Inventors surprisingly discovered and now herein describe that hafnium oxide is able, when properly used in combination with metallic material, to render said metallic material, in particular gold, non toxic, without being detrimental to the metal therapeutic and diagnostic properties, thereby rendering the product of the invention advantageously usable *in vivo* in a mammal.

Inventors further believe that the claimed combination of metallic and hafnium oxide materials may be responsible for an efficient deposit of energy within the tumor structure said deposit being responsible for the dramatical enhancement of tumor destruction *in vivo* when activated by radiations when compared to standard treatments.

SUMMARY OF THE INVENTION

One ~~aspect~~ embodiment of the disclosure provides a nanoparticle comprising a metallic material at least partly covered with an hafnium oxide material or embedded therein. In a particular embodiment, the disclosed nanoparticle is a core-shell metal-oxide nanoparticle which comprises a metallic material fully covered with an hafnium oxide material or embedded therein. They also provide a composition comprising such a nanoparticle together with a pharmaceutically acceptable carrier. This composition may be a diagnostic composition or a pharmaceutical composition. Further embodiments relate to the disclosed nanoparticles for use in a mammal, preferably in a human being, as a diagnostic agent and/or as a therapeutic agent, in particular in oncology, more particularly when the nanoparticle is exposed to a radiation.

In one aspect, there is provided a core-shell metal-oxide nanoparticle comprising a metallic material at least partly covered with an hafnium oxide material or embedded therein for use in a mammal, preferably in a human being, as a therapeutic agent, in particular in oncology, when the nanoparticle is exposed to a radiation.

In another aspect, there is provided a composition comprising a core-shell metal-oxide nanoparticle comprising a metallic material at least partly covered with an hafnium oxide material or embedded therein as described above with a pharmaceutically acceptable carrier.

In another aspect, there is provided a core-shell metal-oxide nanoparticle comprising a metallic material fully covered with an hafnium oxide material or embedded therein for use in a mammal, preferably in a human being, as a diagnostic agent when the nanoparticle is exposed to a radiation.

FIGURES

Figure 1 provides an illustration of the inventive nanoparticle structure.

Figure 1A provides an illustration of metallic crystallite or aggregate of metallic crystallites.

Figure 1B provides an illustration of core-shell metal-oxide nanoparticles which comprise a metallic material fully covered with an hafnium oxide material or embedded therein.

Figure 1C provides an illustration of nanoparticles comprising a metallic material at least partly covered with an hafnium oxide material or embedded therein.

Figure 2 provides an illustration of the benefit over risk ratio of this inventive nanoparticle structure as compared to metallic nanoparticle deprived of hafnium oxide material, in particular in oncology, more particularly when the nanoparticle is exposed to radiations.

Figure 3 provides a transmission electron microscopy picture of 60nm-sized gold nanoparticles from example 1.

CLAIMS

1. Core-shell metal-oxide ~~N~~nanoparticle comprising a metallic material at least partly covered with an hafnium oxide material or embedded therein for use in a mammal, preferably in a human being, as a therapeutic agent, in particular in oncology, when the nanoparticle is exposed to a radiation.

2. Core-shell metal-oxide ~~N~~nanoparticle according to claim 1, wherein the metallic material is selected from gold (Au), silver (Ag), platinum (Pt), palladium (Pd), tin (Sn), tantalum (Ta), ytterbium (Yb), zirconium (Zr), hafnium (Hf), terbium (Tb), thulium (Tm), cerium (Ce), dysprosium (Dy), erbium (Er), europium (Eu), holmium (Ho), iron (Fe), lanthanum (La), neodymium (Nd), praseodymium (Pr), lutetium (Lu) and mixtures thereof.

3. Core-shell metal-oxide ~~N~~nanoparticle according to claim 1 or 2, wherein at least 80% of the metallic material is protected from any interaction with a biological material by the hafnium oxide material.

4. Core-shell metal-oxide ~~N~~nanoparticle according to anyone of preceding claims, wherein the metallic material is a metallic crystallite or an aggregate of metallic crystallites.

5. Core-shell metal-oxide ~~N~~nanoparticle according to claim 4, wherein the nanoparticle comprises one or several metallic crystallites.

6. Core-shell metal-oxide ~~N~~nanoparticle according to anyone of preceding claims, wherein the nanoparticle comprises several hafnium oxide crystallites or hafnium oxide crystallites aggregates.

7. Core-shell metal-oxide ~~N~~nanoparticle according to anyone of preceding claims, wherein the largest dimension of a metallic crystallite is between about 2 nm and about 100 nm and the largest dimension of a hafnium oxide crystallite is between about 5 nm and about 50 nm.

8. Core-shell metal-oxide ~~N~~nanoparticle according to anyone of preceding claims, wherein the largest dimension of a nanoparticle is between 10 nm and 250 nm.

9. Core-shell metal-oxide ~~N~~nanoparticle according to anyone of preceding claims, wherein the metallic material is coated with an agent favoring adhesion between the metal and the hafnium oxide material.

10. Core-shell metal-oxide ~~N~~nanoparticle according to anyone of preceding claims, wherein the metallic material and/or the hafnium oxide material are bonded with drug molecules.

11. Core-shell metal-oxide ~~N~~nanoparticle according to ~~anyone of preceding~~ claim~~s~~ 10, wherein each drug molecule comprise~~s~~ a cleavable portion allowing the release of the drug molecule when the nanoparticle is exposed to a specific stimulus.

12. Core-shell metal-oxide ~~N~~nanoparticle according to anyone of preceding claims, wherein the hafnium oxide material is coated with a biocompatible material selected from an agent exhibiting stealth property, an agent allowing interaction with a biological target, and a combination thereof.

13. Composition comprising a core-shell metal-oxide nanoparticle comprising a metallic material at least partly covered with an hafnium oxide material or embedded therein as described in ~~according to~~ anyone of preceding claims together with a pharmaceutically acceptable carrier.

14. Core-shell metal-oxide ~~N~~nanoparticle ~~according to claims 1 to 12 or composition according to claim 13~~ comprising a metallic material fully covered with an hafnium oxide material or embedded therein for use in a mammal, preferably in a human being, as a diagnostic agent when the nanoparticle is exposed to a radiation.

~~15. Nanoparticle according to claims 1 to 12 or composition according to claim 13 for use in a mammal, preferably in a human being, as a therapeutic agent, in particular in oncology, preferably when the nanoparticle is exposed to a radiation.~~