Contribution ID: **822** Type: **Verbal**

Radioactive Gold Nanoparticles with Beta Energy and Auger Electron Cascades In Nanomedicine: Green Nanotechnology and Radiochemical Approaches

Friday, 18 May 2018 09:45 (15 minutes)

Theranostic Tumor-Specific Gold-198 Nanoparticles Through Green Nanotechnology—Implications In Nanomedicine For Concurrent Molecular Imaging and Tumor Therapy

Kattesh V. Katti, Kavita K Katti, Menka Khoobchandani
Institute of Green Nanotechnology, University of Missouri Cancer Nanotechnology Platform;University of Missouri; Columbia, Missouri 65212, USA
http://katteshkatti.com/
&
Ademar B. Lugao
IPEN, Sao Paulo, Brazil

Auger Electrons were once neglected for oncological applications because of their low energy and consequent short range. However, our recent discovery of the production of well-defined and clinically optimal Au-198 nanoparticles, through green nanotechnology, has changed the landscape of Au-198-derived Auger electron cascades, in oncology. Au-198 provides highly useful biologic toxicity to tumor cells and tumor masses for therapeutic applications in oncology. Internally deposited radionuclides, within tumor cells, result in radiation-induced ionizations, excitations, nuclear recoil, chemical transmutations, and local charge effects. ɣ-Photons, x-ray photons, and energetic negatrons and positrons which have a range of activity equivalent to many cell diameters are characterized by low linear energy transfer and oxygen-dependent biologic effects. In this context, 198Au provides a desirable beta and gamma energy emissions that can be used either to destroy tumor cells/tumor tissue (βmax = 0.96 MeV; half-life of 2.7 days) or to image the neoplasms in real time (gamma-ray energy of = 0.407 MeV). Its penetration range (up to 11 mm in tissue or up to 1100 cell diameters) is sufficiently long to provide cross-fire effects to destroy tumor cells, but short enough to minimize radiation exposure to tissues near the capsule periphery. Au-198 and its nanoparticles comprise of over 85% of the non-radioactive gold. This composition is 'Tailor-Made'for Auger, Coster-Kronig, and super-Coster-Kronig transitions with subcellular ranges (nanometers) as Au-198 decays by electron capture and/or internal conversion to extremely low-energy electrons through Auger effects. Our studies have already generated extensive therapeutic efficacy data (Katti et.al: PNAS 2012) from the treatment of tumors in mice and tumor bearing dogs (where the disease mimics human cancers). These findings have presented compelling prospects for the clinical translation of Auger electron-emitting radionuclides (such as Au-198) in treating human cancers. We envisioned that radioactive gold nanoparticles, which are inherently theranostic, will present realistic prospects in achieving optimal therapeutic payloads in prostate and other solid tumors because of their (i) size; (ii) inherent affinity toward tumor vasculature and (iii) most importantly through their favorable radiochemical properties. We have considered a scientifically sound and futuristic approach, involving green nanotechnology, for the synthesis, stabilization and incorporation of tumor specific features into radioactive theranostic gold nanoparticles. We strongly believe that it is imperative to minimize/eliminate the utility of toxic chemicals in the overall generation of nanoparticles for various medical and allied applications. Our approach to achieving tumor specificity and optimal retention of therapeutic payloads of radioactive gold nanoparticles at prostate tumor sites (and within various disease sites) has involved surface conjugation of radioactive nanoparticles with epigallocatechin-gallate (EGCg) and using a host of tumor specific biomolecules from various herbs and plants. We hypothesized that the redox properties of EGCg (comprised of polyphenolic constitution) could be

effectively utilized by using it as a reducing agent to convert radioactive gold precursor to the corresponding radioactive gold nanoparticles—a 100% green nanotechnological process without the intervention of any toxic chemical. An additional advantage of using EGCg is its ability to target 67kDa Laminin receptor (Lam 67R) which is over expressed on human prostate cancer cells and also in various other human tumors. EGCg has been known to bind to Lam 67R with excellent specificity and selectivity. Therefore, the fabrication of EGCg functionalized radioactive gold nanoparticles (198AuNP-EGCg) in our laboratory may be considered as a genesis of 'Green Nanotechnology in Medicine'. In this lecture, I will present experimental results that validate our hypotheses and also present full details encompassing: (1) synthesis and complete characterization of EGCg and various phytochemical functionalized tumor specific radioactive gold nanoparticles; (ii) evidence of endocytosis due to Laminin receptors on prostate tumor cells and quantitative estimation of AuNP-EGCg within PC-3 cells using neutron activation analysis (NAA) (ii) experimental results on the theranostic applications of Au-198 prostate tumor-specific AuNP-EGCg through in vivo studies in mice and tumor bearing dogs; and (iv) therapeutic efficacy studies of 198AuNP-EGCg in prostate tumor bearing mice and dogs, demonstrating excellent tumor retention resulting in over 85% inhibition of tumor growth through singular intratumoral injection. The overall oncological implications of this and a range of new nano theranostic agents in treating human prostate and various other solid tumors will also be discussed.

References:

1. Katti,. et al; et al. The application of nanotechnology in medicine: treatment and diagnostics. Nanomedicine (Lond.) (2014), 9(9),1291-1294
2. Katti at al., Irradiated chitosan nanoparticle as a water-based antioxidant and reducing agent for a green synthesis of gold nanoplatforms; Radiation Physics and Chemistry; Volume 106, January 2015, Pages 360–370
3. Katti, and Shukla 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

Primary authors: Prof. LUGAO, Ademar (IPEN); KATTI, Kattesh (University of Missouri); Dr KATTI, Kavita (University of Missouri); Dr KHOOBCHANDANI, Menka (University of Missouri)

Presenter: KATTI, Kattesh (University of Missouri)

Session Classification: RPH 2

Track Classification: Radiopharmaceutical Chemistry, Labelled Compounds