Liposome Imaging in Optically Cleared Tissues

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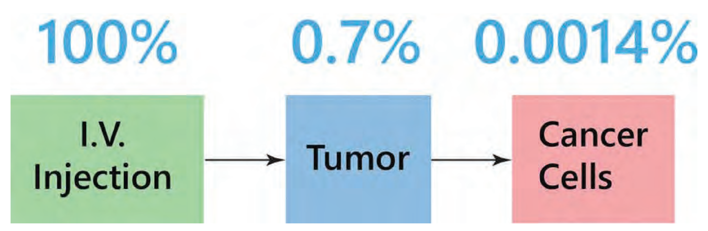
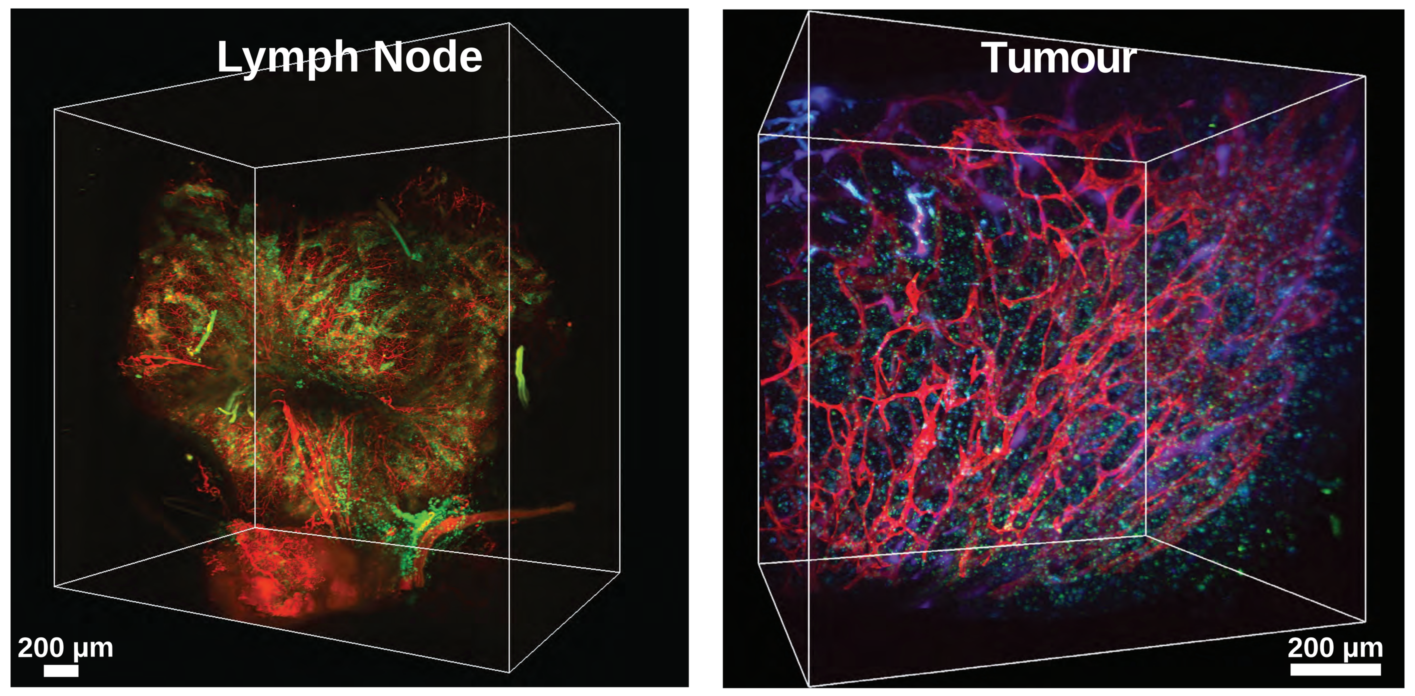
Delivering nanoparticles (NP) to cancer cells remains a challenge

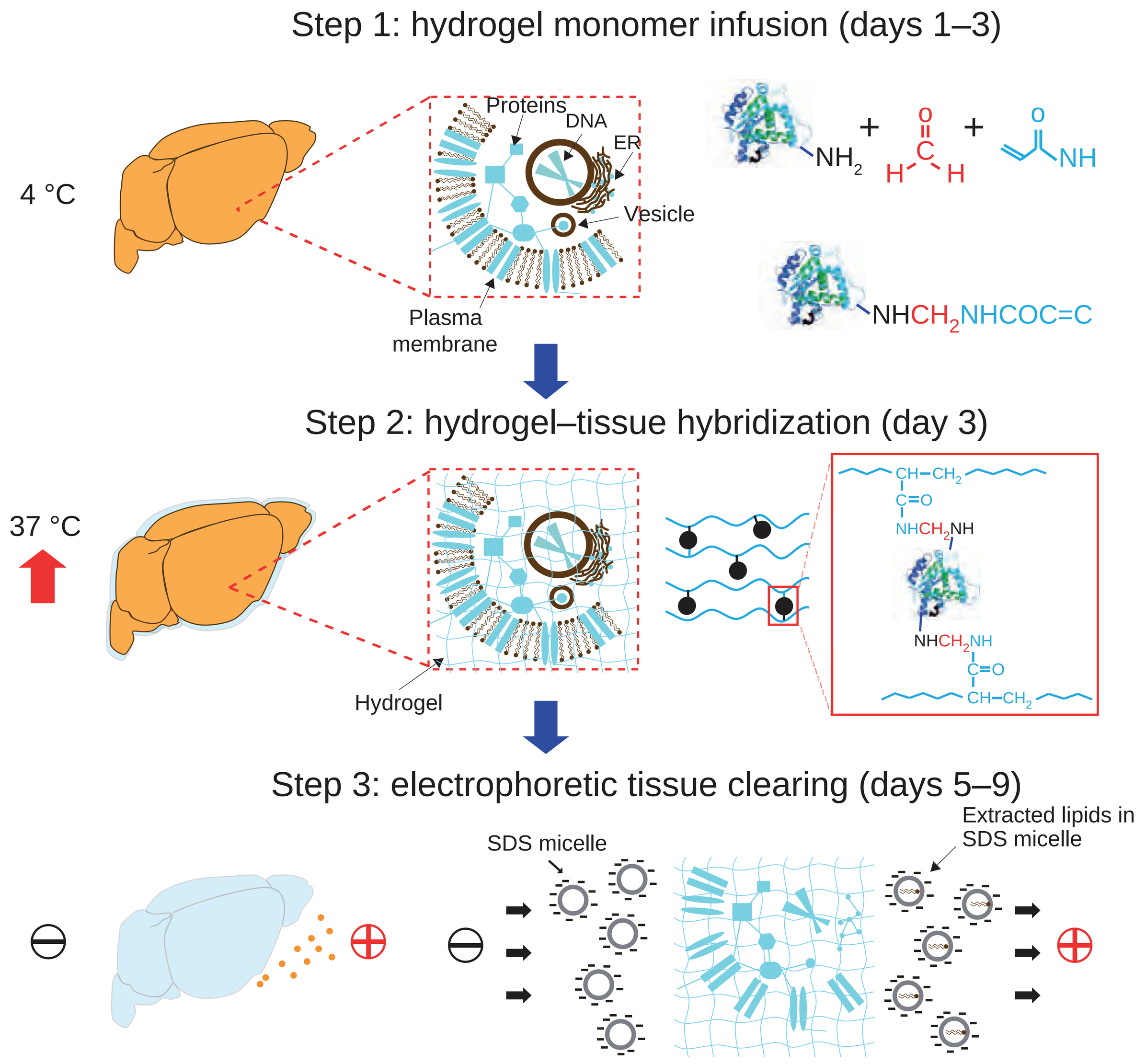


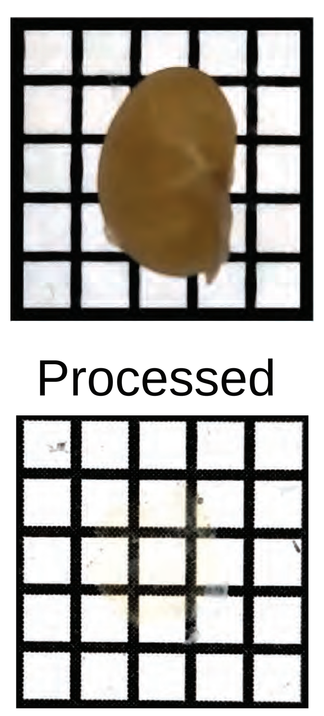
For every 1,000,000 injected nanoparticles, only 14 reach cancer cells.[1]

3D microscopy allows the barriers to NP delivery to be visualized



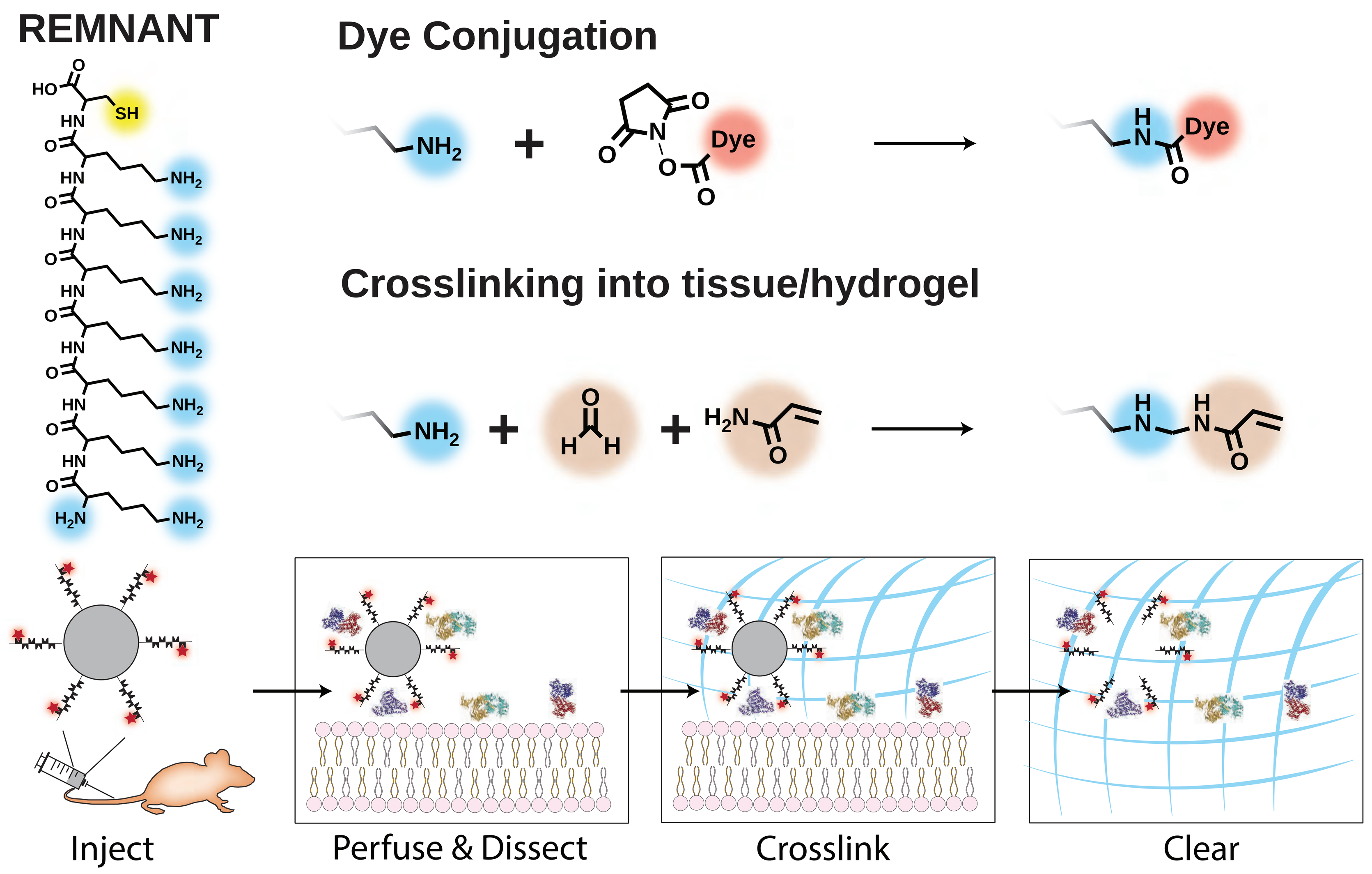
But 3D microscopy requires optically cleared tissues²...





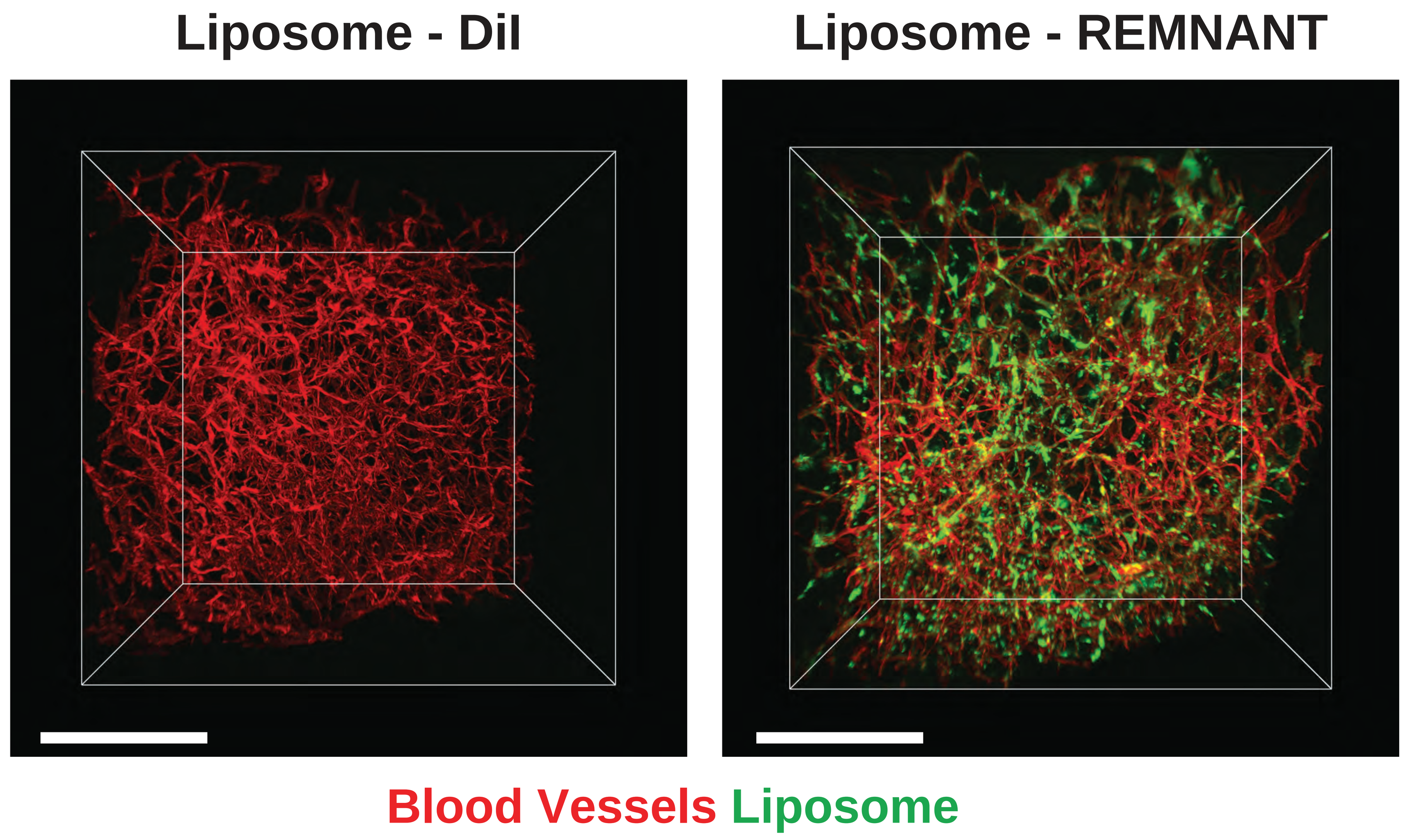
which destroys liposomes and most NP labels

REtained Molecule and NANoparticle Tag



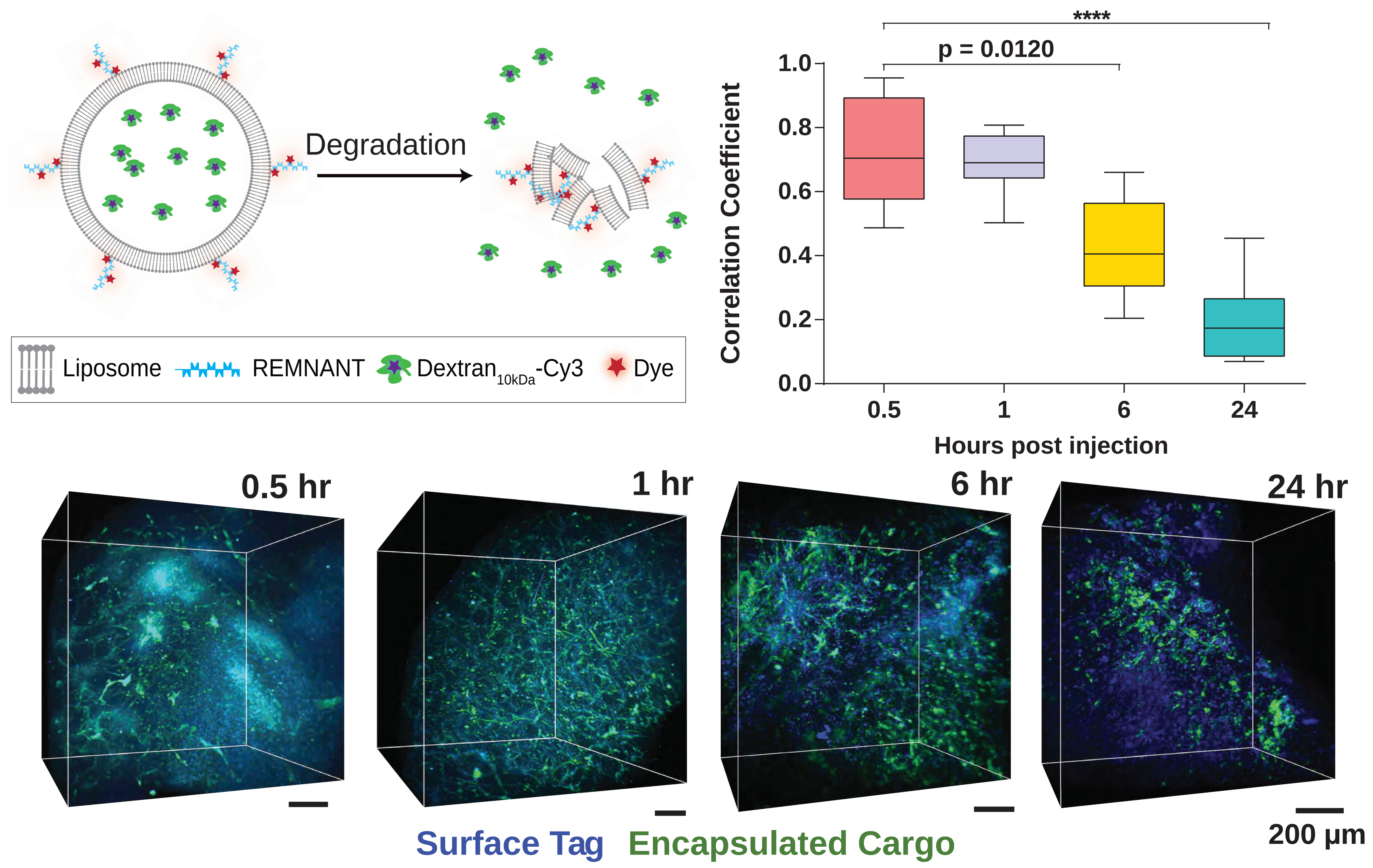
REMNANT is a nanoparticle tag that can be conjugated to the surface of the nanoparticle. REMNANT contains mulitple amine groups which allow it to be fluorescently labeled and crosslinked directly into the tissue hydrogel during tissue clearing. This allows the labeled REMNANT to be retained in cleared tissues even though the nanoparticle is destroyed.

Liposomes can be visualized in cleared tissues using REMNANT



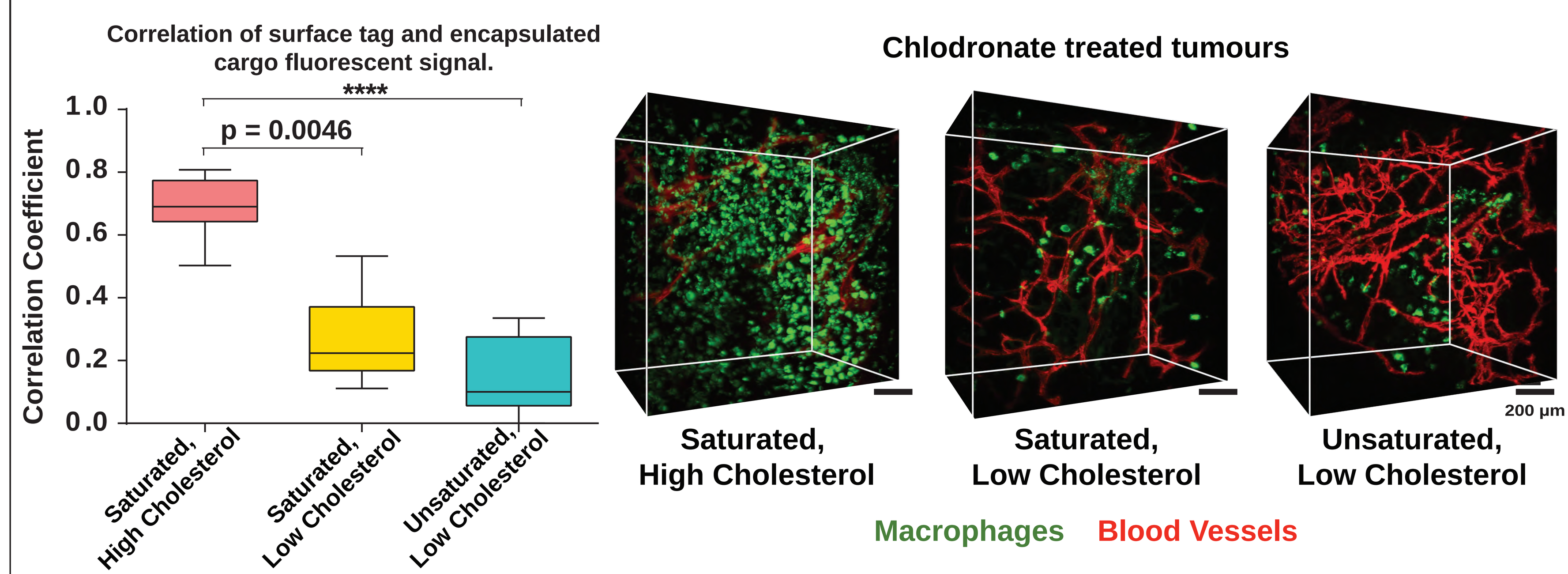
Conjugation of REMANT to the surface of the liposome allows its position to visualized in cleared tissues.

REMNANT can measure *in situ* liposome release rates



The fluorescent signals from the liposome surface and encapsulated cargo can be used to monitor liposome degradation rates. Correlated signals (cyan) indicate intact liposomes. Uncorrelated signals (blue and green) indicate degraded liposomes.

Liposome composition alters relaease rate



Liposome composition was shown to impact its degrataion rate at 1hr post injection. These degradation rates were shown to alter the effect of an encapsulated drug, chlordronate, on the resultant tumour associated macrophage (TAM) population. Fast degrading liposomes were shown to be more effective at killing TAMs.

Conclusion

REMNANT allows clinically relevant NPs to be imaged in 3D at subcellular resolution over large volumes. This provides a method to study liposome degradation *in situ*, and opens up new methods to optimize liposome composition for improved theraputic effect.

References and Acknowledgments

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3. Syed, A. **MacMillan, Presley**. et al. Liposome imaging in optically cleared tissues. *Nano Let. 20,* 1362-1369 (2020)

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