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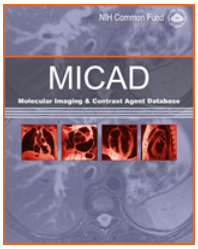

Bovine serum albumin–stabilized gold nanoclusters conjugated with L-methionine and indocyanine green derivative 02

Au-Met-MPA

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Chemical name:	Bovine serum albumin–stabilized gold nanoclusters conjugated with L-methionine and indocyanine green derivative 02	
Abbreviated name:	Au-Met-MPA	
Synonym:	Au-BSA-Met-MPA, Au-BSA-Met-ICG-Der-02, Au-Met-ICG-Der-02	
Agent category:	Compound	
Target:	L-type amino acid transporter 1/2 (LAT1/2)	
Target category:	Transporter	
Method of detection:	Optical, near-infrared fluorescence (NIR) imaging	
Source of signal:	ICG-Der-02 (MPA)	
Activation:	No	
Studies:	• *In vitro* • Rodents	Structure is not available in PubChem.

Background

[PubMed]

Most amino acids are taken up by tumor cells through an energy-independent L-type amino acid transporter system, a Na-dependent transporter system A, or a Na^+-dependent system B^0 (1). They are retained in tumor cells due to their metabolic activities, including incorporation into proteins, which are higher than most normal cells (2). Malignant transformation increases the use of amino acids for energy, protein synthesis, and cell division. Tumor cells have been found to have overexpressed transporter systems (3). *S*-[^{11}C]Methyl-L-methionine ([^{11}C]MET) has been widely used in the detection of brain, head and neck, lung, and breast cancers as well as lymphomas (4) [PubMed]. [^{11}C]MET can cross the blood–brain barrier, and while it is incorporated mainly into proteins, [^{11}C]MET is also incorporated into lipid, RNA, and DNA. Positron emission tomography

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(PET) imaging with [^{11}C]MET is more sensitive to radiotherapy compared to [^{18}F]FDG and is useful for monitoring treatment of cancer.

Among the various optical imaging agents, only indocyanine green (ICG), with NIR fluorescence absorption at 780 nm and emission at 820 nm, is approved by the United States Food and Drug Administration for clinical applications in angiography, blood flow evaluation, and liver function assessment (5-8). It is also under evaluation in several clinical trials for other applications, such as optical imaging and mapping of both the lymphatic vessels and lymph nodes in cancer patients for surgical dissection of tumor cells and endoscopic imaging of the pancreas and colon. Gold (Au) nanoclusters (NCs) are comprised of a few tens of Au atoms that possess the ability to emit strong fluorescence, of which the wavelength is tunable in the range of the visible to near-infrared spectral region (9). Chen et al. (10) prepared bovine serum albumin–stabilized Au NCs (Au-BSA) for conjugation with biomolecules for specific targeting and with near-infrared dye for optical imaging. Met was conjugated to the carboxyl groups of BSA. The ICG derivative 02 (ICG-Der-02, also known as MPA) contains one carboxyl functional group for covalent conjugation to the amino group of BSA on the surface of Au-BSA NCs. MPA is a hydrophilic dye. Chen et al. (10) evaluated Au-BSA-Met-MPA (Au-Met-MPA) for *in vivo* NIR optical imaging in tumor-bearing mice.

Related Resource Links:

- Chapters in MICAD (amino acid transporters, methionine, ICG)
- Gene information in NCBI (L-type amino acid transporter 1, L-type amino acid transporter 2, A-type amino acid transporter)
- Articles in Online Mendelian Inheritance in Man (OMIM) (amino acid transporters)
- Clinical trials (amino acid transporters, L-[^{11}C]methionine, ICG)
- Drug information in FDA (amino acid transporters, ICG)

Synthesis

[PubMed]

Au-BSA NCs were prepared by addition of $HAuCl_4$ solution (10 mM) to BSA solution (50 mg/ml) under vigorous stirring for 30 min at 37°C (10). The mixture was stirred for an additional 12 h at 37°C. Au-BSA NCs were incubated with 1-ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride for 10 min at room temperature. *N*-Hydroxysuccinimide (NHS) was then incubated with the mixture for 2 h, after which Met was added and incubated for 12 h. The product, Au-BSA-Met, was isolated with column chromatography. MPA (1.0 mg) was activated with *N*,*N*'-dicyclohexylcarbodiimide (DDC) and NHS (molar ratio of MPA:DCC:NHS was 1:1.5:1.5) for 3 h at room temperature. Finally, the above activated MPA was evenly mixed with purified Au-BSA-Met and then incubated for 12 h at room temperature with stirring to produce Au-Met-MPA. The mean hydrodynamic diameter of Au-BSA (measured with laser particle size analysis) was 3.9 nm (polydispersity = 0.303), whereas Au-Met-MPA exhibited a relatively larger diameter of 5.6 nm (polydispersity = 0.118), indicating the successful addition of Met and MPA molecules. The absorption spectra of Met, Au-BSA, MPA, Au-BSA-Met, and Au-Met-MPA exhibited absorbance peaks at 215, 232, and 780 nm, which corresponded to Met, Au, and MPA, respectively. The number of Au, BSA, Met, and MPA moieties per Au-Met-MPA was not reported. Au-Met-MPA displayed spectral properties similar to those of MPA, with maximum absorption at 750 nm and maximum emission at 830 nm.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

The cytotoxic effects of Au-BSA, Au-BSA-Met, Au-BSA-MPA, and Au-Met-MPA (0.01–1,000 μM) were assessed in human cell lines L02 (normal human liver cell), Bel 7402 (liver cancer), A549 (lung cancer), and MCF-7 (breast cancer) for 24 h at 37°C (10). Approximately 90% viability was observed with 0.01–1 μM, with 80% at 1 mM. Fluorescence microscopy analysis showed little binding of Au-BSA and Au-Met-MPA to L02 cells (low LAT1/2 expression), whereas strong fluorescence signal was observed in the MCF-7 cells (high LAT1/2 expression) with Au-Met-MPA but not with Au-BSA-MPA. No blocking studies were performed with excess Met.

Animal Studies

Rodents

[PubMed]

Chen et al. (10) performed *in vivo* whole-body NIR fluorescence imaging studies in nude mice (the number of mice used was not reported) bearing MDA-MB-231 human breast cancer (high LAT1/2 expression) and A549 human lung cancer xenografts (low LAT1/2 expression) at 0.5–96 h after intravenous injection of Au-Met-MPA (10 mg/kg body weight). Images showed that NIR fluorescence spread all over the body at 0.5 h and then concentrated in the liver and kidneys. Most NIR fluorescence of the normal tissues was cleared from the body by 10 h. MDA-MB-231 tumors were clearly visualized at 2 h, and the NIR fluorescence peaked at 10 h. The tumor NIR fluorescence was still detectable at 96 h. On the other hand, A549 tumor exhibited weak NIR fluorescence at 2–4 h, and fluorescence was almost indistinguishable from the background by 7 h. The tumor/background ratio was 1.47 ± 0.16 at 0.5 h for MDA-MB-231 tumors, reaching a peak at 10 h (6.86 ± 0.12) and slowly declining to 2.83 ± 0.18 at 96 h. Au-Met-MPA exhibited little histological change in the excised organs from normal mice at 7 d after injection of Au-Met-MPA.

Other Non-Primate Mammals

[PubMed]

No publication is currently available.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

No publication is currently available.

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