|Tuning hydrophobicity of gold nanoclusters to enhance membrane penetration

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Abstract

Understanding how ultra-small gold nanoparticles (metal core ~ 1–1.5 nm), so-called gold nanoclusters (Au NCs), interact with biological barriers has become highly important for their future bioapplications. The properties of Au NCs with tunable hydrophobicity were extensively characterized in 3 different biological situations: i) interaction with serum in solution, ii) interaction with synthetic free-standing lipid bilayers integrated in a microfluidic device, and iii) cell studies with two different cell types (U87MG human primary glioblastoma and A375 melanoma cell lines). Our results indicate a significant impact of the precise tailoring of the hydrophilicity/hydrophobicity balance on the Au NC surfaces, which could prevent the formation of biomolecular absorption while maintaining excellent colloidal stability in solutions with high serum contents. Increasing the surface hydrophobicity of the Au NCs enabled more efficient lipid bilayer membrane insertion and induced faster cellular uptake. We showed the existence of a hydrophobicity threshold, which resulted in colloidal instability, lipid bilayer damage, and acute cytotoxicity.