GOLD NANOPARTICLE-BIOCONJUGATES AS CONTRAST AGENTS FOR CANCER CELL RECOGNITION AND DELIVERY AGENTS OF ANTI-LEUKEMIC TYROSIN-KINASE INHIBITORS FOR ACUTE MYELOID LEUKEMIA.

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Introduction.

Gold nanoparticles are extensively exploited in biomedical applications because of their easy preparation, ready bioconjugation and potential biocompatibility. Moreover, the reduced size of nanoparticles facilitates their delivery and incorporation into biological systems. Nevertheless, noble-metal nanoparticles have unique optical properties dominated by the excitation of so called localized surface plasmon resonances (LSPR) from the visible to the near-infrared (NIR) region of the electromagnetic spectrum which facilitates their detection in vivo using innovative, non-invasive techniques such as Surface-Enhanced Raman Scattering (SERS) spectroscopy. In the view of the above mentioned properties, one recent application of nanoparticles is their use for the development of new pharmacological molecular entities which can be delivered to targeted locations within the body in order to maximize therapeutic ratio and minimize systemic side effect.

Methods.

Having in mind the design of a specific, individualized therapeutic agent which relies on nanoparticle-structure properties, we chemically synthesized gold nanoparticles of various plasmonic responses (from Vis to NIR) and conjugated the particles either with fluorophores (eg. fluorescein isothiocyanate, cresyl violet perchlorate) for imaging applications or anti-leukemic drugs (quizartinib, midostaurin, sorafenib, lestauritinib) for therapeutic effect. Bioconjugated particles were characterized by transmission electron microscopy, UV-Vis-NIR absorption spectroscopy, dynamic light scattering, zeta potential, fluorescence and/or surface enhanced Raman scattering (SERS) and found to be biochemically stable and detectable inside cells. The functional tests included MTT assay, cell counting, cell cycle analysis and apoptosis assay.

Results.

Since a prerequisite for any therapeutic agent to be applicable in vivo is to be compatible with the healthy tissue nearby the targeted zone of malignancy, biological effects (proliferation and citotoxicity) of conjugated nanoparticles were investigated on OCI-AML3 acute myeloid leukemia cells and THP-1 human monocytic leukemia cells. Comparative tests between non-conjugated and conjugated nanoparticles revealed a direct dependence of cytotoxicity on particle concentration and also on their morphological and surface chemistry features. We have found that quizartinib, lestauritinib and sorafenib had an enhanced in vitro effect of conjugated with gold nanoparticles.

Conclusion.

The presented results evidence the potential of spectroscopic-active nano-conjugates to serve to combined purpose: as ultra-sensitive imaging tools for cancer cell identification and drug delivery vehicles for cancer nanotherapy.