^{18}F-Labeled neogalactosylalbumin

[^{18}F]FNGA

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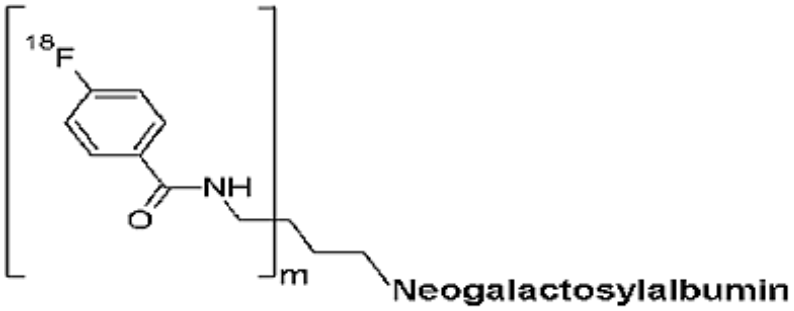
Chemical name:	^{18}F-Labeled neogalactosylalbumin
Abbreviated name:	[^{18}F]FNGA
Synonym:	
Agent Category:	Protein
Target:	Asialoglycoprotein receptor (ASGP-R)
Target Category:	Receptor
Method of detection:	Positron emission tomography (PET)
Source of signal / contrast:	^{18}F
Activation:	No
Studies:	• *In vitro* • Rodents



Structure of [^{18}F]FNGA according to Yang et. al. (1). Click here for human asialoglycoprotein receptor 1 nucleotide and protein sequence.

Background

[PubMed]

Asialoglycoprotein receptors (ASGP-R; exist as subtypes 1 and 2) are located on the surface of hepatic cell membranes and are involved in the binding and endocytosis of glycoproteins that have exposed carbohydrate or *N*-acetylgalactosamine residues (2). In

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addition, the decreased level of ASGP-R on the hepatic cells has been shown to correlate clinically with the degree of liver function retained due to the development of cirrhosis, cancer, or viral hepatitis (2). Therefore, ^{99m}Tc-labeled galactosyl human serum albumin (HSA), a single-photon emission computed tomography (SPECT) imaging agent that targets the ASGP-R, was developed and evaluated, and it is commercially available in Japan for clinical diagnosis of diseases of the liver or to assess the hepatic functional status (1). As an alternative to the SPECT imaging compound, Yang et al. developed ^{18}F-labeled neoglycoalbumin ([^{18}F]FNGA) for imaging of the liver with positron emission tomography (PET) (1). The biodistribution of [^{18}F]FNGA was studied in normal mice with or without pretreatment of non-radioactive NGA. In addition, imaging was performed on rats treated with [^{18}F]FNGA in the presence or absence of non-labeled NGA.

Synthesis

[PubMed]

The synthesis of [^{18}F]FNGA from HSA was detailed by Yang et al. (1). On average, 38 units of galactose were reported to be attached to each HSA molecule (1). The radiochemical yield of the final labeled product was typically 8–10%, and the time required to complete the entire procedure was 150 ± 20 min. The radiochemical purity of [^{18}F]FNGA was >99% as determined with instant thin-layer chromatography (ITLC), with a specific activity of 1.92–7.10 TBq/mmol (51.8–191.7 Ci/mmol). [^{18}F]FNGA was reported to be stable for >4 h in saline at room temperature and maintained a radiochemical purity of >95% as determined with ITLC. The purified radiocompound was also stable for >4 h when stored at 37°C in murine plasma as determined with high-performance liquid chromatography.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

No references are currently available.

Animal Studies

Rodents

[PubMed]

Yang et al. investigated the biodistribution of [^{18}F]FNGA in normal mice (1). The animals were injected with the radiochemical through the tail vein and euthanized at 5 min and 30 min (n = 5 mice per time point) after injection. Major tissues and organs were subsequently removed from the animals to determine the amount of accumulated radioactivity. The data was presented as percent of injected dose per gram tissue (% ID/g) for the various samples. To determine the binding specificity of [^{18}F]FNGA, the animals

(n = 5 mice) were injected with non-radioactive NGA (10 mg/kg body weight) followed by an injection of [^{18}F]FNGA 5 min later. The animals were euthanized 5 min after treatment with the radiochemical, and samples were treated as before to determine the amount of radioactivity accumulated in the various tissues and organs.

Within 5 min of treatment with [^{18}F]FNGA, >75% ID/g of the label was detected in the liver, and all the other organs (heart, lung, kidney, spleen, stomach, blood, muscle, and small intestine) showed an accumulation of <3% ID/g radioactivity at this time point (1). By 30 min after injection, radioactivity in the liver had reduced to <15% ID/g with an accumulation of ~17.5%ID/g in the kidneys. Compared with the normal animals, mice pretreated with a blocking dose of non-radioactive NGA had significantly ($P < 0.01$) less accumulation of radioactivity in the liver (<15% ID/g) at 5 min after injection of [^{18}F]FNGA. In these animals, significantly ($P < 0.01$) increased radioactivity was detected in the blood (>45% ID/g), lungs (>15% ID/g), kidneys (>10% ID/g), and spleen (>5% ID/g), indicating that the radiolabeled compound bound specifically to the ASGP-R in the liver.

MicroPET imaging with [^{18}F]FNGA was performed on rats (n = 1 mouse per group) with or without blocking with non-radioactive NGA as before (1). The images were acquired 5 min and 15 min after treatment with the radiotracer. From the images it was evident that the radiolabel accumulated in the liver within 5 min after injection, and by 15 min some of the radioactivity had been lost from this organ, although the liver outline was clearly visible. Low uptake of the radiotracer was observed in the kidneys, spleen, and other organs during this time. Treatment of the animals with non-radioactive NGA followed by an injection of [^{18}F]FNGA was reported to reduce the level of accumulated radioactivity in the liver and make the outline of the organ unclear on imaging. During the same time period, the label was observed to accumulate in the kidney with quick clearance through the bladder.

From these studies the investigators concluded that [^{18}F]FNGA can be used for imaging the liver in a preclinical setting and after further evaluation could help evaluate the risk of hepatic surgery in humans (1).

Other Non-Primate Mammals

[PubMed]

No references are currently available.

Non-Human Primates

[PubMed]

No references are currently available.

Human Studies

[PubMed]

No references are currently available.

Supplemental Information

[Disclaimers]

No information is currently available.

References

1. Yang W., Mou T., Peng C., Wu Z., Zhang X., Li F., Ma Y. *Fluorine-18 labeled galactosyl-neoglycoalbumin for imaging the hepatic asialoglycoprotein receptor.* Bioorg Med Chem. 2009;17(21):7510–6. PubMed PMID: 19796957.
2. Lee S.M., Casey C.A., McVicker B.L. *Impact of asialoglycoprotein receptor deficiency on the development of liver injury.* World J Gastroenterol. 2009;15(10):1194–200. PubMed PMID: 19291819.