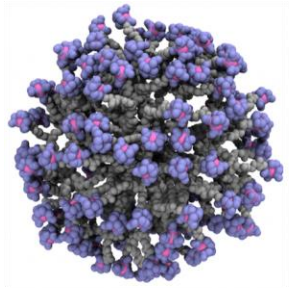

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NANO2CLINIC

CANCER NANOMEDICINE - FROM THE BENCH TO THE BEDSIDE

Effect of particle shape and size on the interactions of gold nanoparticles with proteins of different glycosylation status

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Gold and cancer nanomedicine

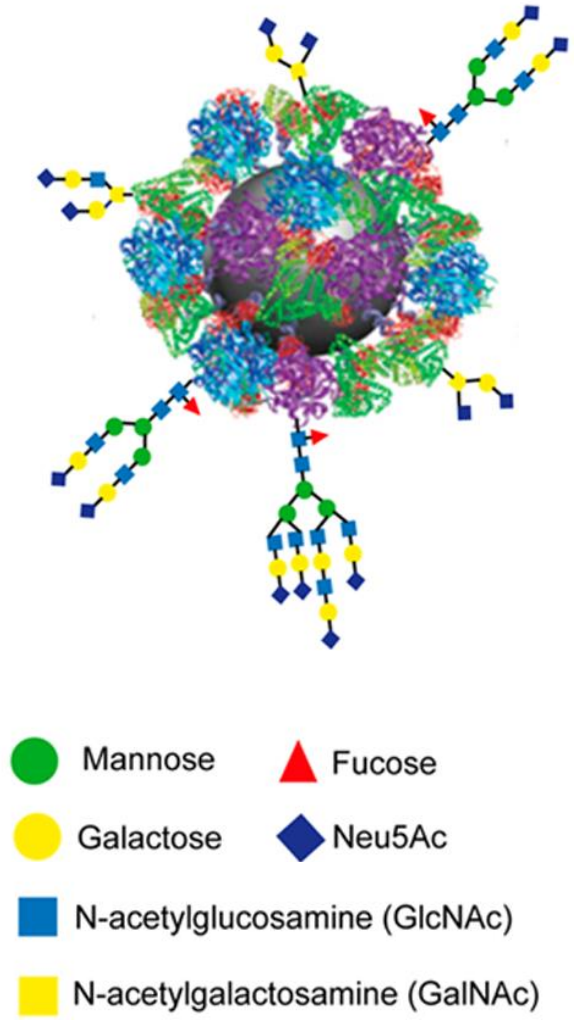
- Diagnostics, bioimaging and biosensing
- Targeted drug delivery
- Photothermal therapy

- Advantages: inert, biocompatible, tunable properties, easy functionalisation

Source: Sztandera et al. Mol. Pharmaceutics, 2019, 161, 1-23

Protein corona and glycans

- Protein corona
  - layer of adsorbed proteins on NP surface
  - Impacts NP stability and behaviour
- A lot of serum proteins are glycosylated
- Glycosylation patterns change in cancer cells



Sources:
Liu et al. Nanoscale 2013, 5, 1658–1668
Stowell et al. Annu Rev Pathol. 2015, 10, 473-510
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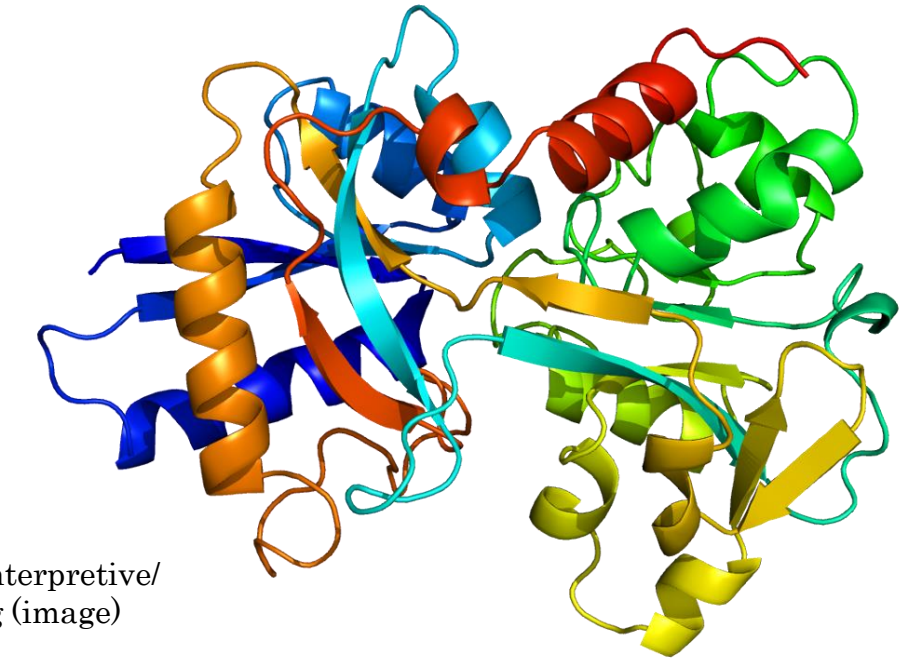
Transferrin

- Iron-binding blood plasma glycoprotein, 679 amino acids, 80 kDa
- Human blood reference range 2.040–3.60 mg/mL
- Used in nanomedicine to increase NP uptake through the blood-brain barrier or target cancer cells
- 2 N-linked glycans



Sources:
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Chung. Biochemical education, 1984, 12(4)
Li et al. Cancer Lett, 2009, 274(2), 319-26
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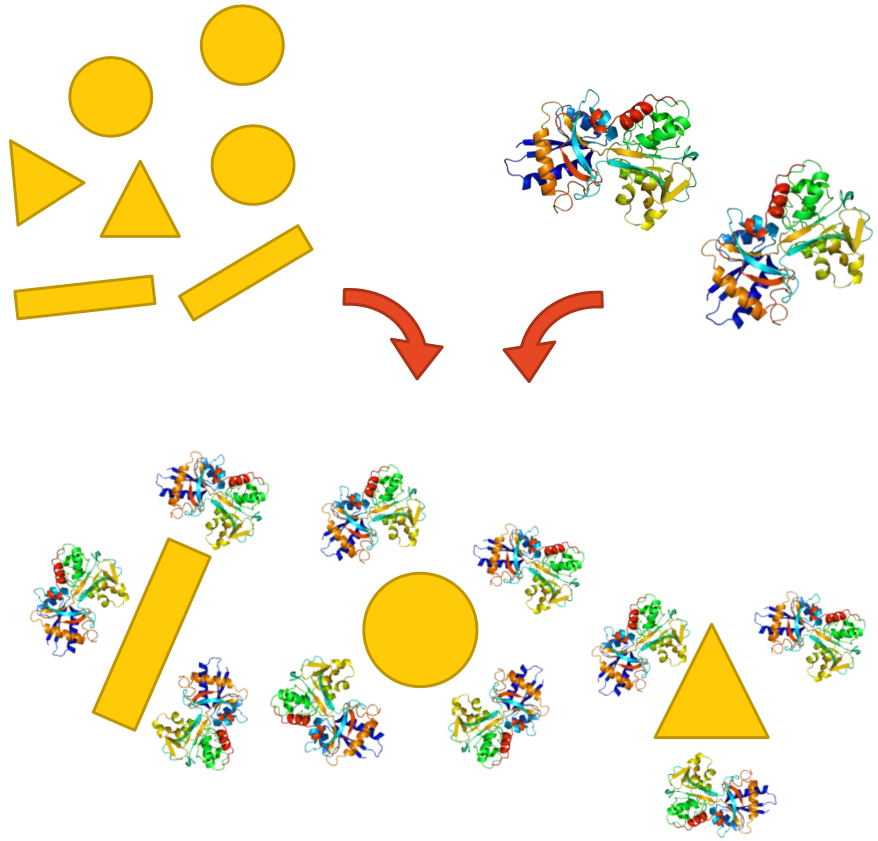
https://en.wikipedia.org/wiki/File:Protein_TF_PDB_1a8e.png (image)

Aim

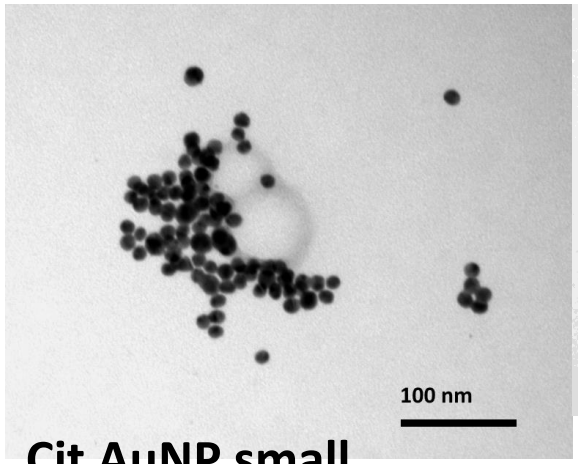
- Investigate the difference in binding of human (glycosylated) and recombinant (non-glycosylated) transferrin to gold NPs of different shapes and sizes
- NPs selected: spheres, prisms and rods of different sizes



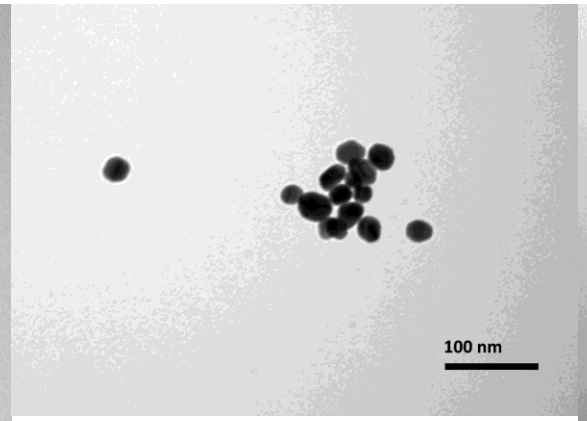
Methods

- Synthesis – Zaragoza, Spain
- Size and morphology determination – TEM
- Hydrodynamic diameter measurement – DLS
- Zeta potential measurement – ELS
- Determination of binding constants – fluorescence spectroscopy
- Secondary structure estimation – circular dichroism

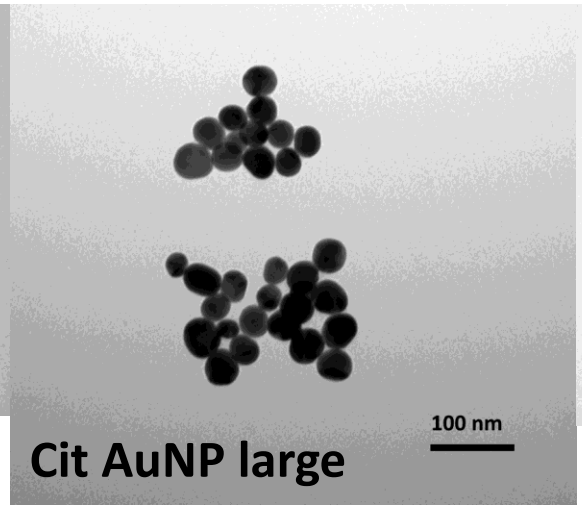
Characterisation



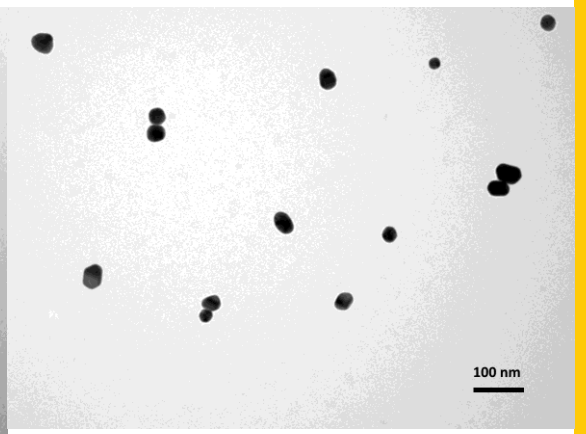
Cit AuNP small



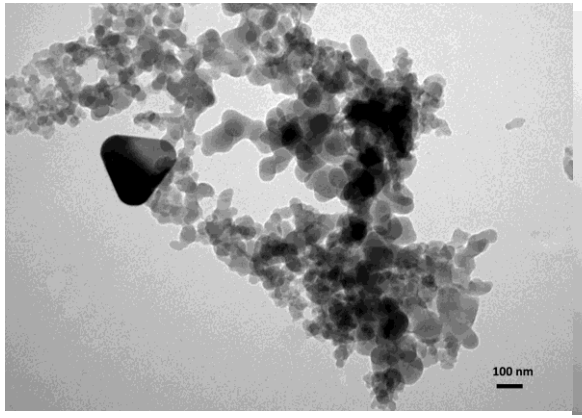
Cit AuNP medium



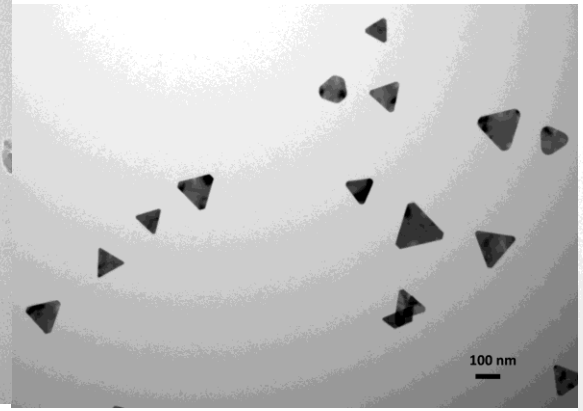
Cit AuNP large



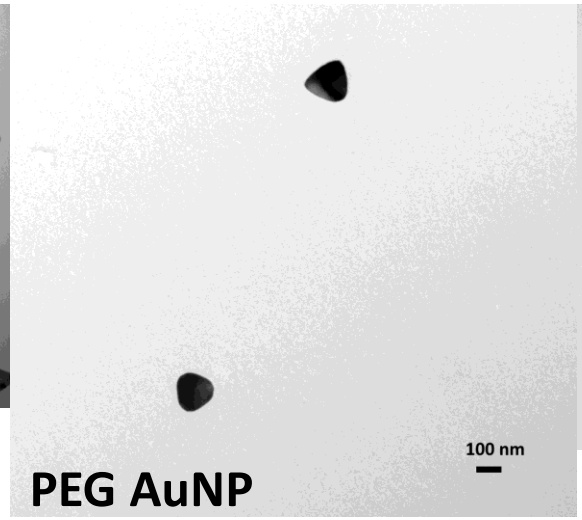
Cit PEG AuNP



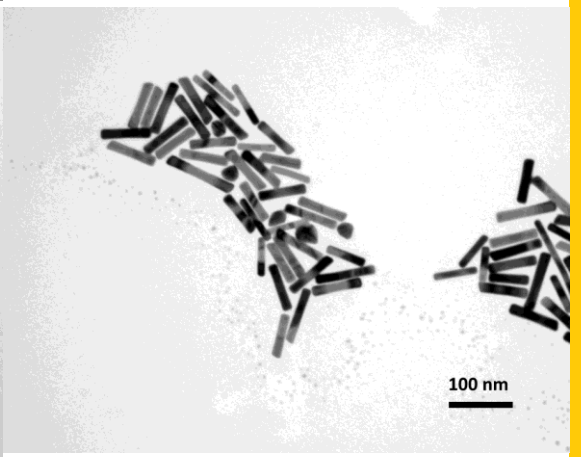
GSH PEG AuNP small



GSH PEG AuNP large



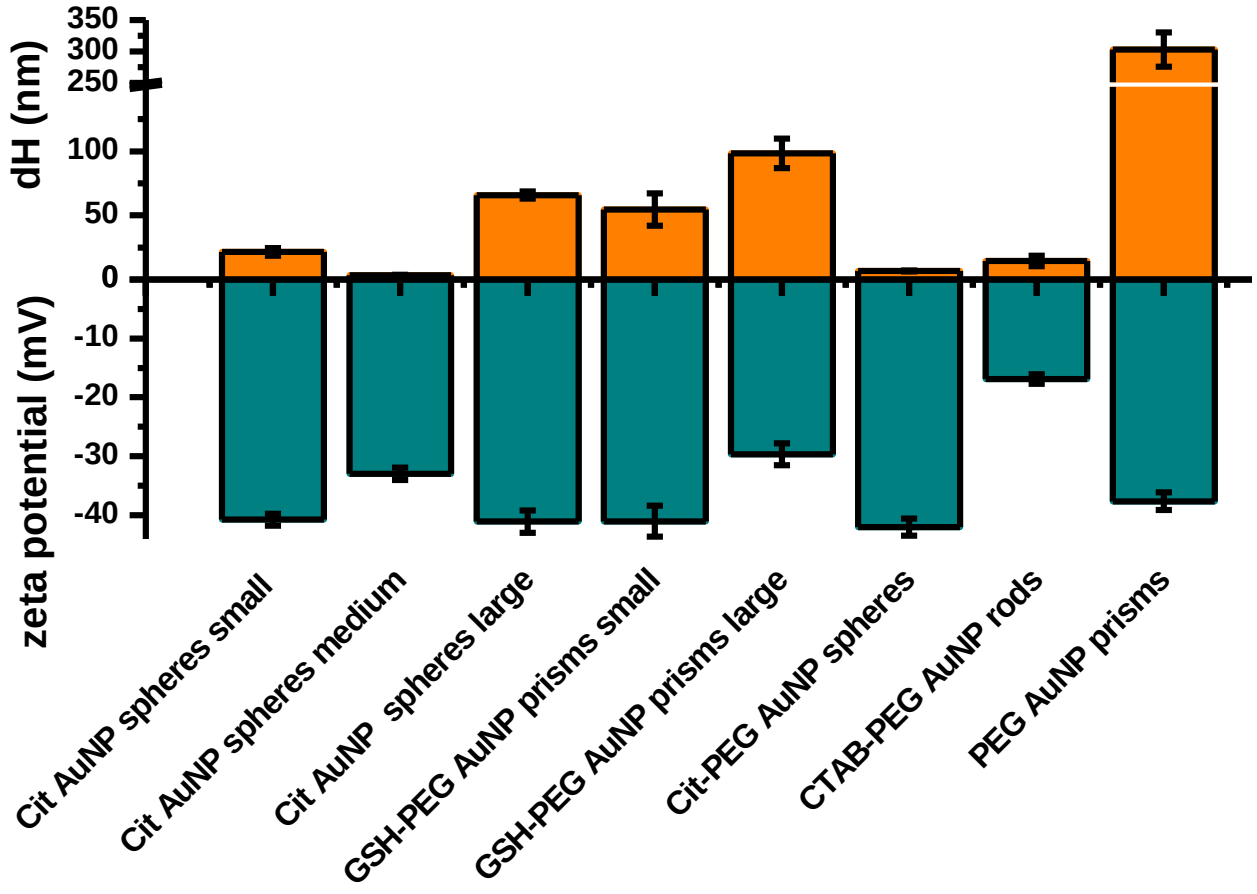
PEG AuNP



CTAB PEG AuNP

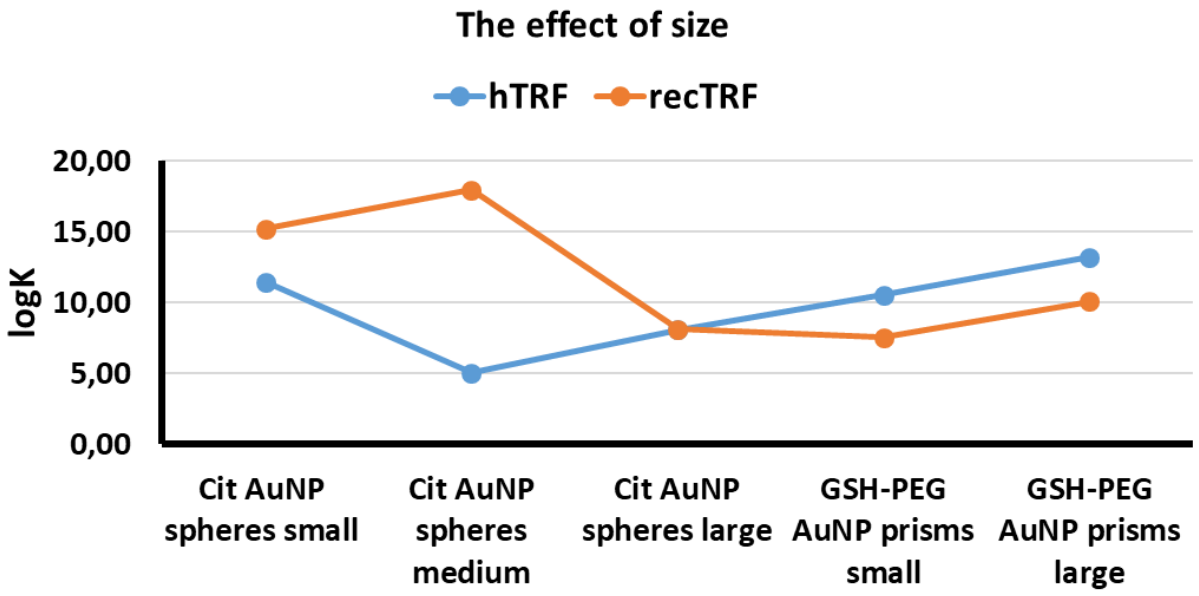
Characterisation

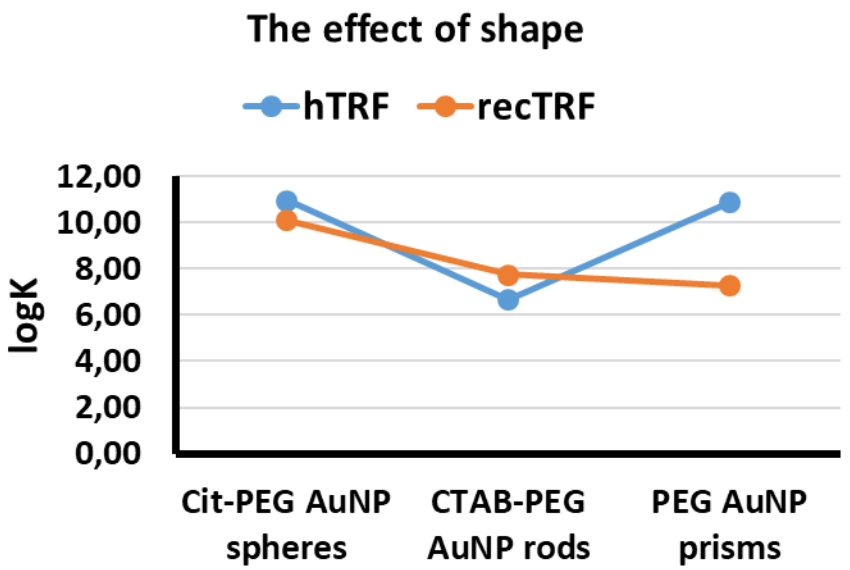
Nanoparticle	diameter by TEM (nm)
Cit AuNP spheres small	13
Cit AuNP spheres medium	36
Cit AuNP spheres large	60
GSH-PEG AuNP prisms small	125
GSH-PEG AuNP prisms large	150
Cit-PEG AuNP spheres	36
CTAB-PEG AuNP rods	77
PEG AuNP prisms	197



Fluorescence spectroscopy and binding constants

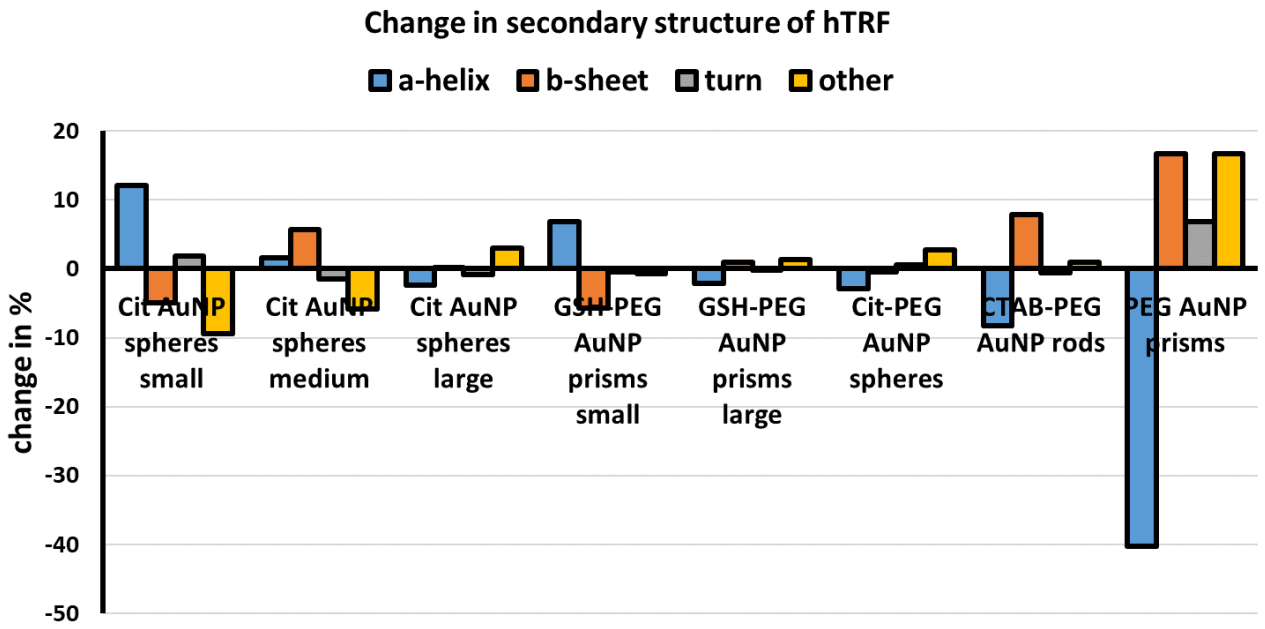
- Non-glycosylated protein binds more strongly to smaller spherical NPs, while glycosylated form prefers nanoprisms of either size

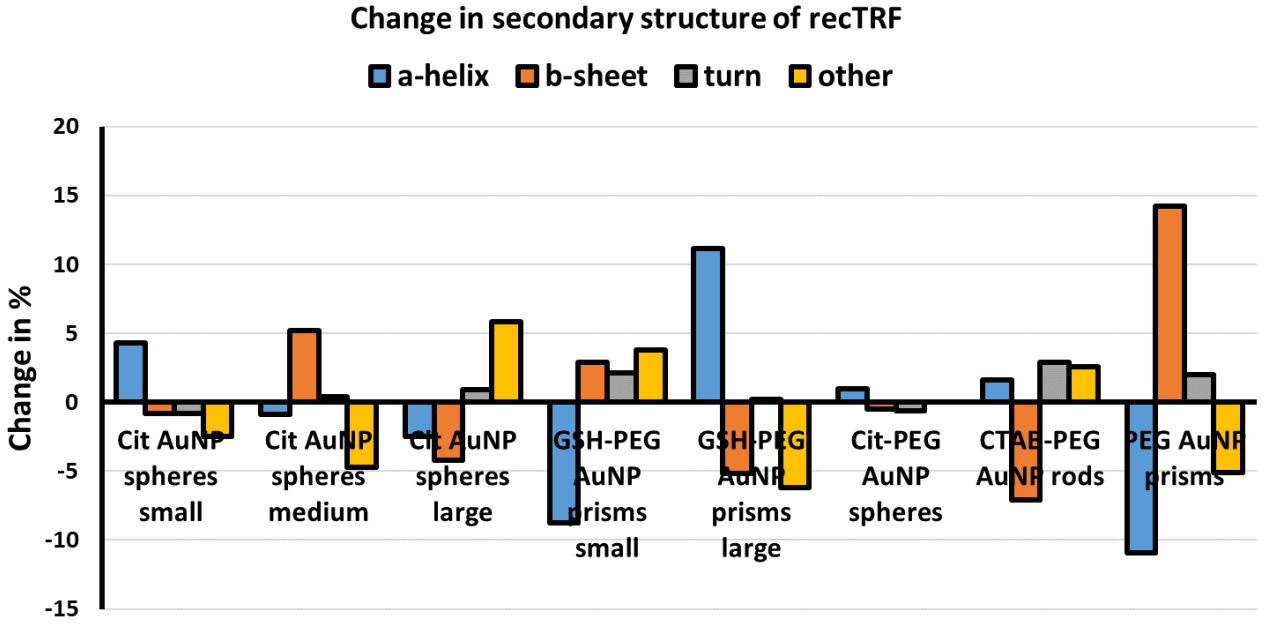




Secondary structure determination

- Protein-NP interactions result in changes of secondary structure due to changes in hydrogen bonding
- Significantly different patterns of change between glycosylated and non-glycosylated forms for nanoprisms and nanorods





Conclusions

- Glycans are involved in NP-protein interactions
- Binding of glycosylated proteins to the NP surface is size and shape dependent

Acknowledgements

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