2-[2-[2-Chloro-3-[2-[1,3-dihydro-3,3-dimethyl-1-(4-sulfobutyl)-2H-indol-2-ylidene]-ethylidene]-1-cyclohexen-1-yl]-ethenyl]-3,3-dimethyl-1-(4-sulfobutyl)-3H-indolium

IR-783

Kam Leung, PhD[1]

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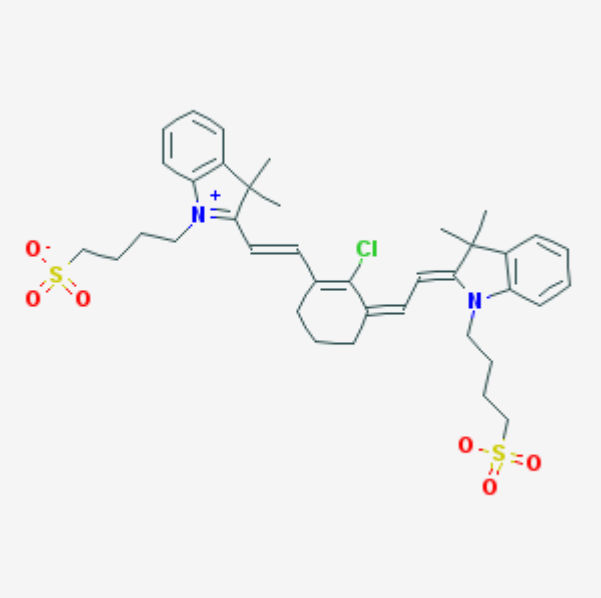
Chemical name:	2-[2-[2-Chloro-3-[2-[1,3-dihydro-3,3-dimethyl-1-(4-sulfobutyl)-2*H*-indol-2-ylidene]-ethylidene]-1-cyclohexen-1-yl]-ethenyl]-3,3-dimethyl-1-(4-sulfobutyl)-3*H*-indolium
Abbreviated name:	IR-783
Synonym:	
Agent category:	Compound
Target:	Lysosomes and mitochondria
Target category:	Unknown
Method of detection:	Optical, near-infrared (NIR) fluorescence imaging
Source of signal:	IR-783
Activation:	No



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Studies:	• *In vitro* • Rodents	Click on the above structure for additional information in PubChem.

Background

[PubMed]

Optical fluorescence imaging is increasingly being used to monitor biological functions of specific targets (1-3). 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 natural background fluorescence interference of biomolecules, which provides a high contrast between target and background tissues in small animals. NIR fluorophores have a wider dynamic range and minimal background fluorescence as a result of reduced scattering compared with visible fluorescence detection. NIR fluorophores also have high sensitivity, attributable to low background fluorescence, and high extinction coefficients, which provide high quantum yields. The NIR region is also compatible with solid-state optical components such as diode lasers and silicon detectors. NIR fluorescence imaging is a non-invasive complement to radionuclide imaging in small animals.

Among the various NIR agents, only indocyanine green (ICG), with 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 (4). It is also under evaluation in several clinical trials for other applications. However, ICG has a plasma half-life of 2–4 min because it forms aggregates in the blood and is rapidly cleared from blood circulation (5). ICG is prone to photobleaching and non-specific quenching *via* its extensive binding to proteins. On the other hand, the fluorescence efficiency of some cyanine dyes can increase by ~1,000-fold upon binding to proteins and nucleic acids (6).

Organic anion transporters (OATPs) are responsible for the transport of a diverse group of substances (hormones, xenobiotics, and bile acids) (7). Some OATPs have been shown to be overexpressed in various human cancer tissues and cancer cell lines (8, 9).

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Lysosomes are membranous vesicles found in most mammalian cells (10). Lysosomes contain various types of proteases, which have been implicated in migration, invasion, and metastasis of malignant cancer cells by degradation of extracellular matrix (11). Lysosomes are found to be larger in malignant cancer cells than in benign cancer cells (12). 2-[2-[2-Chloro-3-[2-[1,3-dihydro-3,3-dimethyl-1-(4-sulfobutyl)-2*H*-indol-2-ylidene]-ethylidene]-1-cyclohexen-1-yl]-ethenyl]-3,3-dimethyl-1-(4-sulfobutyl)-3*H*-indolium (IR-783) has been shown to accumulate in the mitochondria and lysosomes of cancer cells (13). Uptake of IR-783 may be dependent upon OATPs. Yang et al. (13) have evaluated the usefulness of IR-783 as a probe for NIR imaging of tumors.

Related Resource Links:

- Chapters in MICAD
- Gene information in NCBI (Organic anion transporters).
- Articles in OMIM (Organic anion transporters)
- Clinical trials (Indocyanine green)
- Drug information in FDA (Indocyanine green)

Synthesis

[PubMed]

IR-783 is commercially available. IR-783 has an extinction of coefficient of 157,000 $M^{-1}cm^{-1}$ and a quantum yield of 0.11, with a maximal excitation wavelength of 768 nm and a maximal emission wavelength of 784 nm in saline (14). The fluorescence intensities at pH 3–5 were higher than those at pH 6.4–7.2.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Yang et al. (13) showed that 0.02 mM IR-783 exhibited a two-phase uptake in human prostate $ARcAP_M$ tumor cells competed at 12 min and 30 min with minimal cell cytotoxicity in cultures. The measured fluorescence intensity correlated with the concentrations (0.001, 0.01, 0.02, and 0.05 mM) of IR-783 in $ARcAP_M$ cells. In normal prostate epithelial cells, the uptake of IR-783 (0.02 mM) only began at 12 min with 3-fold lower signal intensity. The uptake in $ARcAP_M$ cells was abolished with 0.25 mM bromosulfophthalein, a competitive inhibitor of OATPs. Most of the IR-783 signal was co-localized with the lysosomal and mitochondrial tracking dyes. IR-783 accumulated preferentially in a panel of human and mouse cancer cells *versus* normal tissues and cells.

Animal Studies

Rodents

[PubMed]

Yang et al. (13) performed studies of IR-783 (~10 nmol/mouse) in nude mice bearing subcutaneous human bladder tumors (T-24), subcutaneous pancreas tumors (MIA PaCa-2), orthotopic prostate tumors ($ARCaP_M$), and kidney tumors (SN12C, intraosseously to tibia) using a whole-body fluorescence detection system. IR-783 showed a clear fluorescence signal in all four tumors at 24 h after injection with no background interference. IR-783 was also able to detect the primary tumors and metastatic tumors in two transgenic mouse models (TRAMP mouse model for prostate cancer and $Apc^{Min/+}$ mouse model for colon cancer) with high degrees of tumor metastases. Histopathological analysis of all tumor sections confirmed uptake of IR-783 in tumor cells but not in normal cells. An e*x vivo* biodistribution study showed that the $ARcAP_M$ tumor exhibited >5-fold greater fluorescence intensity than the liver, kidney, lung, heart, and spleen at 24 h after IR-783 injection ($n = 3$; $P < 0.05$). No blocking studies were reported.

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.

NIH Support

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