

Engineering Nanoparticle Shape for Increased Uptake by Breast Cancer Cells

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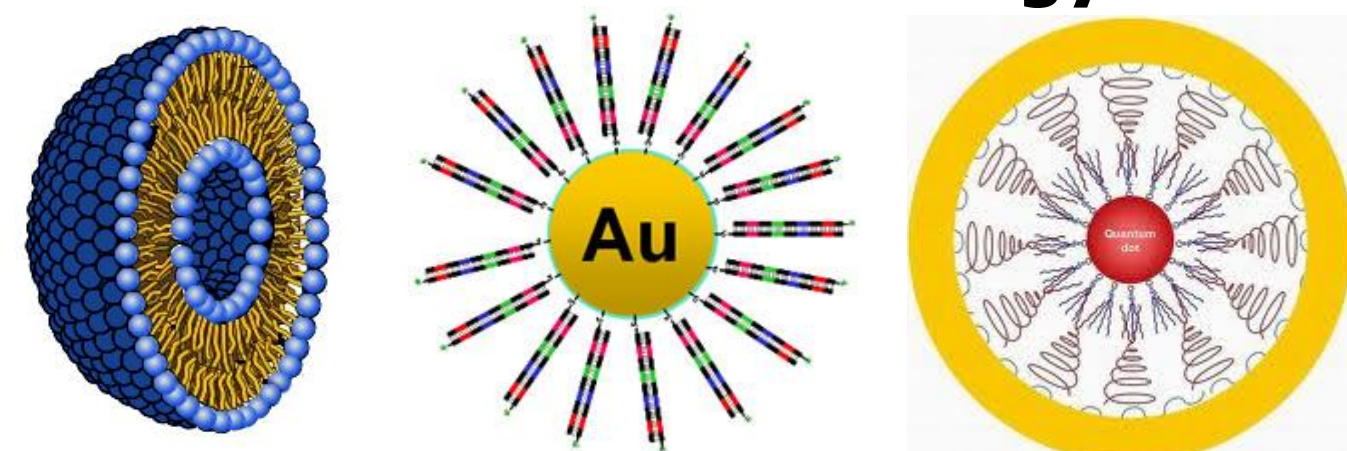
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Objective

The objective of this project is to better design nanoparticle geometry, specifically shape, for active binding and distribution of drug molecules among diseased cells such as cancer.

Background

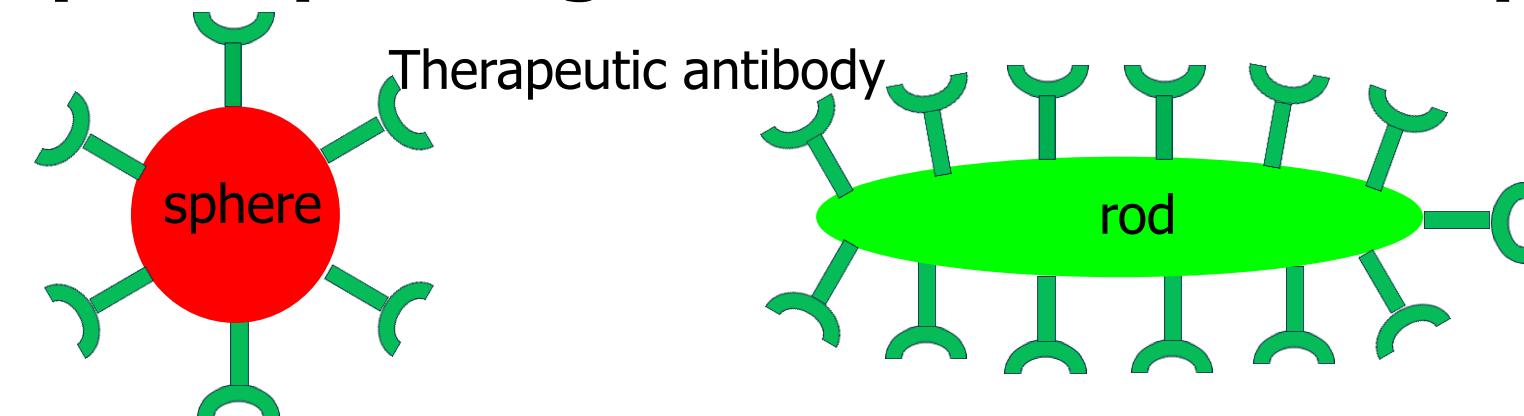
Cancer Nanotechnology



Current nanoparticle therapies including liposomes, gold nanoparticles, and quantum dots (from left to right), are spherical in shape and have not shown much efficacy in drug delivery.

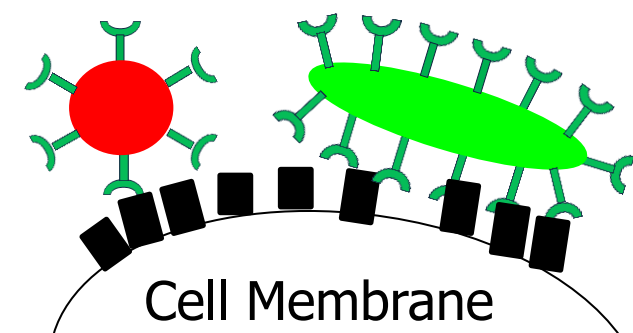
Hypothesis: Shape Does Matter

Rod-shapes expose higher surface area than spheres



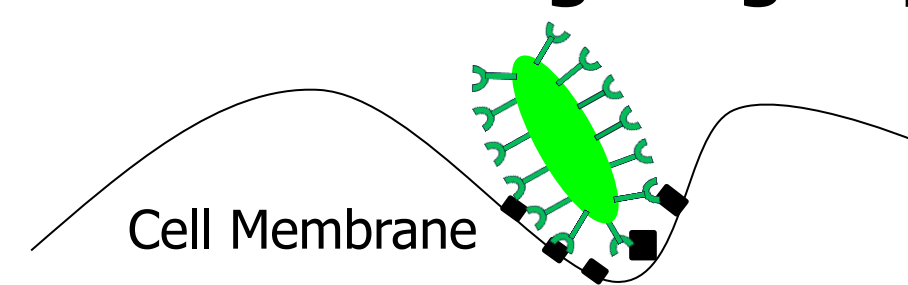
Changing the nanoparticle shape from spheres to rods exposes more surface area to interact with the cell membrane. The cartoon depicts nanospheres and nanorods coated with herceptin anti-bodies.

Shape matters for targeting cell membrane



Nanorods bind more than nanospheres through Herceptin antibody binding to HER2 cell surface receptor proteins.

Better targeting improves uptake by cells



Nanorods are taken up more than nanospheres by breast cancer cells via receptor mediated endocytosis.

Significance for the treatment of cancer

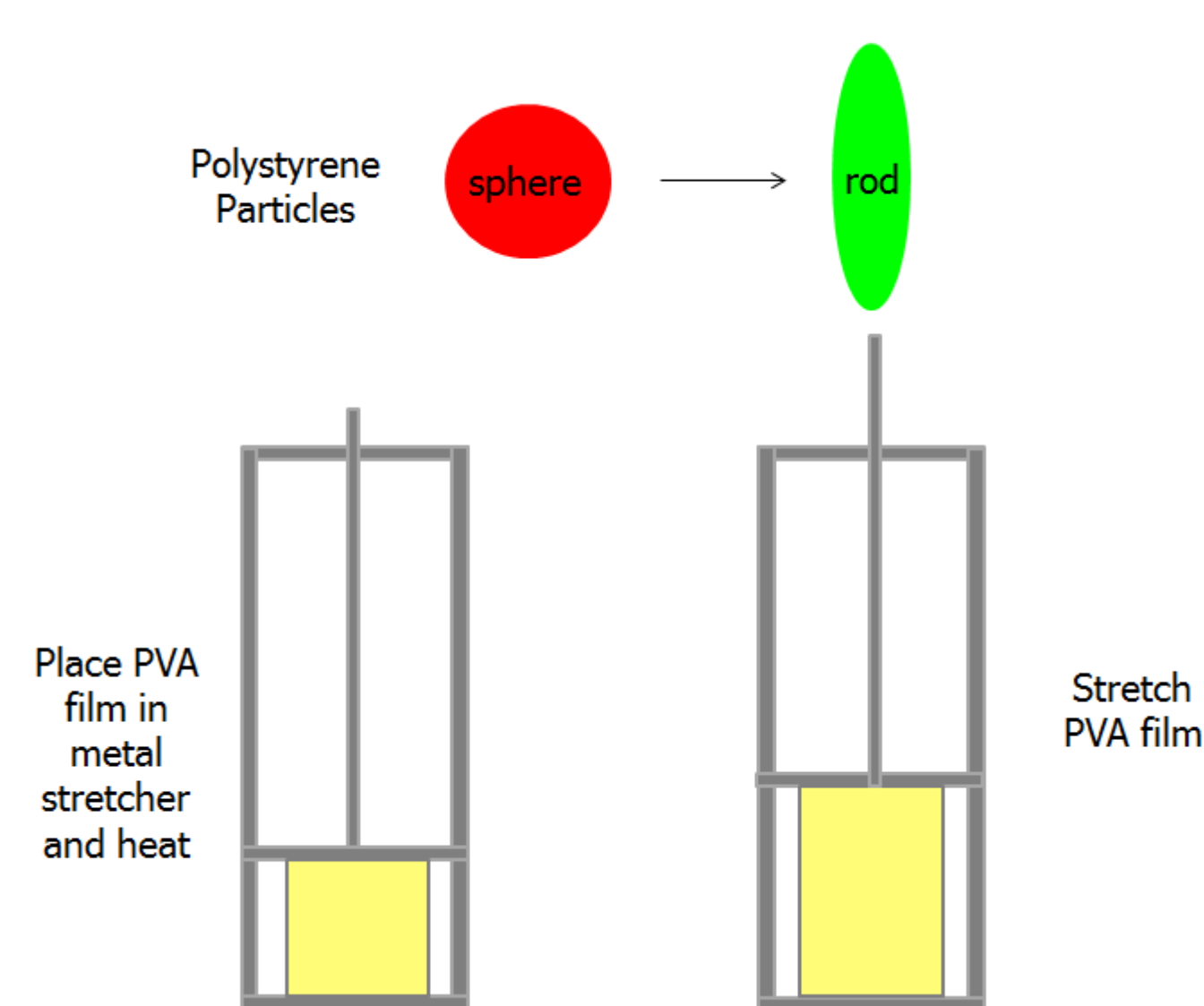
The therapeutic activity of Herceptin alone is low in a variety of cancer cells, including breast cancer. Presentation of the antibody on nanorods improve its efficacy.

3D breast cancer cell work

In actual breast cancer cells, nanoparticles cannot penetrate deep into cancer cells. In this study, we investigate the effect of nanoparticle shape to improve penetration into 3D breast cancer cells.

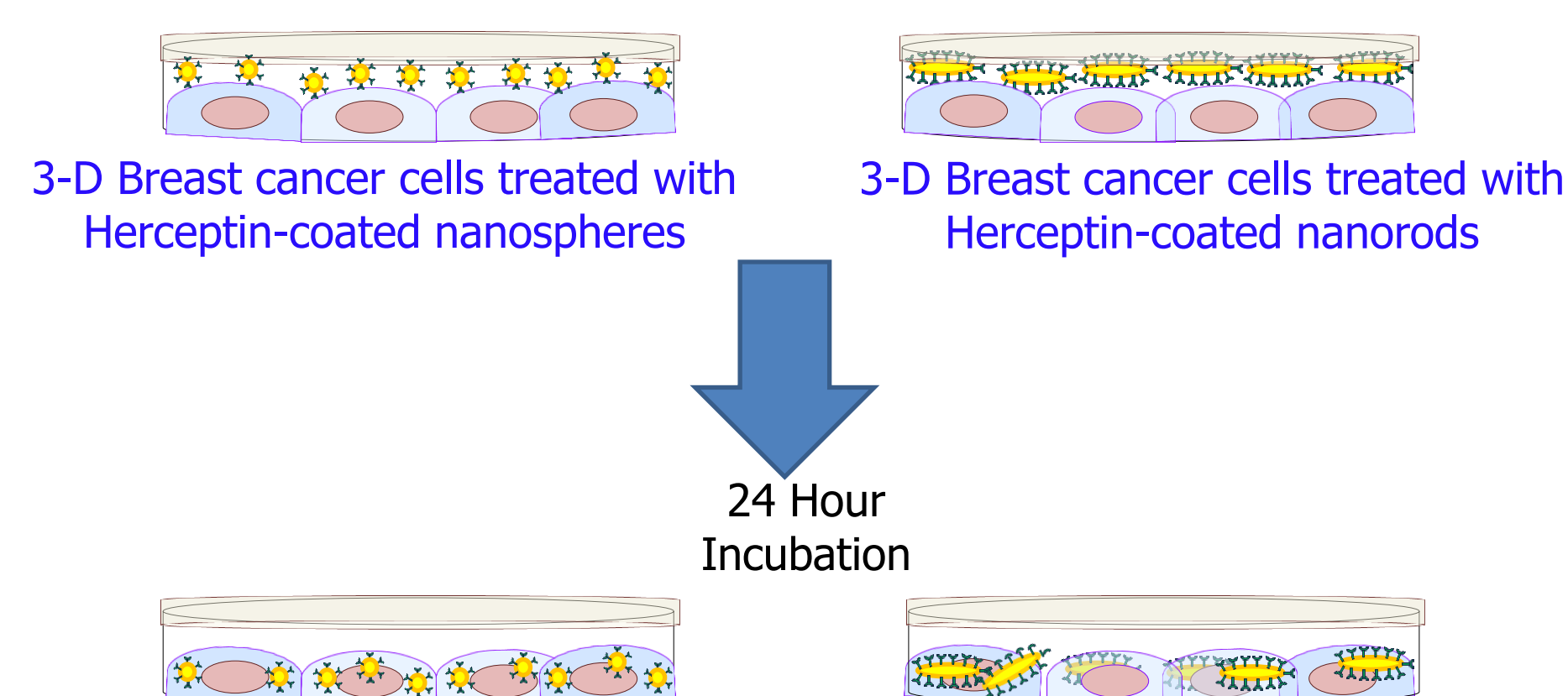
Methods

Nanoparticle Stretching



Nanospheres can be stretched into different shapes using nanoparticle stretching techniques. The nanospheres are entrapped in a polymer film which is then heated and stretched to create various nanoparticle shapes. The nanoparticles are then recovered through a series of isopropyl alcohol and water washes.

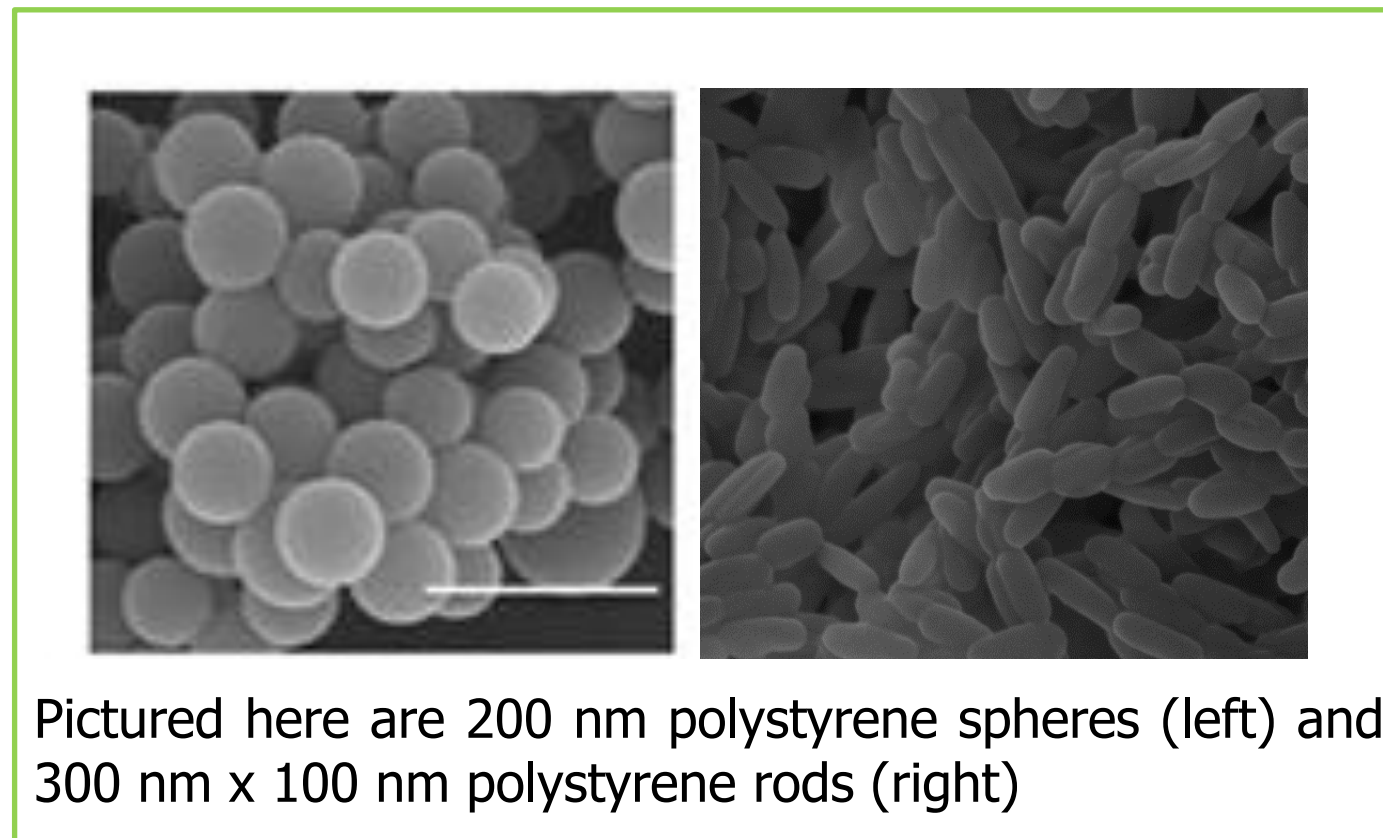
3D Cell Culture



By forming 3D cells using matrigel, we incubate these cells with Herceptin coated nanoparticles and use confocal microscopy to visualize and quantify the differences in nanoparticle penetration.

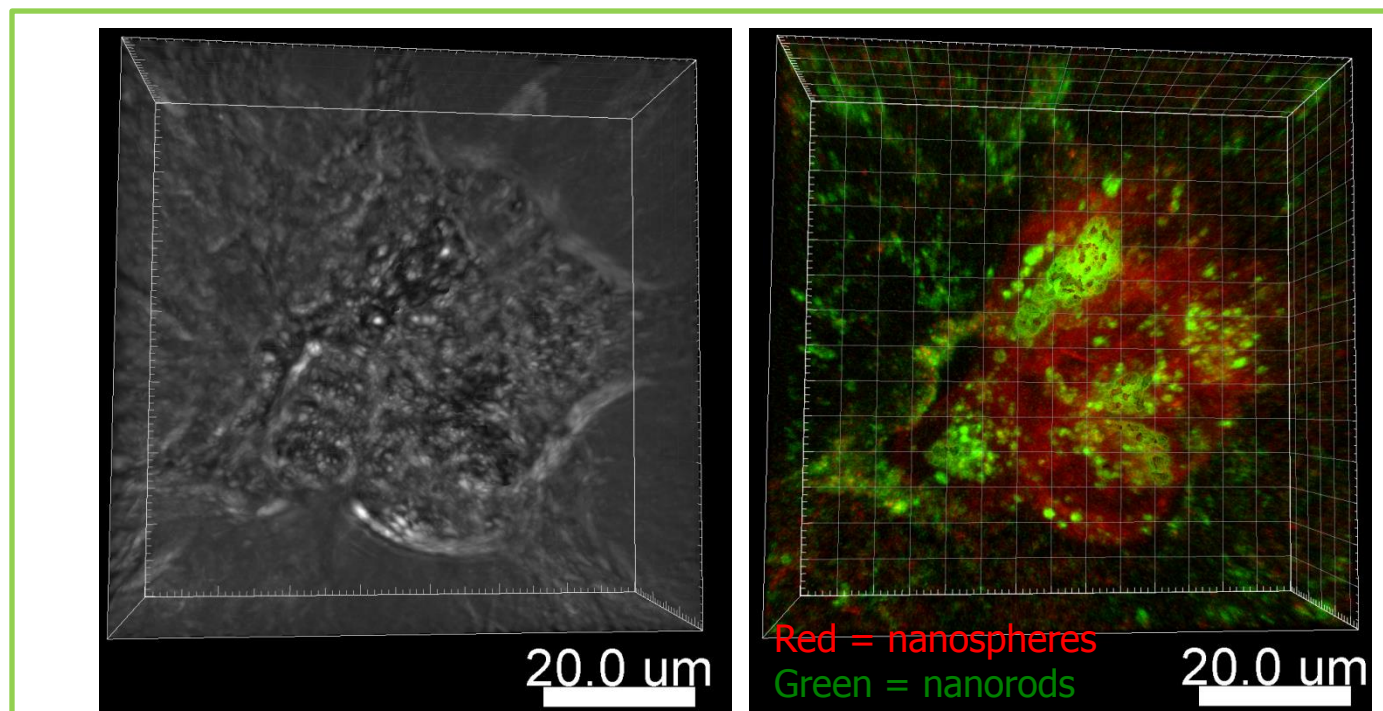
Results

Figure 1: Spherical and Rod-Shaped Nanoparticles

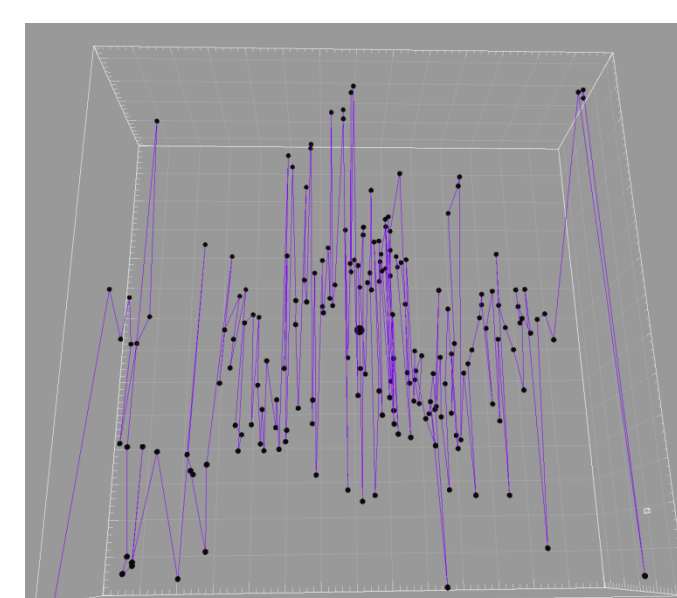


Pictured here are 200 nm polystyrene spheres (left) and 300 nm x 100 nm polystyrene rods (right)

Figure 2: Confocal Images of 3D Breast Cancer Cells

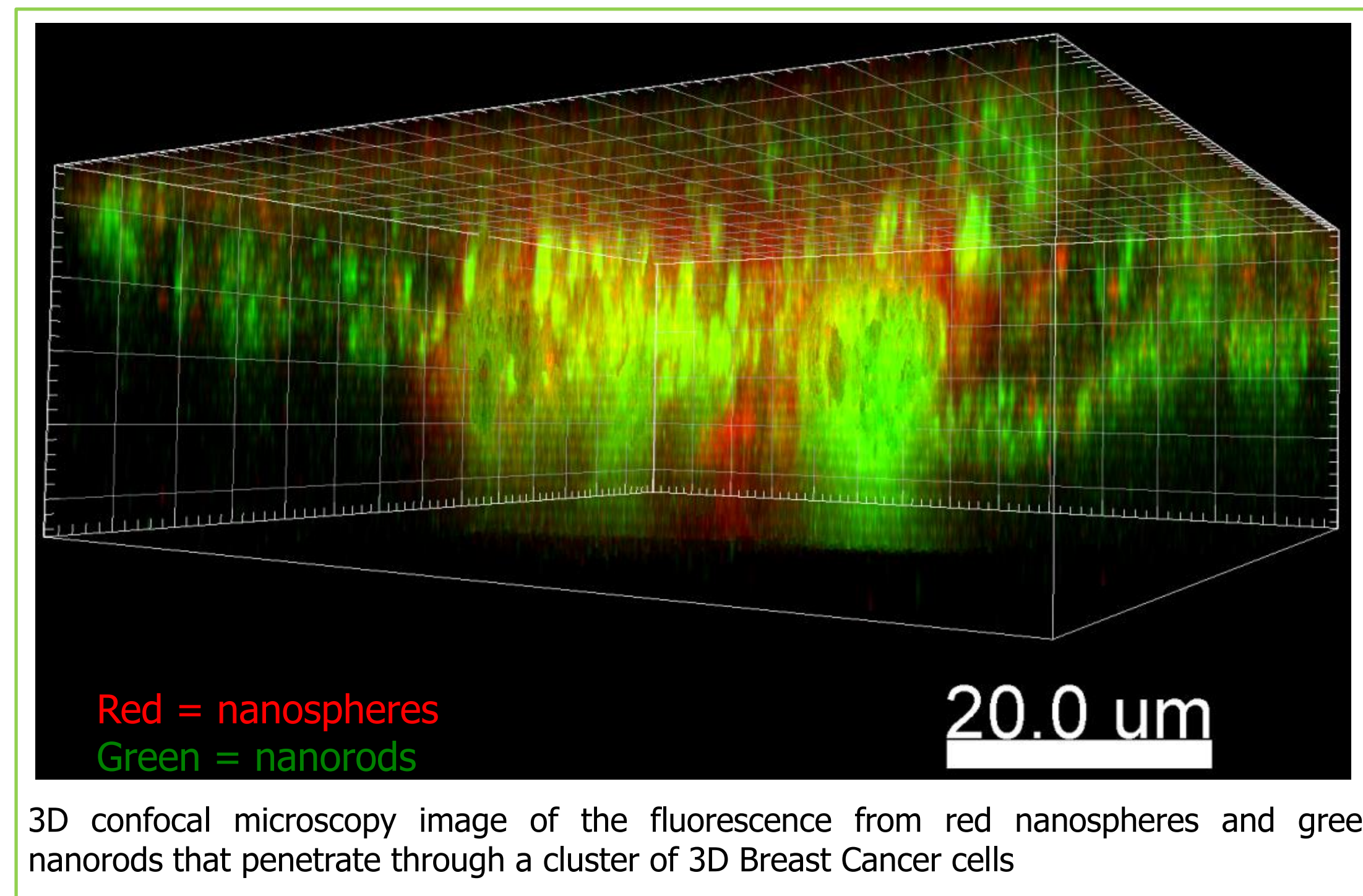


3D confocal microscopy image of a cluster of 3D cancer cells on the right. On the left, the fluorescence from the nanoparticles is visualized.



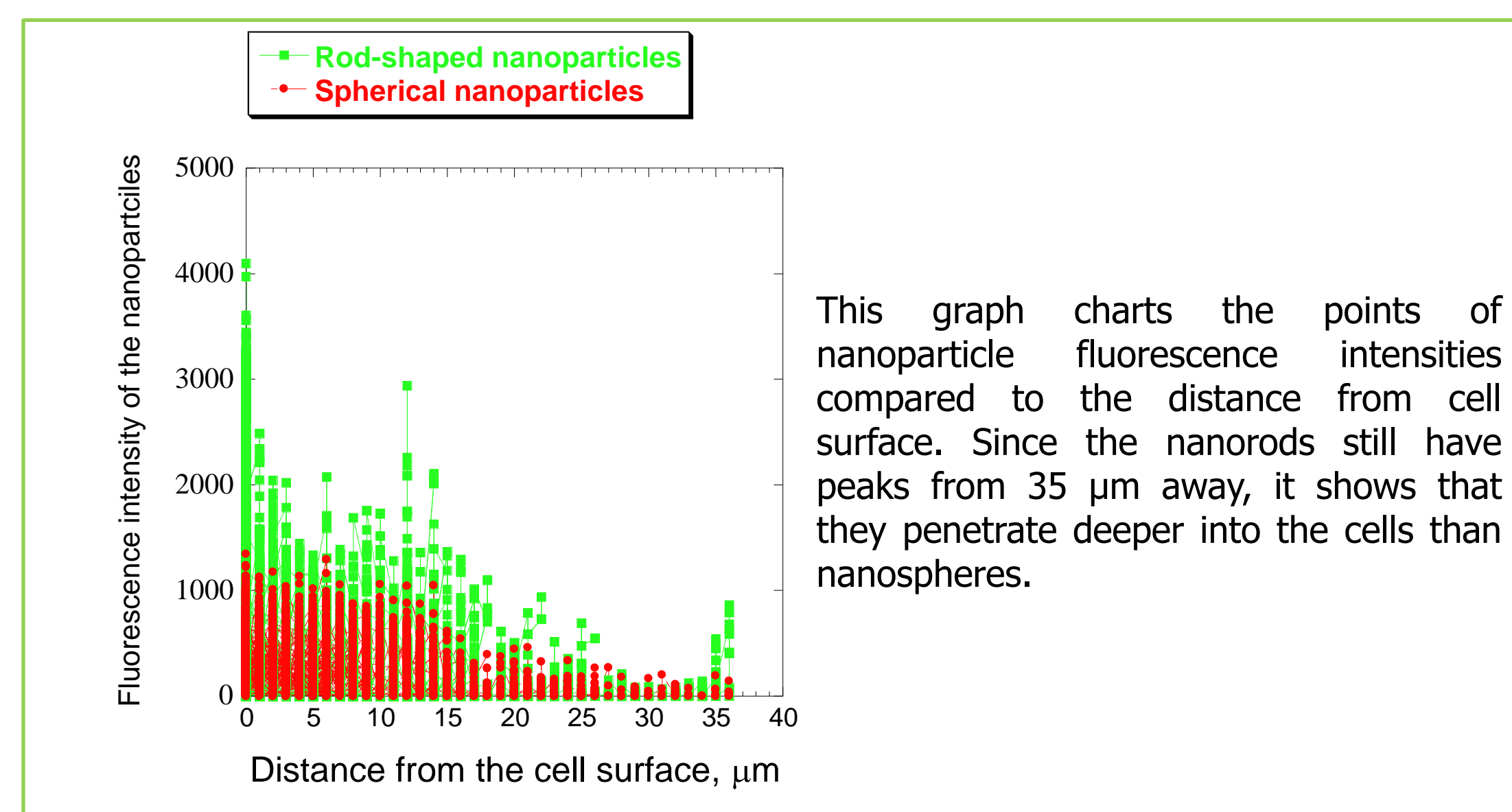
The dots symbolize points of fluorescence intensity which is further quantified on the graph to the right.

Figure 3: Nanoparticle Penetration in 3D Breast Cancer Cells



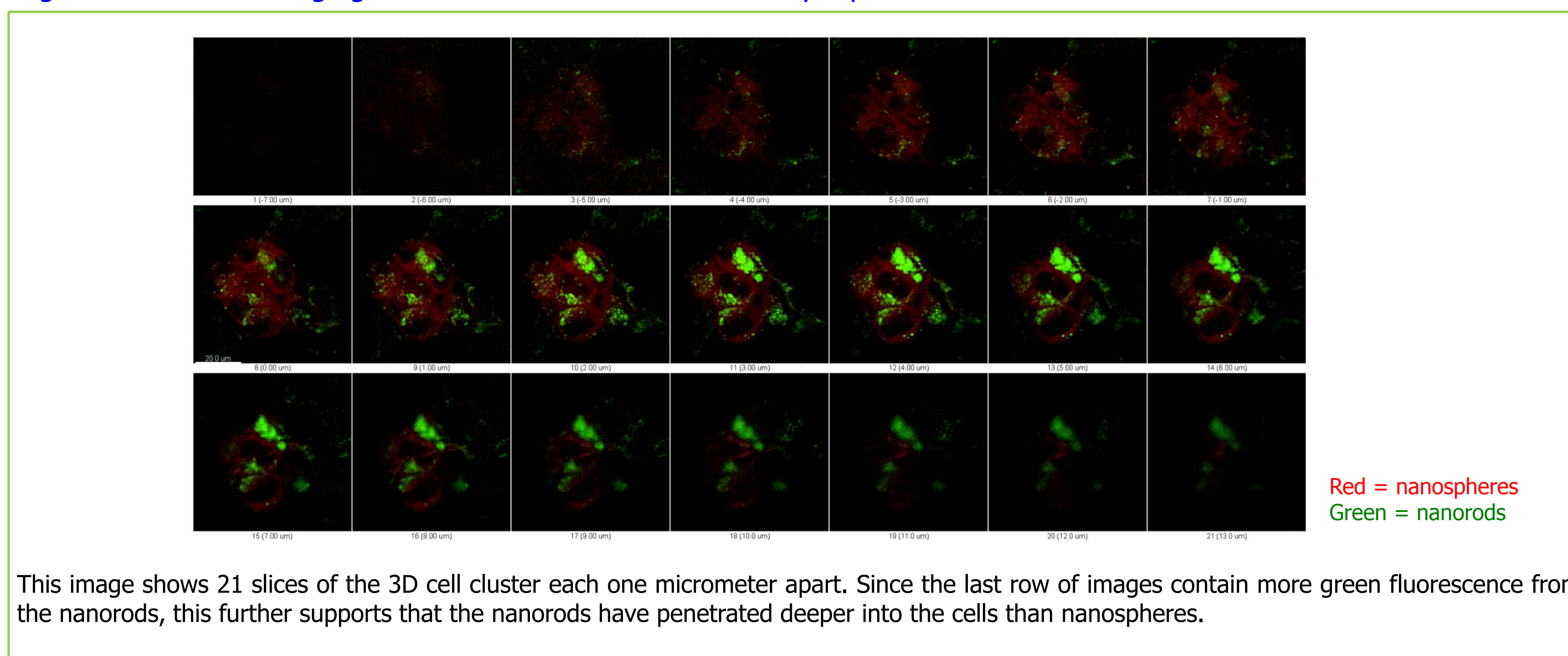
3D confocal microscopy image of the fluorescence from red nanospheres and green nanorods that penetrate through a cluster of 3D Breast Cancer cells

Figure 4: Quantitative Measurements of Nanoparticle Fluorescence Intensity



This graph charts the points of nanoparticle fluorescence intensities compared to the distance from cell surface. Since the nanorods still have peaks from 35 μm away, it shows that they penetrate deeper into the cells than nanospheres.

Figure 5: Confocal Imaging of 3D Breast Cancer Cells at Every 1 μm Distance



This image shows 21 slices of the 3D cell cluster each one micrometer apart. Since the last row of images contain more green fluorescence from the nanorods, this further supports that the nanorods have penetrated deeper into the cells than nanospheres.

Summary

Nanorods penetrate deeper into cells than nanospheres leading to more effective drug delivery to cancer cells.

Future Work

More trials of this study will be done to further quantify our work. Further modeling of the work will be done using a 3D tumor model.

Significance

This work has a tremendous impact in the field of drug delivery not only for the treatment of cancer but also other diseases which suffer from poor transport of drugs to the complex tissue microenvironment.

References

Barua, Sutapa, Yatin R. Gokarn, Poornima Kolhara, Samir Mitragotri, Aditya Wakankarc, and Jin-Wook Yoob. "Particle shape enhances specificity of antibody-displaying nanoparticles." *Proceedings of the National Academy of Sciences* 110.9 (2013): 3270-3275.
Champion, Julie A., Yogesh K. Katare, and Samir Mitragotri. "Making polymeric micro-and nanoparticles of complex shapes." *Proceedings of the National Academy of Sciences* 104.29 (2007): 11901-11904.

Acknowledgements

Thank you to CNSI and CSEP for providing the funding for my research through the EUREKA Internship. I would also like to thank Maarten Bakker for working alongside my mentor and I. Lastly, I would like to acknowledge Sutapa Barua for all of her patience and support.