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Early Diagnosis of Colorectal Cancer Using Gold Nanoparticles – a Pilot Study

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Introduction: Colorectal cancer (CRC) is ranked amongst the top three most diagnosed cancers in humans worldwide. Colorectal cancer is the fourth most common cancer in South Africa and the sixth most common cause of death. If diagnosed during the early stages, the 5year relative survival rate can be as high as 90%. However, in most cases, the diagnosis is only made at a later stage when the cancer has metastasized, as the detection depends on the symptoms and non-specific screening. Many attempts have been made to achieve an early detected of CRC.

Due to their beneath systemic toxicity, faster kidney clearance, and for better the tumor accumulation, ultrasmall gold nanoparticles (less than 10 nm in diameter) are proved to be promising in biomedical applications. However, their potential applications in cancer imaging and treatment haven't been reviewed yet. This review summarizes the efforts to develop systems supported ultrasmall gold nanoparticles to be used in cancer diagnosis and therapy. First, we describe the methods for controlling the dimensions and surface functionalization of ultrasmall gold nanoparticles. Second, we review the investigation on ultrasmall gold nanoparticles in cancer imaging and treatment. Specifically, we focus on the applications of ultrasmall gold nanoparticles in tumor visualization and bioimaging in different fields such as magnetic resonance imaging, photoacoustic imaging, fluorescence imaging, and X-ray scatter imaging. We also highlight the uses of ultrasmall gold nanoparticles in tumor chemotherapy, radiotherapy, photodynamic therapy, and gene therapy.

The promising application of GNs in cancer treatment depends largely on their ability to penetrate tumor tissues. The studies of Liang et al. and Hong et al. showed that ultrasmall GNs displayed obvious superiority in penetration of tumor tissue in mice. Liang et al. quantified the cellular uptake of two, 4, and 6 nm core GNs featuring neutral (zwitterionic), anionic, and cationic headgroups. They found that changes in particle size and surface ligand coverage can be used synergistically to control cell uptake. Lei et al. found that GNs inhibit the CpG oligodeoxynucleotide (CpG-ODN)-induced production of TNF-α during a manner that trusted the concentration and size of GNs. Specifically, GNs (4 nm) are stronger than larger GNs (11, 19, 35 or 45 nm). These studies confirmed that the dimensions of GNs affect their cellular uptake which smaller GNs are haunted more readily. On this basis, researchers also analyzed the ability of GNs to enter the nucleus. Kumar et al. and Huang et al. proved that GNs (2 nm and 6 nm) can effectively penetrate into the nucleus

We focus specifically on ultrasmall GNs, which have diameters of less than 10 nm. We will firstly discuss the methods for synthesizing and surface functionalization of ultrasmall GNs. The use of ultrasmall GNs in imaging techniques for cancer diagnosis is going to be reviewed briefly. The applications of ultrasmall GNs in cancer therapy, including chemotherapy, gene therapy, and radiotherapy then on, are going to be discussed in additional detail. This information may be significant in the further development of clinical applications for GNs.

Over the last few decades, the use of gold nanoparticles (GNs) in biomedical applications has piqued interest owing to their intrinsic properties, which make them suitable for the diagnosis and treatment of cancer. GNs, like many precious metals, have a unique optical property known as surface plasmon resonance (SPR), which allows them to be used in near-infrared (NIR)-resonant biomedical imaging modalities such as magnetic resonance imaging (MRI), photoacoustic imaging (PAI), fluorescence imaging and X-ray scatter imaging 1, 2. GNs also generate heat when exposed to NIR laser light, which makes them suitable for the photothermal treatment of cancer 3, 4. In addition, GNs have low toxicity and are nonimmunogenic by nature. Their synthesis methods are simple, and their size, shape and surface modifications can be readily controlled. All these properties mean that GNs can be functionalized in many different ways for local hyperthermia of cancer tissue and delivery of multiple drugs in a controlled and targeted manner 5. Based on these excellent characteristics, gold nanostructures have been studied and administered in phase I and II clinical trials for cancer treatment 6. Size is one of the key parameters of GNs that influence half-life time, systemic toxicity, tumor accumulation and so on, which are important properties for imaging and therapeutic applications. As the range of applications of GNs continues to increase, it is necessary to better understand the biological effects of GNs of different sizes.

Colonoscopy, an examination of the liner of the colon and therefore the rectum employing a fiber-optic camera, is that the most generally used screening test for colorectal cancer. Colonoscopies allow doctors to detect small growths or polyps that have formed in colorectal tissue and take away them before they turn cancerous. The accuracy of colonoscopy will be depending on several factors, including the speed with which the examination is performed and thus the way thoroughly doctors look for flat or depressed lesions.

Researchers are trying to find ways to enhance the accuracy of colonoscopy and to detect colorectal cancer even before it is currently possible. Abnormalities detected at the earliest stages would be much less likely to have spread by the time they are found. Nanotechnology, the branch of engineering that deals with the manipulation of individual atoms and molecules, has the potential to help identify cancerous or precancerous cells well before a transparent growth has formed and to deliver cancer-killing drugs on to the cancerous cells.

In one application of this approach, the middle of Cancer Nanotechnology Excellence at Stanford University, a part of the National Cancer Institute's (NCI) Alliance for Nanotechnology in Cancer, has developed a system during which gold nanoparticles are wont to hunt down and bind to cancer cells. When light shined from a tool that's inserted into a typical endoscope (a colonoscope) reaches cancer cells that have bound the gold nanoparticles, they stand out from the traditional cells and may be removed. Researchers hope to start a clinical test to check the security of this approach in humans by early next year.

Another promising appeal which will be applicable to colorectal cancer is being developed by researchers at the University of Buffalo and for the scientists at the Roswell Park Cancer Institute. This approach uses a silica-based nanoshell that encases molecules of light-sensitive drugs referred to as photosensitizers. The nanoshells are readily haunted by tumor cells grown within the laboratory, and, when the cells are exposed to light, the photosensitizers are activated and trigger the assembly of reactive oxygen molecules that kill the cancer cells. This technology is currently being tested for safety in clinical trials. The researchers also are developing a second-generation photosensitizer-loaded nanoshell that comes with tumor-targeting and imaging agents to deliver tumor-specific, image-guided therapy for cancer. Nanoparticles are often used for molecular imaging of malignant lesions, enabling earlier detection and targeted drug delivery. Nanoshells can selectively link to cancer cells, delivering therapeutic treatment on to kill tumor cells and not harm neighboring healthy cells.

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Aim: To induce CRC in rats to investigate the use of targeted gold nanoparticles (AuNPs) as a diagnostic tool for CRC.

Methods: Ten Wistar rats were injected with 1,2-dimethylhydrazine (DMH), 25 µg/Kg bodyweight once per week, for 5 consecutive weeks to induce CRC. This was followed by an incubation period of 22 weeks. At the end of the incubation period, AuNPs were synthesized using Turkevich's citrate reduction method, and conjugated with peptide p.L. The rats were then injected intraperitoneally with p.L-PEG-AuNPs to detect CRC. Six rats were kept as controls and did not receive any treatment.

Results: Five injections of DMH did not induce CRC in the rats.

Conclusion: Even though CRC could not be induced using DMH in this study, 14 nm p.L-AuNPs were synthesized successfully.