Galactosamine-serum albumin-rhodamineX$_{20}$

GmSA-20ROX

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Chemical name:	Galactosamine-serum albumin-rhodamineX$_{20}$	
Abbreviated name:	GmSA-20ROX	
Synonym:		
Agent Category:	Polypeptide	
Target:	β-D-galactose receptor	
Target Category:	Receptor binding	
Method of detection:	Optical fluorescence imaging	
Source of signal:	RhodamineX	
Activation:	Yes	
Studies:	• *In vitro* • Rodents	No structure is currently available in PubChem.

Background

[PubMed]

Optical fluorescence imaging is increasingly used to study biological functions of specific targets (1, 2). However, the intrinsic fluorescence of biomolecules poses a problem when fluorophores that absorb visible light (350–700 nm) are used. Near-infrared (NIR) fluorescence (700–1,000 nm) detection avoids the background fluorescence interference of natural biomolecules, providing a high contrast between target and background tissues. NIR fluorophores have a wider dynamic range and minimal background as a result of reduced scattering compared with visible fluorescence detection. They also have high sensitivity, resulting from low infrared background, and high extinction coefficients, which provide high quantum yields. The NIR region is also compatible with solid-state

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optical components, such as diode lasers and silicon detectors. NIR fluorescence imaging is becoming a non-invasive alternative to radionuclide imaging in small animals.

A variety of cancer cells express on their cell surface receptors (lectins) that bind to glycosylated proteins (3, 4). The β-D-galactose receptor binds and internalizes proteins that contain galactose sugar residues. Galactosamine-serum albumin (GmSA) was labeled with rhodamine green (RhodG) to study *in vivo* biodistribution of the tracer in tumor-bearing mice and was found to have a high accumulation in a variety of human ovarian adenocarcinomas in nude mice (5). A self-quenching GmSA complex was create by conjugating 20 rhodamineX (ROX) molecules to GmSA (GMSA-rhodamineX_{20} (GmSA-20ROX)) (6). ROX is an optical fluorescence dye with an absorbance maximum at 595 nm and an emission maximum at 610 nm. GmSA-20ROX was found to have a high accumulation in peritoneal micrometastases of human SHIN3 ovarian adenocarcinomas in nude mice (6).

Synthesis

[PubMed]

Commercially available GmSA (7.0 nmol), which contains 23 galactosamine residues, was incubated with ROX-succinimidyl ester (360 nmol) for 15 min at room temperature (6). GmSA-20ROX was isolated by column chromatography. There were ~20 ROX per GmSA as determined by spectroscopy. GmSA-1ROX was also synthesized using 14 nmol ROX-succinimidyl ester.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Flow cytometry and fluorescence microscopy confirmed intracellular accumulation of GmSA-20ROX into SHIN3 cells (6). The mean fluorescence intensity (MFI) for cells treated with GmSA-20ROX progressively increased with time of incubation (0.5–6 h). The rate of MFI increase was 5.574 a.u./h for GmSA-20ROX and 0.485 a.u/h for GmSA-1ROX. GmSA-20ROX became more than five-fold more fluorescent than cells treated with GmSA-1ROX. GmSA-20ROX was bound to the cell surface and internalized into intracellular lysosomes and endosomes where the GmSA-20ROX molecules were unfolded and digested, resulting in increased fluorescence signals because of dequenching. GmSA-20ROX fluorescence was markedly activated by trypsin, cathepsin D, and matrix metalloproteinase 2 (MMP-2), whereas GmSA-1ROX was mildly activated by MMP-2 only.

Animal Studies

Rodents

[PubMed]

Hama et al. (6) performed studies of GmSA-20ROX in nude mice bearing intraperitoneal (i.p.) xenografts of the SHIN3 cell line. Images were obtained after i.p. injection of 50 μg (~0.7 nmol) GmSA-20ROX or GmSA-1ROX. Higher fluorescence intensity was observed with GmSA-20ROX than with GmSA-1ROX at 1 h and 3 h after injection in the tumors formed in the exposed abdomen. Tumors that were <1 mm in diameter were visible. Sensitivity and specificity for GmSA-20ROX (n = 336 tumor foci) were 99% and 99%, whereas these values were 24% and 100%, respectively, for GmSA-1ROX (n = 388 tumor foci). *Ex vivo* study of subcellular localization in the tumors was not performed. No blocking experiment was performed.

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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