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Radioactive Gold Nanoparticles In Nanomedicine: Neutron Activation and Radiochemical Approaches In Green Nanotechnology

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Effective delivery of radiopharmaceuticals, chemotherapeutic, hormonal and biological pharmaceuticals to the tumor tissue and cancer cells selectively continue to be the most vexing problems in cancer oncology. Radioactive nanoparticles with diagnostic and therapeutic capabilities provide intelligent drug delivery systems to maximize therapeutic activity and to minimize undesirable side-effects. For example the radioisotope of gold metal, Au-198, provides a desirable beta energy emission and half-life that destroys tumor cells/tumor tissue (βmax = 0.96 MeV; half-life of 2.7 days). Its penetration range (up to 4 mm in tissue or up to 1100 cell diameters) is sufficiently long to provide cross-fire effects to destroy tumor cells/tissue, but short enough to minimize radiation exposure to adjacent tissues. One particularly attractive feature of radioactive gold nanoparticles is that it does not have to be incorporated into every tumor cell to have a therapeutic effect. The path length of the emitted radiation is sufficient to allow effective therapy following uptake into a subpopulation of tumor cells. It is this feature that has attracted recent attention to apply nanotechnology for the effective delivery of therapeutic doses of beta emitting nanoparticles selectively to tumor tissue and tumor cells. We have recently carried out extensive in vitro and in vivo investigations to validate the hypothesis that glyco protein (gum Arabic) functionalized radioactive Au-198 nanoparticles are stable and biocompatible under in vivo conditions. Our research efforts have demonstrated that the complex polysaccharides and protein structures within the GA backbone can effectively lock gold nanoparticles on the protein matrix to produce non-toxic gold nanoparticulate constructs (GA-AuNP) which are stable under in vivo conditions for potential applications in tumor therapy (1). Our detailed in vivo studies, through intratumoral administration of GA-198AuNP (1.5⊠Ci/tumor), in SCID mice bearing human prostate cancer xenografts, have demonstrated retention of over 154.05 ±40.7 %ID/gm within the tumor at 30 min that declined to 87.0±16.9 %ID/gm by 24 h. The overall reduction in tumor volume was 80% three weeks after a single dose intratumoral administration of GA-198AuNP (408μCi).

In our continued efforts to apply Green Nanotechnology for the development of therapeutic radioactive gold nanoparticles, recently we have discovered that the high antioxidant capacity of Epigallocatechin gallate (EGCG), which is the most abundant catechin polyphenol in tea, can be used to convert radioactive Gold-198 precursor to the corresponding biocompatible radioactive gold nanoparticles functionalized with Laminin receptor specific EGCG. Laminin receptors are overexpressed in a large number of human tumors and the high in vivo affinity of EGCG toward Laminin receptors has allowed to develop Laminin receptor specific radioactive gold nanoparticles to achieve tumor specificity (2,3). This lecture will provide: (a) scope and prospects of beta emitting radioisotopes in nanomedicine; (b) details on the intervention of nuclear activation analysis and various radioanalytical approaches for the production of tumor specific radioactive gold-198 nanoparticles; and (c) full in vivo investigations on therapeutic properties of EGCG-198-AuNP agent in treating prostate tumors and (d) the overall implications of Green Nanotechnology of therapeutic beta emitting nanoparticles in oncology.

1. Katti, et.al: Functionalized Radioactive Gold Nanoparticles in Tumor Therapy. Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, 2012; vol. 4, no. 1, pp. 42–51,
2. Katti, et.al; Laminin Receptor Specific Therapeutic Gold Nanoparticles (198AuNP-EGCg) Show Efficacy in Treating Prostate Cancer; Proceedings of the National Academy of Sciences-PNAS-2012 2012 vol. 109 no. 31; 12426-12431
3. Katti, et.al: EGCG-Functionalized Radioactive Gold Nanoparticles in Tumor Therapy. W

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