Raman Spectroscopy Monitoring of Intracellular Anticancer Drug Release

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Dark-field microscopy (DFM) and surface-enhanced Raman scattering (SERS) provided the evidence of the intracellular drug-coated AuNP loads.[1] *In vitro* and *in vivo* glutathione (GSH)-induced purine or pyrimidine anticancer drug releases on gold nanoparticle (AuNP) surfaces were investigated by means of label-free Raman spectroscopy.[2,3] Releases of 6-mercaptopurine (6MP), 6-thioguanine (6TG), gemcitabine (GEM), acycloguanosine (ACY), and fadrozole (FAD) were examined in a comparative way by means of SERS. We observed fairly strong SERS signals of the anticancer drugs in cell culture media solution. Direct monitoring of GSH-triggered release of 6MP and 6TG was achieved in real time. Live cell imaging technique provides a nanomolar range release of 6MP and 6TG from AuNP surfaces after the injection of external GSH. *In vivo* SERS spectra of 6TG were obtained from the subcutaneous sites in living mice after GSH treatment. GSH-triggered releases of Cy5-dye assembled on 6TG-capped AuNPs were also compared using independent fluorescence measurements. The GSH-induced dissociation constant of GEM (or ACY/FAD) from AuNPs was estimated to be larger by more than 38 times than that of 6TG from the kinetic relationship. After their cellular uptake, GEM, ACY, and FAD would not show SERS intensities as strong as 6TG. This may be due to easier release of GEM, ACY, and FAD than 6TG by intracellular reducing species including GSH. Our work demonstrates that the time-lapse Raman spectroscopic tools are useful for monitoring of the controlled release of thiopurine drug molecules *in vitro* and *in vivo*.

References

1. Analytical and Bioanalytical Chemistry 401 (2011) 1635.
2. Analytical Chemistry 84 (2012) 2172.
3. Analyst 137 (2012) 2852.

