidation product.



5 Thermal heating

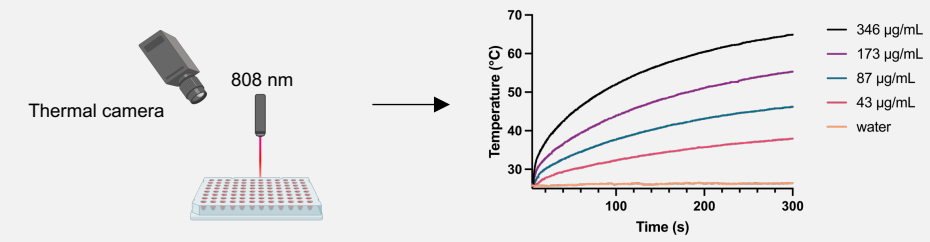
H-Pro-Gly-Trp-NH$_2$-coated AuNPs

TEM image and absorption spectrum



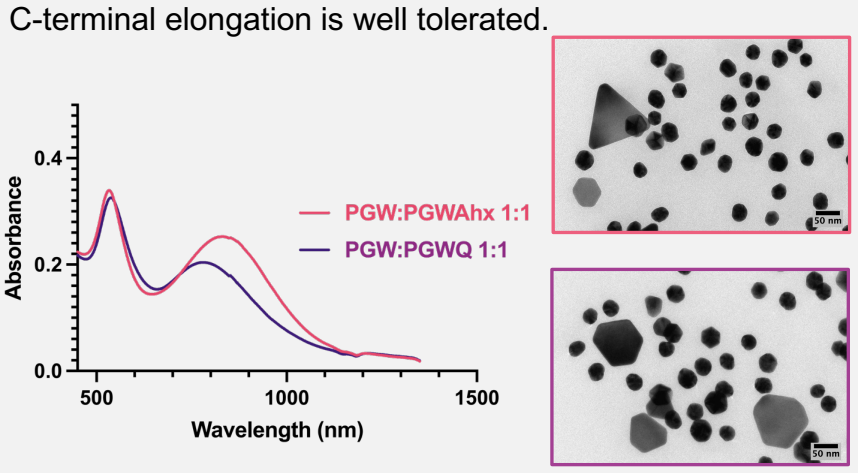
Photothermal effect

The AuNPs were irradiated by an 808 nm laser with a power density of 1.5 W/cm^2 for 5 min.



6 Functionalization of the lead peptide

Modification of the N-terminus resulted in AuNP aggregation, but C-terminal elongation is well tolerated.



Absorption spectra and TEM images of peptide-coated AuNPs formed with 1:1 mixtures of H-Pro-Gly-Trp-NH$_2$ and H-Pro-Gly-Trp-Ahx-NH$_2$ or H-Pro-Gly-Trp-Gln-NH$_2$.

Derivatization opens up the possibility to equip the peptide at the C-terminus with a targeting moiety to form functionalized AuNPs tailored to specific applications.

References

[1] L. Wang, M. H. Kafshgari, M. Meunier, *Adv. Funct. Mater.*, **2020**, *30,* 2005400.
[2] K. Bhattacharjee, B. L. V. Bhagavatula, *Chem Soc Rev*, **2023**, *52,* 4121.

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