Parallel conjugation of PEG and peptide

Gold nanoparticles are nontoxic nanocarriers of biomolecules for potential therapeutic delivery applications. Peptides can function as targeting and therapeutic agents. The most direct way of conjugation of peptides with gold nanoparticles is to tether thiolated peptides onto gold surfaces (Fig. 1a). Such conjugates often lack colloidal stability and have short circulating life time. It is also widely practiced to pre-link the peptides with PEG molecules (Fig. 1b) to improve circulation time. However this route requires complex protocol, is time consuming, and can be challenging for quality control.

Partially PEGylated i-colloid Au nanoparticles

With i-colloid Au nanoparticles, we provide a simple protocol where the gold nanoparticles are pre-loaded with sub-monolayer PEG molecules (Fig. 1c). Peptide conjugation proceeds simply by adding peptides to the colloid of the partially PEGylated gold nanoparticles. The result is a conjugate comprising gold nanoparticles and dual molecules loaded in parallel. Such easy-to-use protocol can significantly save process time and improve quality control.

Why i-colloid Au?

PEGylation process can trigger colloid instability unless PEG molecules are provided in excess amount to saturate the gold surface. However this often leaves no space for loading other functional biomolecules. The colloidal stability of partially PEGylated i-colloid Au nanoparticles is ensured by the high colloid purity (see Technical note T01). Figure 2 demonstrates the stability of i-colloid Au with various loadings of PEG molecules (top). With traditionally synthesized gold colloids of less purity, aggregation is observed at partial PEG coverage.

Cell uptake

Partially PEGylated i-colloid Au nanoparticles conjugated with RGD peptide are tested for cell uptake by cancer cells. Under optical microscope, it is observed that the gold nanoparticles are concentrated in the cell nucleus region (Fig. 3), demonstrating satisfactory cell membrane penetration capability and high mobility of the conjugates inside the cells.