

X-Ray Triggered Release of Hybrid Protein-Gold Nanoparticles

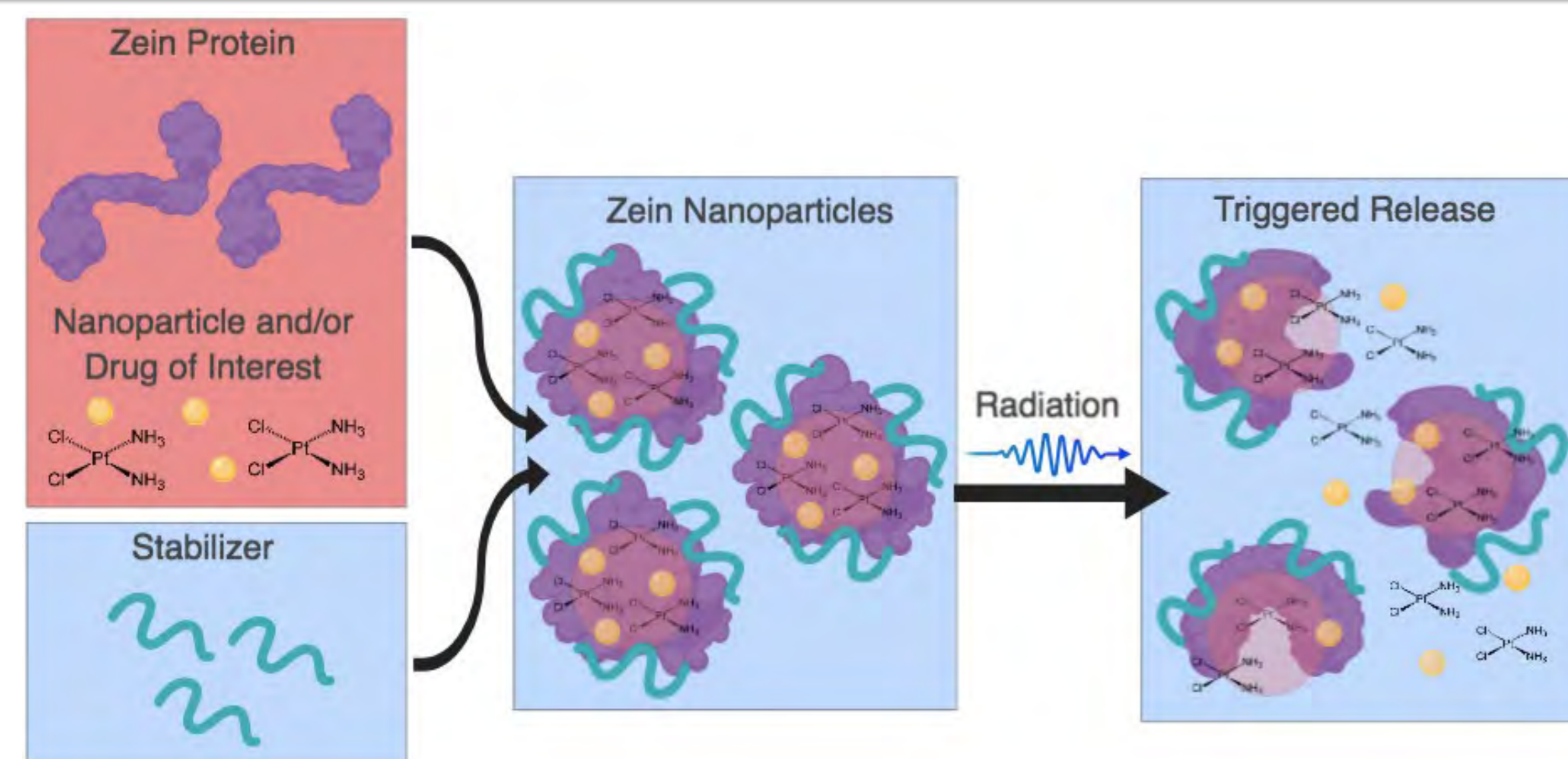


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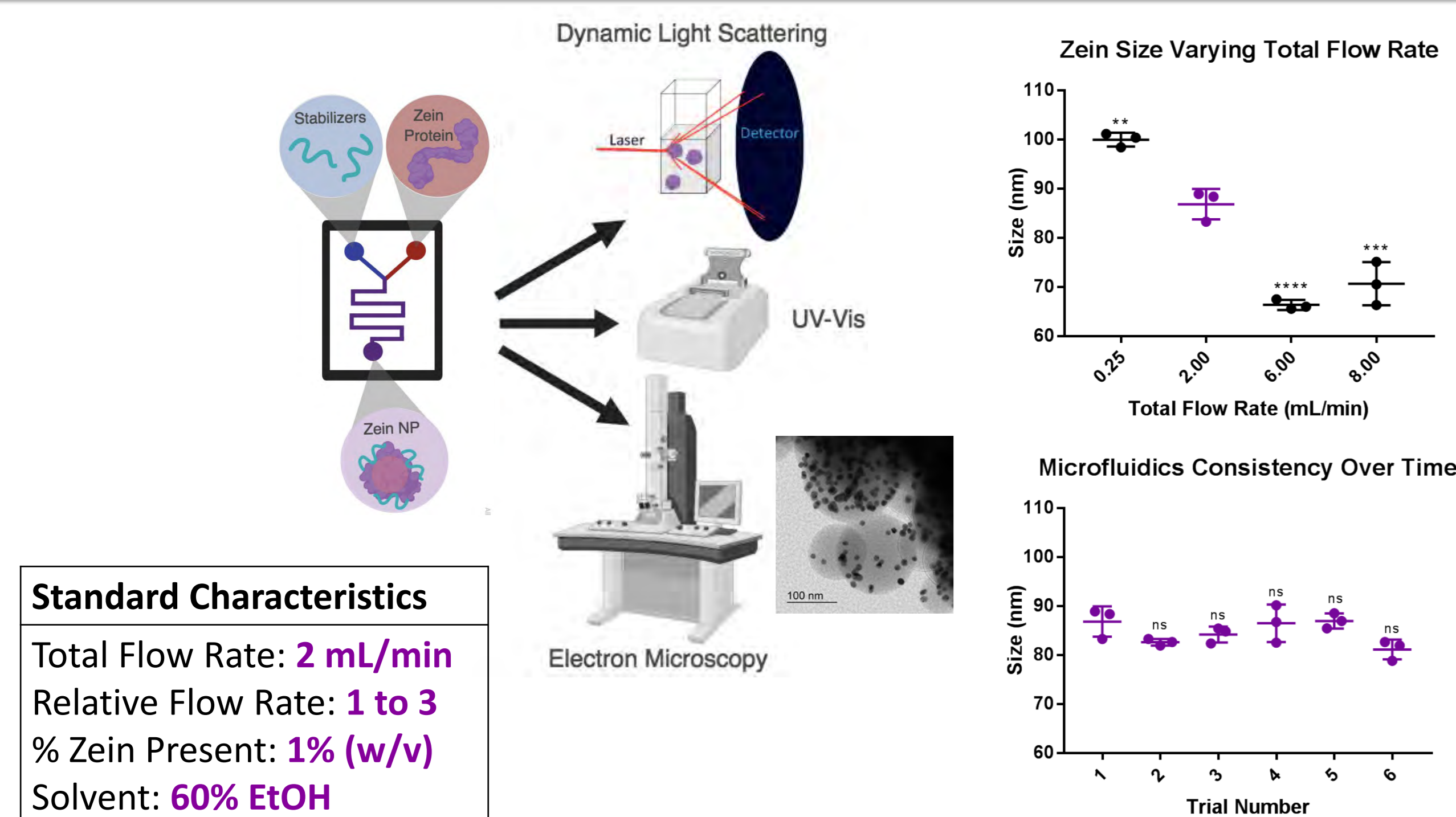
Introduction

Cancer treatments using combined modality approaches, such as high dose cisplatin with radiotherapy (RT), often result in patients experiencing significant toxicities during treatment.¹ In order to better control the side effects, we are examining the use of X-rays as an external trigger to release drugs from Zein nanoparticles (NPs). The radiolysis of water by X-rays generates reactive oxygen species (ROS) which, under certain conditions, is enhanced by the presence of gold (AuNPs). ROS are known to react with surrounding materials, such as DNA and proteins, to degrade and destabilize their structure.² The destabilization of Zein NPs could potentially be used to release drug on-demand with the application of X-rays. Herein, we present the preliminary design of a Zein AuNP hybrid system that is destabilised by exposure to X-rays.

Graphical Abstract



Microfluidic Synthesis of Zein Nanoparticles

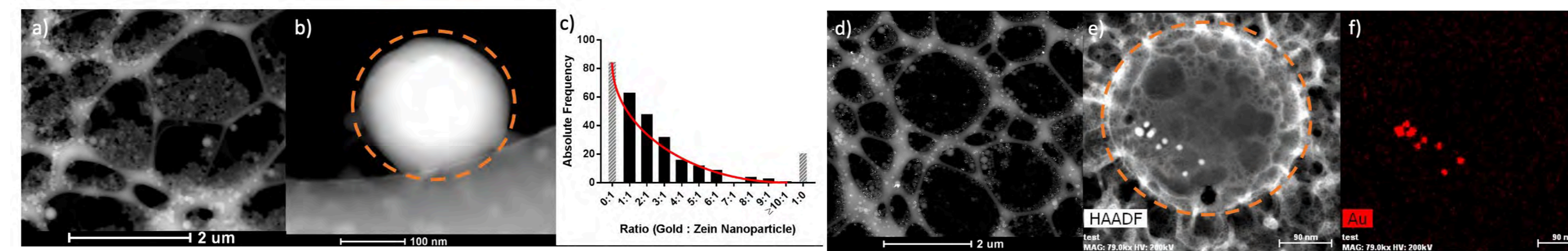


Zein NPs and Zein AuNPs were generated using "standard characteristics" in our microfluidic system. Samples were characterized using dynamic light scattering (DLS; above graphs demonstrate how NP size can be controlled by changing the total flow rate as well as the consistency of the synthesis), ultra violet visible spectroscopy (UV-Vis; data not shown), and transmission electron microscopy (TEM; above image showing Zein AuNP hybrids).

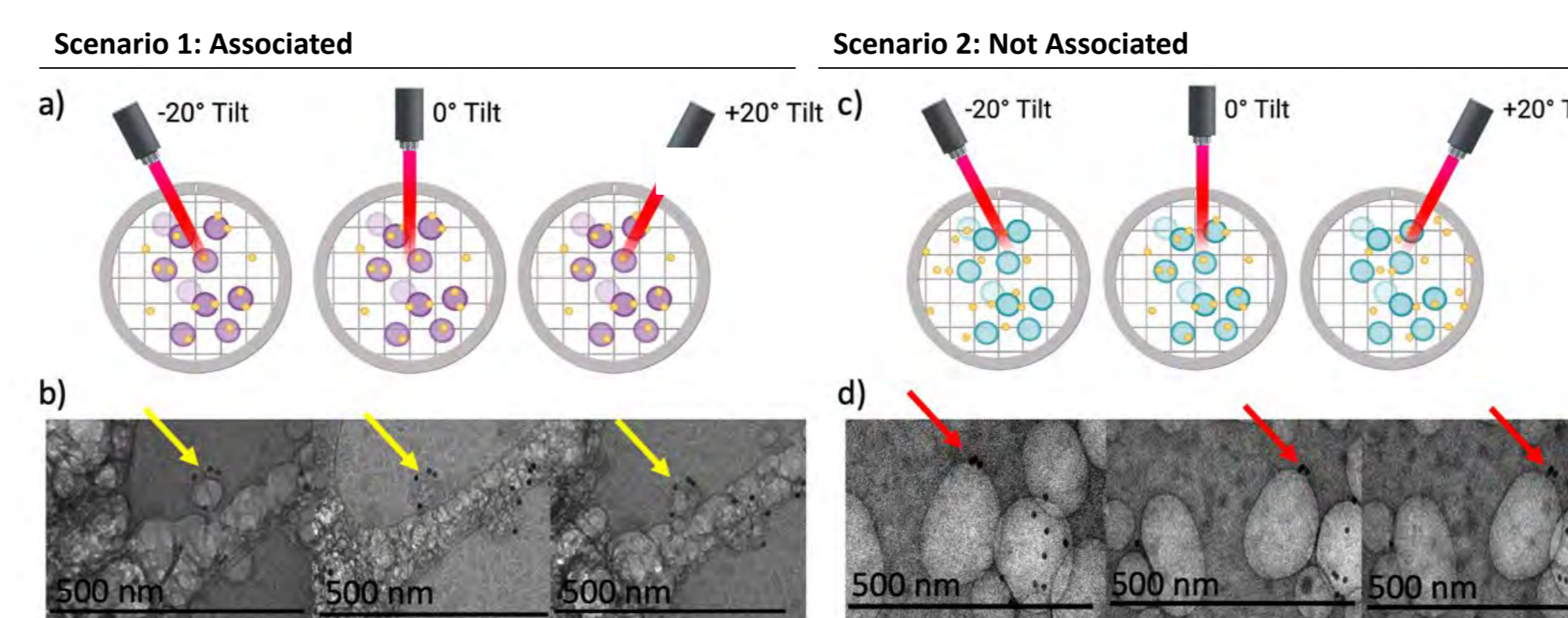
All other variables are held constant for each experiment other than the one being investigated * p<0.05; ** p<0.01; *** p<0.001; **** p<0.0001

Hybrid Characterization

Step1: Identify Stable Formulations Varying The Ratio Of Protein To Gold Nanoparticles

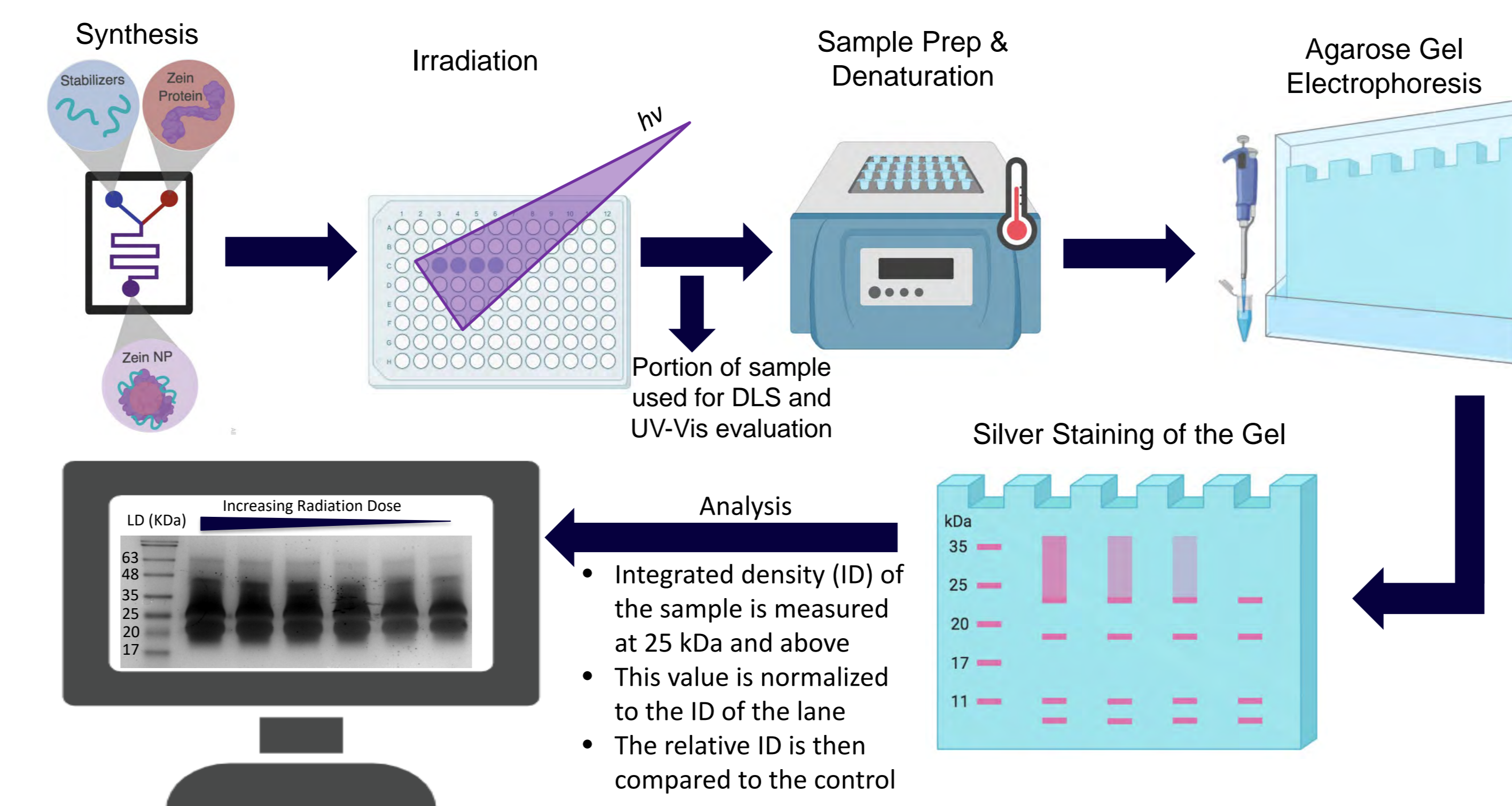


Step2: Further Confirm Association Using Cryo-TEM

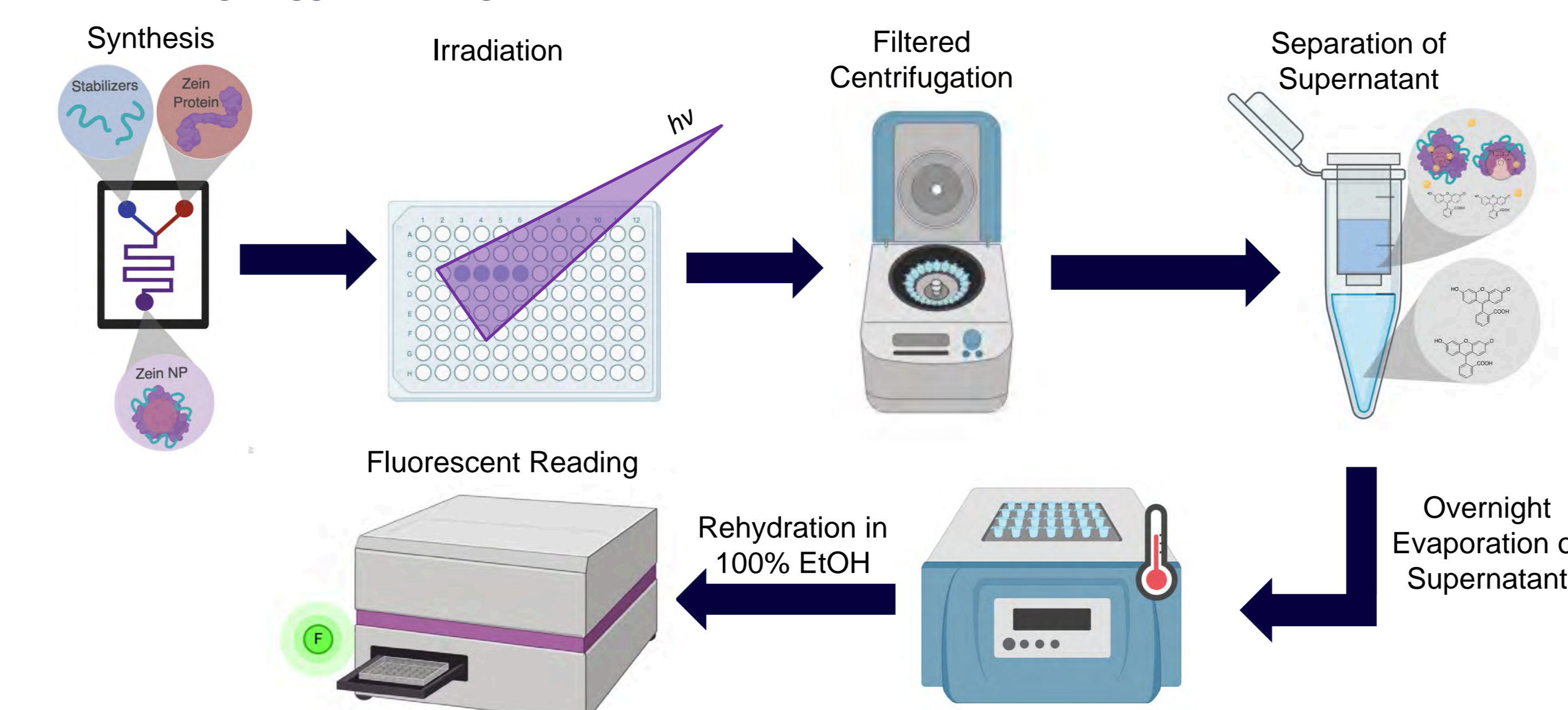


X-Ray Zein Interactions: Methods

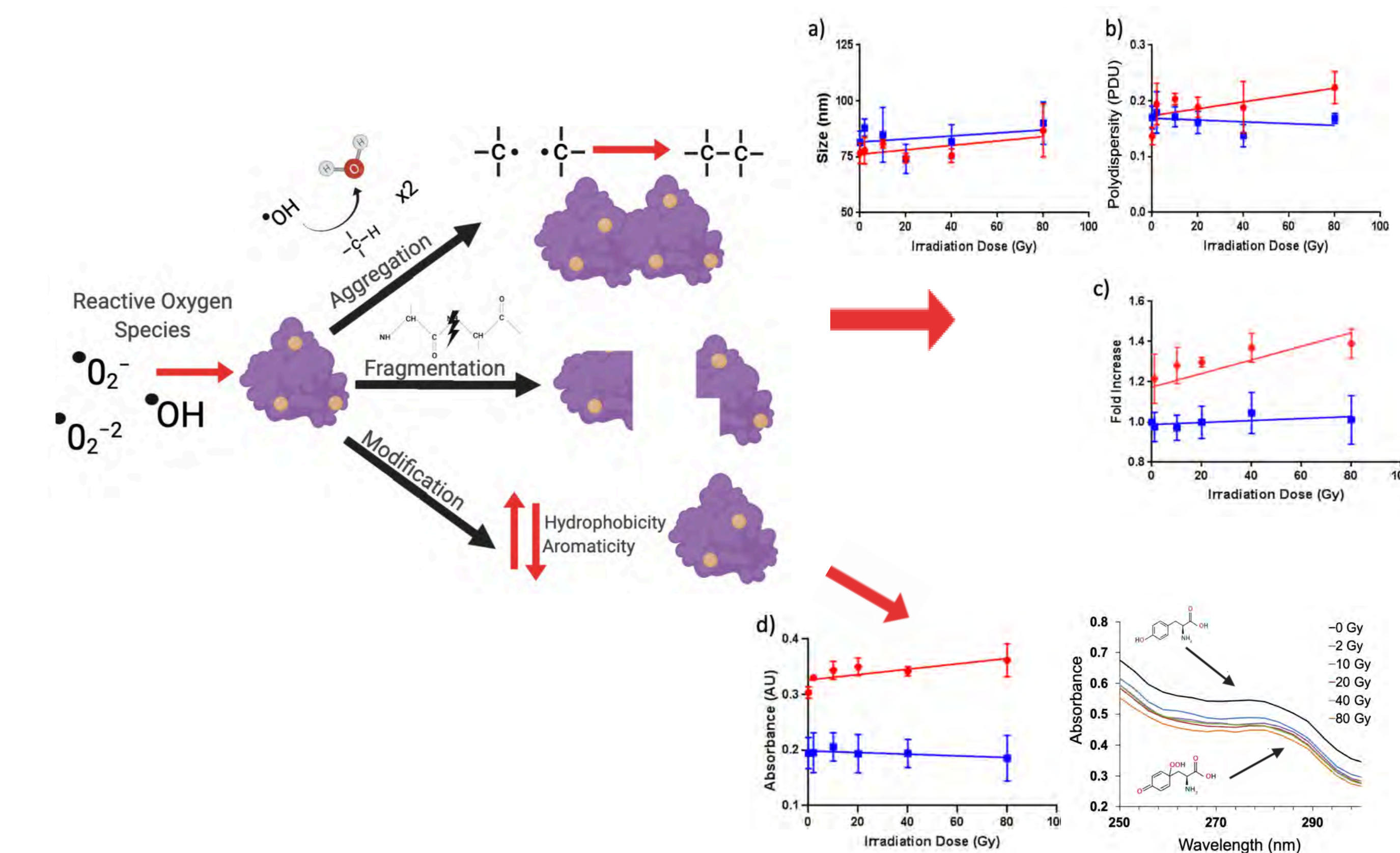
Measuring Primary Structure Changes of Zein NPs and Zein AuNPs Post Irradiation:



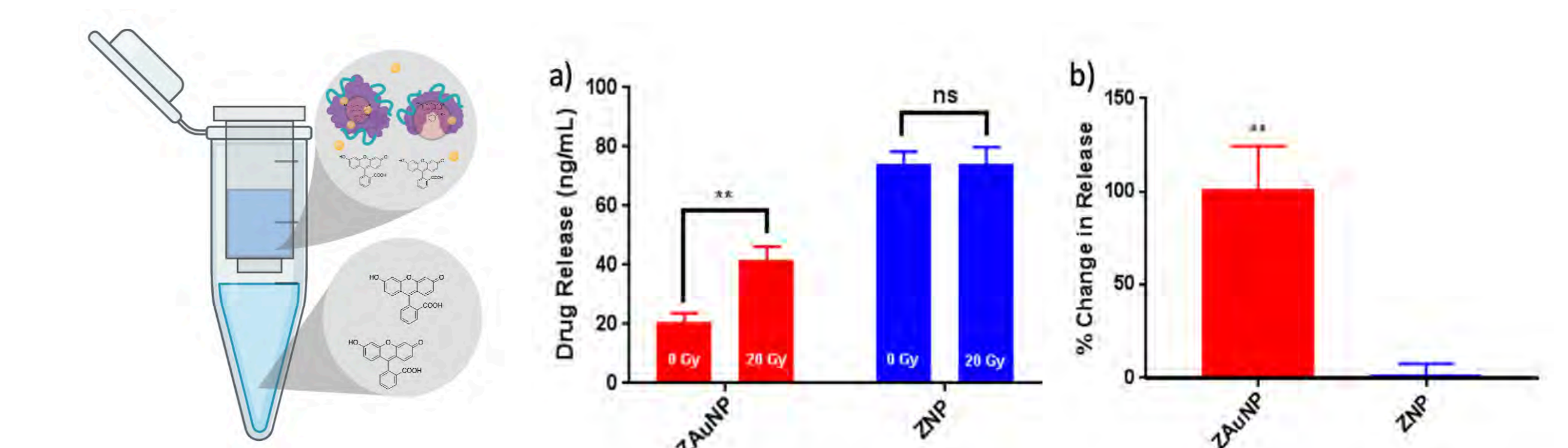
Measuring Triggered Drug Release of Zein NPs and Zein AuNPs Post Irradiation:



Protein Structure Changes



Triggered Drug Release



Conclusion and Future Work

While X-Ray triggered hybrid Zein AuNPs has shown to be a promising method for on-demand drug delivery, further experiments are still required:

- Cisplatin release studies with Zein NPs and Zein AuNPs
- Cell toxicity studies of the Zein NP and Zein AuNP systems
- Efficacy drug release studies in the presence of cells
- Vehicle safety and organ distribution studies *in vivo*

References

1. Brockstein, B., Vokes, E., and Eisbruch, A. Locally Advanced Squamous Cell Carcinoma of the Head and Neck: Approaches Combining Chemotherapy and Radiation Therapy. UpToDate, 2019.
2. van Ballegoie, C., Man, A., Win, M., Yapp, D. Spatially Specific Liposomal Cancer Therapy Triggered by Clinical External Sources of Energy. *Pharmaceutics*, 2019. 11(125).
3. Images generated using BioRender

