TomoWave Laboratories

Imaging Sensing Monitoring

Functional Gold Nanorods (GNR) as Targeted Contrast Agents for Optical and Opto-Acoustic Imaging and Cancer Therapy

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Contrast Agents

➢Nanotechnology combined with molecular biology offers abundant opportunities for development of contrast agents for biomedical imaging with exceptional molecular specificity.

➢Gold nanorod (GNR) based contrast agents designed for optical and optoacoustic imaging possess exceptionally strong absorption in the near-infrared (NIR) spectral range, 1000 times stronger than any organic dye in the same concentration

➢Synthesis, Purification and Conjugation of GNR with Monoclonal Antibodies or peptides was optimized to yield a contrast agent with precisely controlled properties and performance validated in a range of biomedical applications.

Optimized Protocol for Gold Nanorods:

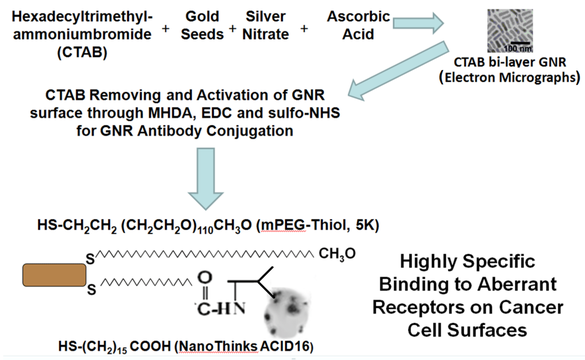
➢After synthesis of GNR, toxic CTAB removed and GNR surface is activated through thiol group Mercaptohexadecanoic Acid (MHDA or Nanothinks Acid16)

➢Monoclonal antibody or specific peptides are attached with Zero-Length Heterobifunctional Crosslinkers between Carboxyl Group MHDA and Amine Group of molecular target

➢Polyethylene glycol (PEG) molecules are attached to GNR via thiol functional group

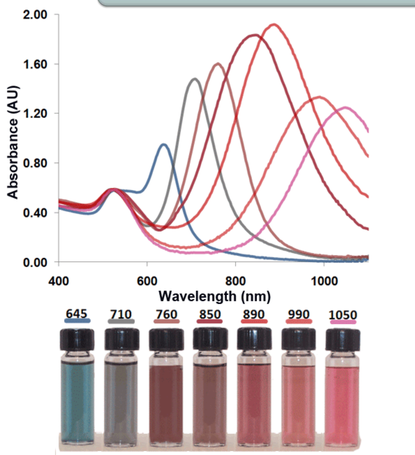
➢GNR-PEG and GNR-mAb-PEG conjugates are purified with differential centrifugation and filtration to achieve consistent performance in biomedical applications

Synthesis and Conjugation of Gold Nanorods

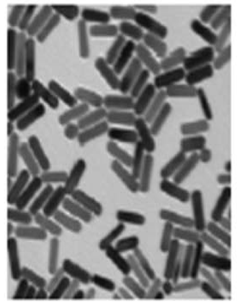


GNR Conjugates fabrication: protocol design

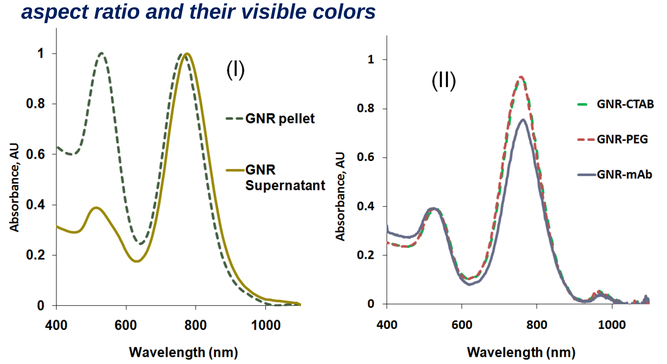
Product Characterization



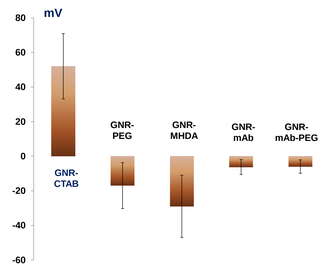
Near-Infrared Absorption Spectra of GNR with gradually increasing aspect ratio and their visible colors



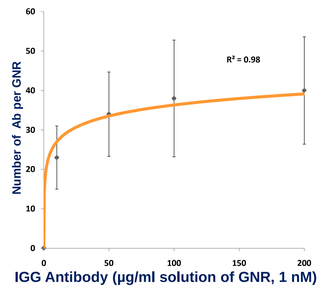
Transmission Electron Microphotograph of Gold NanoRods with aspect ratio of 4



UV-VIS Spectra of GNR-based contrast agent: (I) after Centrifugation ; (II) after PEGylation and Conjugation

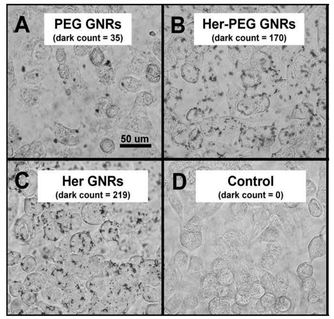


Zeta-Potential for Different GNR Surface Ligands: Confirmation of Chemistry Modification



Binding of mAb on the Surface of GNR: Concentration Effects

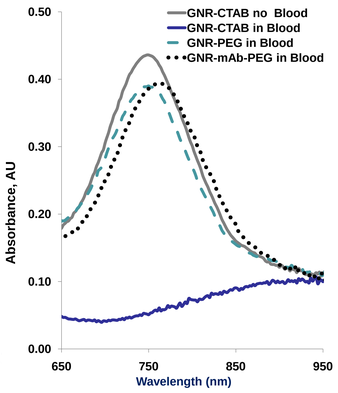
Imaging Applications



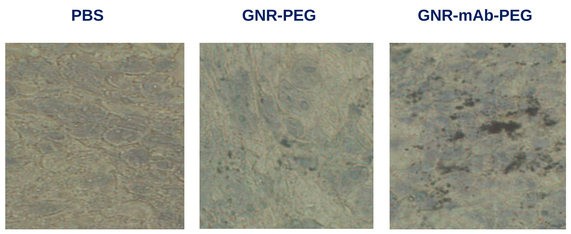
Cell cultures targeted with GNR contrast agent were stained with Silver to reveal GNR as dark spots. Concentration of these dark spots is much higher in case of targeting with Her-PEG GNR or Her-GNR, which demonstrates selective targeting of cancer cells.

Optical microscopic images of breast cancer cells SKBR3 cell cultures incubated with (A) PEG-GNR; (B) Her-PEG-GNR; (C) Her-GNR and (D) control no GNR.

The absence of NIR optical absorbance in GNR-CTAB following incubation in blood indicated aggregation and destruction of the contrast agent by the immune system. The presence of only slightly reduced absorbance with GNR-PEG and Her-PEG following incubation in blood confirmed the stability of this contrast agent in a live system.

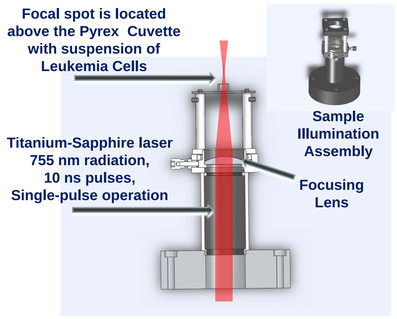


Absorption Spectra of Different Types of GNR after 3 hours incubation in Mouse Heparinized Blood

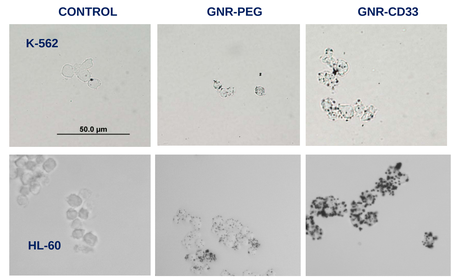


Mouse tumor (breast cancer) tissue slices were silver stained and imaged under microscope to reveal accumulation of GNR contrast agent after intravenous injection into the tail vein.

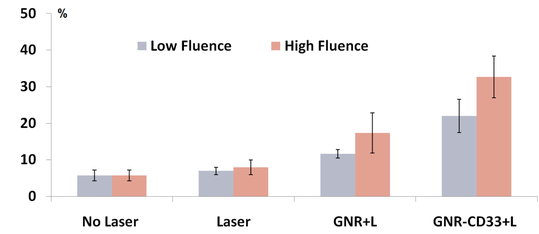
Therapy Applications



Schematic diagram of Pulsed-Laser Nanothermolysis



Silver Staining of Chronic (K562) and Acute (HL-60) Leukemia Cells with Pegylated (GNR-PEG) and Conjugated with CD33 Antibody (GNR-CD33)



Percentage of Leukemia Tumor Cells targeted with GNR CD-33 Antibody Conjugates, then killed with a single laser pulse.

GNR Product Properties

➢Strong optical absorption in the near-infrared spectral range provides for high detection sensitivity of molecular targets

➢Highly specific peptides and antibodies assure effective and selective targeting of biomolecules

➢Conjugation with PEG coat results in the stealth properties that help to avoid interactions with immune system and enables long circulation time.

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