

# MOLECULAR TARGETING TECHNOLOGIES, INC. www.mtarget.com

# Novel molecular and cellular imaging reagents for life sciences and drug discovery



2012 Catalog

- · CellVue®
- P\$Vue®
- NeuroVue<sup>®</sup>
- SRfluor®
- Cyanine Dyes
- Immobilized
   Steroid Beads
- IRIS™ Dyes
- CyAl-5 Dye and analogs for

### Message from the President

Dear Colleague,

I want to take this opportunity to introduce to you our new 2012 catalog which contains a wide range of innovative products for your research needs. Molecular Targeting Technologies, Inc., (MTTI) continues to offer PTIR products such as CellVue® for general cell membrane labeling of live cells and NeuroVue® dye for neuronal tract tracing in fixed tissue,



as well as steroid-coated affinity beads for purification of steroid receptors. In our continuing effort to broaden the scope of products offered to researchers we have introduced our PSVue® reagents (based upon Zn-DPA technology licensed from the University of Notre Dame). PSVue® reagents have been found to bind with high selectivity to membrane surfaces enriched with anionic phospholipids, especially phosphatidylserine (PS) exposed on cell membranes. We have launched the IRIS™ dyes which exhibit favorable photo stability and versatility. In addition, we are introducing the novel proprietary Cy5 dyes for labeling drugs, proteins and antibodies. We are also pleased to introduce CyAL-5 2-deoxyglucose and CyAL-5 cyclic RGD for molecular imaging applications. You can find additional information on all our products in our

website: www.mtarget.com.

Sincerely, Chris Pak, Ph.D. President and CEO

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#### **About MTTI**

Molecular Targeting Technologies, Inc. (MTTI) is a Pennsylvania-based biotechnology company with a focus on preclinical and clinical development of novel small molecules for the targeting and imaging of lifestyle diseases and cancer. Our business also includes development of molecular imaging reagents for the research and drug discovery markets inclusive of academia and pharmaceutical R&D. These generally include novel and cost-efficient fluorescent probes for *in vitro* and *in vivo* imaging of cellular plasma membranes, apoptotic and bacterial cells, tracing of neuronal tracts, tools for chromatography and general dye labeling. We are also continually innovating and improving to ensure the highest standards of performance on all our products.

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Translating innovative technologies into

### **Ordering Information**

#### How to order:



Online store:

http://www.mtarget.com/mttistore



For orders of 6 items or more: MTTI telephone: +1 610 738 7938 MTTI fax: +1 610 738 7928

N N

MTTI Email: info@mtarget.com

Please include the following information if ordering by phone:

- 1) Catalog number and product name
- 2) Quantity
- 3) Your contact number, institution and address
- 4) Purchase order (P.O.) number

#### **International Orders**



MTTI has a list of distributor contacts for each product. Please refer to the index of distributors listed on pages 34-35 for more information.

#### **Technical Support**



For all inquiries on reagents purchased from MTTI, please contact briangray@mtarget.com or call +1 610 738 7938.

#### **Payment Options**



By phone: Credit cards accepted are VISA and Mastercard Online: Paypal only (www.mtarget.com/mttistore)

**Purchase Order:** Terms are net 30 for purchase orders sent to briangray@mtarget.com or dspencer@mtarget.com.

#### Delivery



All items are shipped via UPS 2nd Day Air for delivery within the U.S., and via UPS Standard for destinations outside the U.S. Approximate prices are shown below and exact shipping charges will be reflected in the invoice. For orders of 6 items or more or shipping outside the U.S., please contact us at **info@mtarget.com** for a quote on shipping charges. Expedited shipping, declared value, insurance and other services are charged additional.

Number of items Within the US		Outside the U.S.	
1-5	\$35.00 (flat rate)	Contact for quote	
6 or more	Contact for quote	Contact for quote	

#### **Material Safety Data Sheets**



MSDS will be included and delivered together with each product ordered.

#### **Quality Assurance**



Our products go through rigorous chemical and biological quality testing, leveraging on inhouse chemical expertise and our external collaborations with the life sciences. In addition, a Certificate of Analysis is included with each product kit. For questions on product quality, please contact briangray@mtarget.com.

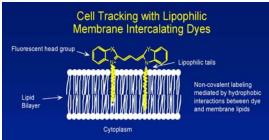
### Reagent Products: Summary

MTTI holds specialized expertise in the organic synthesis of fluorochromes, chromatography reagents, heterocyclics, bioconjugates and lipophilic probes. Our most important aim is to keep our items cost-efficient, innovative and affordable for regular usage. A certificate of analysis and MSDS sheet (s) are included with each individual order. We strive for the highest quality in performance and technical support. For enquiries on products or customization to suit your needs, please contact us at info@mtarget.com.

Product type	General usage	Page
CellVue®	Fluorescent dye kits for general cell membrane labeling	7
PSVue®	Fluorescent dye kits for <i>in vitro</i> and <i>in vivo</i> imaging of apoptotic cells, cancers and bacterial infections	9
NeuroVue®	Dye filters for tracing of neuronal connections in fixed animal tissues	12
SRfluor®	Squaraine rotaxane encapsulated dyes with superior photochemical stability	17
Cyanine Dyes	Unique lipophilic imaging probes for labeling of cellular membranes or membrane potential	20
Novel Immobilized Steroid Beads	Sepharose®-linked beads for chromatography and crystallography studies	22
IRIS™ Dyes	Suitable for conjugation to any biomolecules carrying free primary amines, such as proteins, peptides, amino-modified antibodies and biopolymers.	24
CyAl-5 Dyes	Monofunctional cyanine dye containing a free carboxylic acid group for conjugation with targeting agents containing a free amine group; use for in vivo and in vitro imaging applications	27
CyAl-5 RGD	Fluorescence imaging agent comprising a potent cyclic RGD peptide, c(RGDfK) designed to target integrins and a CyAL-5 dye with emission at 658 nm.	28
CyAl-5 2DG	Fluorescent imaging agent designed to target a wide spectrum of cancers such as breast, glioblastoma, colon and prostate in vitro as well as in vivo.	29

# CellVue® for general cell membrane labeling





#### Description

CellVue® dyes are fluorescent probes for the irreversible labeling of plasma membranes on viable cells using a proprietary labeling method. The dye molecules consist of long aliphatic tails which insert into phospholipid regions on the cell membrane. The diluent provided with the dye kits is an aqueous solution designed to maintain maximal cell viability and dye solubility, thus enhancing staining efficiency.

#### Advantages of CellVue® over traditional membrane labeling

- Versatility—Can be used to label cell or bioparticle membranes
- Stability— Minimal cell-to-cell transfer
- Fast and uniform labeling
- Modularity— For use with fluorescent antibodies or cellular biomarkers
- Applicability—Suitable for cell tracking and proliferation studies
- Convenience—Several colors (UV to NIR) for multi-parameter studies
- Reliability—Far-Red and NIR versions can provide greater signal-to-noise ratio due to lower background autofluorescence
- Compatability— With flow cytometers, confocal and in vivo imaging equipment
- Easy-to-use kit format

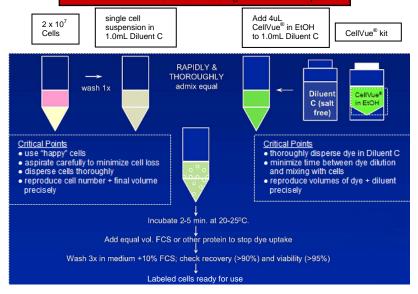
CellVue® is a trademark of PTI Research, Inc used under license. CellVue® products are sold under sublicense from PTI Research, Inc. US Patent Numbers 5,665,328; 7,462,347 B2 and 8,029,767 B2

# CellVue® products

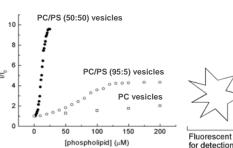
CellVue® kits are available in 3 sizes:	Price
$\label{eq:MiniKit} \textbf{Mini Kit (small): } 0.1 \text{ ml of } 1 \text{ mM ethanolic dye stock and } 1 \times 10 \text{ ml of diluent} \\ \textbf{Midi Kit (medium): } 0.2 \text{ ml of } 1 \text{ mM ethanolic dye stock and } 6 \times 10 \text{ ml of diluent} \\ \textbf{Maxi Kit (large): } 0.5 \text{ ml of } 1 \text{ mM ethanolic dye stock and } 6 \times 10 \text{ ml of diluent} \\ \end{cases}$	\$171.00 \$359.00 \$563.00
<b>Diluent C</b> : 6 vials containing 10 ml of Diluent for use with CellVue <sup>®</sup> dyes	\$154.00

Catalog number	Name	Excitation max (nm)	Emission max (nm)	All sizes available
C-1001	CellVue® Maroon	647	667	Yes
C-1002	CellVue® Claret	655	675	Except Maxi
C-1003	CellVue® Plum	652	671	Yes
C-1004	CellVue® Burgundy	683	707	Yes
C-1005	CellVue® Lavender	425	461	Yes
C-1006	CellVue® NIR815	786	814	Yes
C-1007	CellVue® NIR780	745	776	Yes
C-1008	Diluent C	-	-	N.A.
C-1009	CellVue® Jade	478	508	Yes
C-1011	CellVue® Red	567	588	Except Maxi

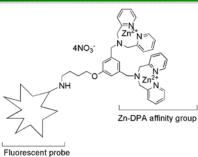
#### Tricks of the Trade for Cell Labeling with CellVue® Dyes



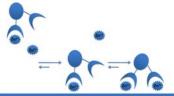
# PSVue® for imaging of cell death and bacterial infections



PSVue® dyes bind selectively to unilamellar vesicles with significant proportion of membrane phosphatidylserine, as reflected by the increase in fluorescence intensity (PC/PS 50:S0).



PROPOSED MECHANISM OF BINDING OF PSVue® TO APOPTOTIC MEMBRANES: A TWO-POINT INTERACTION A B C



Negatively Charged Membrane Surface - Exposed PS

#### Description

PSVue® products are a family of fluorescent dyes with the ability to bind selectively to the surfaces of apoptotic/necrotic cells, cancer cells and tumors, Grampositive and -negative bacteria under *in vitro* or *in vivo* conditions. The molecular structure of PSVue® consists of a positively-charged bis(zinc-dipicolylamine) (Zn-DPA) group which can bind with high affinity to the surfaces of these cells which are enriched with anionic phospholipids due to the activation of membrane scramblases. The Zn-DPA group is conjugated to a variety of reporter elements which enables probe localization by fluorescence detection upon binding.

#### Advantages of PSVue® over other reagents such as Annexin V

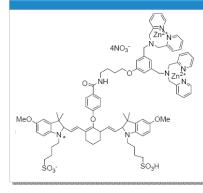
- Faster binding kinetics
- Binding is Ca<sup>2+</sup> independent, avoiding non-specific scramblase activation and thus false-positives
- Cheap compared to most Annexin V analogs
- Apoptosis can be detected under a wide variety of conditions (e.g. in presence of 10% serum, temperatures from 4 to 37°C)
- Can provide more intense labeling due to their much smaller size (i.e. >10 PSVue® molecules can bind to the same area as 1 Annexin V molecule)
- Ability to distinguish between bacterial infection and sterile inflammation in in vivo bacterial infection models

PSVue® is a trademark of Molecular Targeting Technologies, Inc. PSVue® products are sold under an exclusive license from the University of Notre Dame.US Patent # 7,179,616 and others pending.

# PSVue® products

#### P-1001: PSVue® 794

#### Type: Cy7 (Near-Infrared) analog



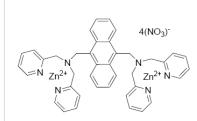
Final quantity: 0.68 ml (1mM) in water Excitation maximum: 794 nm Emission maximum: 810 nm Uses: *In vivo/in vitro*Kit also includes:

• Instructions for usage

Price: \$281.00

#### P-1002: PSVue® 380

#### Type: Anthracene analog



Final quantity: 0.40 ml (2mM) in water Excitation maximum: 380 nm Emission maximum: 440 nm

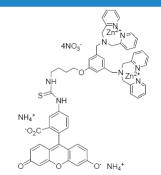
Uses: In vitro
Kit also includes:

Instructions for usage

Price: \$239.00

#### P-1003: PSVue® 480

#### Type: FITC analog



Final quantity: 0.50 ml (1mM) in water Excitation maximum: 480 nm Emission maximum: 519 nm Uses: *In vitro* Kit also includes:

• Instructions for usage

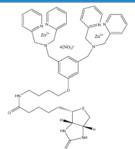
Price: \$239.00

\*mixture of isomers (5-carboxyfluorescein isomer shown)

## PSVue® products

#### P-1004: PSVue® biotin

Type: Biotin analog



#### Final quantity: 1 mg solid

(Can be complexed with streptavidincoated quantum dots (not provided) for *in vivo* and *in vitro* use.

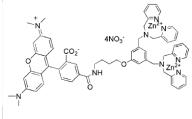
#### Uses: In vivo/in vitro Kit also includes:

 Procedures to formulate PSVue® biotin and prepare PSVue® biotin-streptavidin -coated quantum dot complex

Price: \$186.00

#### P-1005: PSVue® 550

Type: Rhodamine analog



Final quantity: 0.50 ml (1mM) in water Excitation maximum: 553 nm Emission maximum: 615 nm Uses: *In vitro* 

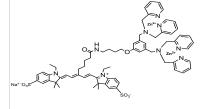
Kit also includes:
• Instructions for usage

Price: \$239.00

\*mixture of isomers (5-carboxytetramethylrhodamine shown)

#### P-1006: PSVue®

Type: Cy5 analog



Final quantity: 0.25 ml (1mM) in water Excitation maximum: 643 nm Emission maximum: 658 nm Uses: *In vitro and In Vivo* Kit also includes:

• Instructions for usage

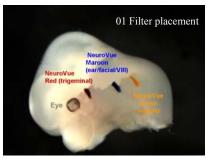
Price: \$232.00

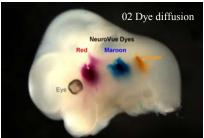
#### Applications and tips for usage of PSVue probes

- Concurrent multiple wavelength detection from long-UV to near-infrared
- $\bullet~$  Suitable for high-throughput drug screening assays or in vitro/in vivo apoptosis assays
- Enables in vivo drug biodistribution studies via intravenous probe injection
- May allow molecular imaging of disease state in response to therapeutic intervention
- Compatible for use with most imaging equipment for fluorescence microscopy and flow cytometry

# NeuroVue® for visualization of neuronal connections







#### Description

NeuroVue® dye filters are available as a set of microstrips which can be inserted into animal tissues fixed in formaldehyde, from which these lipophilic dye tracers diffuse into neuronal membranes and diffuse laterally from the insertion site. This enables labeling of the entire cell body as well as the finest axonal and dendritic branches, up to several millimeters distance from the point of dye insertion. NeuroVue® dyes can be conveniently visualized via light or fluorescence microscopy.

#### Advantages of using NeuroVue® for neuronal labeling

- Convenient, ready-to-use coated filter format
- Precise control of dye insertion point, and avoids tissue damage caused by high pressure microinjection
- No messy oils, pastes or hard-to-position crystals
- Comparable or better diffusion properties than other commercially available neurotracing dyes
- More focal results (e.g. labeling of small sets of axons within pathway)
- Available in multiple colors, including far red, for multi-tract tracing as well as similar diffusion rates among colors

NeuroVue® is a trademark of PTI Research, Inc. used under license. NeuroVue products are sold under license from PTI Research, Inc. US Patent Numbers 7,462,347 B2 and 8,029,767 B2.

# NeuroVue® Products

NeuroVue® products are available as  $1\,\mathrm{cm}^2$  filters coated with lipophilic dyes of varying excitation and emission characteristics, or as a solid dye which can be formulated as desired for application.

Catalog number	Name	Excitation max/ Emission max	Applications	Price (1 mg)
FS-1001	NeuroVue <sup>®</sup> Maroon	647/667 nm (in ethanol)	Useful for tract tracing studies of up to 3-4 weeks. Spectrally compatible with most fluorescent genetic tags, and NeuroVue® Red, Orange and Jade.	\$188.00
FS-1002	NeuroVue® Red	567/588 nm (in ethanol)	Useful for tract tracing studies of up to 3-4 weeks. Spectrally compatible with eGFP, YFP in many systems, and NeuroVue® Maroon and Jade. Spectral unmixing required for use with NeuroVue® Orange.	\$188.00
FS-1003	NeuroVue® Orange	550/570 nm (in ethanol)	Useful for tract tracing studies of up to 3-4 weeks. Spectrally compatible with eGFP and YFP in many systems, and NeuroVue® Maroon and Jade. Spectral unmixing required for use with NeuroVue® Red.	\$188.00
FS-1005	NeuroVue® Burgundy	683/707 nm (in ethanol)	Useful for tract tracing studies of up to 7 days. Spectrally compatible with most fluorescent genetic tags and NeuroVue® Red, Orange, Jade. Spectral unmixing required for use with NeuroVue® Maroon.	\$188.00
FS-1006	NeuroVue® Jade	478/508 nm (in ethanol)	Useful for tract studies of up to 5 days. Spectrally compatible with NeuroVue® Maroon, Orange and Red.	\$188.00
FS-1007	NeuroVue® Red Plus	567/588 nm (in ethanol)	Useful for tract tracing studies of up to 3-4 weeks. Spectrally compatible with eGFP, YFP in many systems, and NeuroVue® Maroon and Jade. Spectral unmixing required for use with NeuroVue® Orange. Provides faster and more extensive labeling than FS-1002 in many cases.	\$205.00

## NeuroVue® Products

Catalog number	Name	Excitation max/ Emission max	Applications	Price (1 mg)
DY-1001	NeuroVue® Red Solid	567/588 nm (in ethanol)	Can be formulated as desired for application.	\$171.00
DY-1002	NeuroVue® Maroon Solid	647/667 nm (in ethanol)	Can be formulated as desired for application.	\$171.00
DY-1003	NeuroVue® Jade Solid	478/508 nm (in ethanol)	Can be formulated as desired for application.	\$171.00

#### Overview of labeling strategy for NeuroVue® dye-coated filters

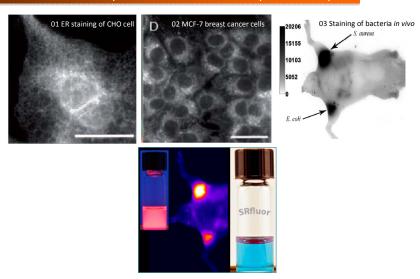
Fix tissue in 4% buffered formaldehyde

Initiate labeling by inserting NeuroVue® micro-strip(s) into nerve tract(s) to be traced. NeuroVue® dyes transfer into nerve cell membranes and diffuse laterally in both directions.

Monitor the progress of dye diffusion using light microscopy and/or fluorescence microscopy Incubate tissue in 4% phosphate buffered formaldehyde at 37°C.

When dyes have reached the regions to be studied, remove NeuroVue® microstrips and prepare whole mounts or tissue sections for fluorescence imaging

# SRfluor® Stable Squaraine Rotaxane Encapsulated Dyes



#### Description

SRfluor® dyes are a class of dyes based on the squaraine rotaxane structure, which enable them to exhibit absorption and emission properties in the far-red region of the spectrum. SRfluor® dye products offer many superior features to regular labeling dyes, and are available with a wide range of functionalities allowing conjugation with biomolecules for *in vitro* and *in vivo* imaging. SRfluor® dyes have been successfully used to visualize intracellular structures such as ER and lipid droplets, metal ions, as well as bacterial cells and infections in mouse models. SRfluor® dyes are also under development for conjugation to molecular targeting probes for imaging of other diseases such as cancer.

#### Advantages of SRfluor® dyes over regular fluorescent dyes

- Better chemical and photochemical stability than squaraines, cyanines, Alexa® and Atto dyes
- Sharp absorption and emission characteristics reduce cross-channel talk
- Does not exhibit aggregation-induced spectral broadening under biological conditions at micromolar concentrations
- Stronger staining intensity (5-20X) compared to cyanines, Alexa® and Atto dyes
- Stable photophysical properties over pH 2-12
- Compatible with 633 nm and 647 nm lasers on flow cytometers, confocal and in vivo imaging equipment

SRfluor® is a trademark of MTTI and Alexa® is a trademark of Molecular Probes, a subsidiary of Invitrogen.

# SRfluor® Products

Catalog number	Name	Abs max/ Emission max	Applications	Price (1 mg)
SR-1001	SRfluor® 680 Phenyl (crystalline Powder)	650 nm/ 678 nm (in DMSO)	Lipophilic squaraine rotaxane analog that emits in the far- red region of the spectrum and is known to accumulate at lipophilic sites inside living cells.	\$173.00
SR-1002	SRfluor® 680 Carboxyl (crystalline Powder)	650 nm/ 678 nm (in DMSO)	Carboxyl functionalized squaraine rotaxane analog that emits in the far-red region of the spectrum. This compound can be readily coupled to amino functionalities of biomolecules to provide fluorescent conjugates for use in multiple applications.	\$199.00
SR-1003	SRfluor® 680 Crown (crystalline Powder)	641 nm/ 661 nm (in ethanol)	Squaraine rotaxane analog that emits in the far-red region of the spectrum and is functionalized with a crown ether which can bind to cations such as Na <sup>+</sup> and K <sup>+</sup> .	\$226.00
SR-1004	SRfluor® 680 maleimide (crystalline Powder)	641 nm/ 664 nm (in ethanol)	Squaraine rotaxane analog that emits in the far-red region of the spectrum and is functionalized with a maleimide group that can readily undergo conjugation with thiol groups.	\$256.00
SR-1005	SRfluor® 680 NHS ester (crystalline Powder)	650 nm/ 678 nm (in DMSO)	Squaraine rotaxane analog that emits in the far-red region of the spectrum and is functionalized with a hydroxysuccinimide ester group that can readily undergo conjugation with amino groups of biomolecules to provide fluorescent conjugates for use in multiple applications.	\$226.00

# SRfluor® Products

Catalog number	Name	Abs max/ Emission max	Applications	Price (1 mg)
SR-1006	SRfluor® 680 azide carboxylate (crystalline Powder)	645 nm/ 668 nm (in DMSO)	Squaraine rotaxane analog that emits in the far-red region of the spectrum and is functionalized with an azide group that can readily undergo click chemistry reactions with reagents or biomolecules with a terminal alkyne group to provide fluorescent conjugates for use in multiple applications. A free carboxyl group is also present in this molecule which can be coupled to amino groups of biomolecules.	\$226.00
SR-1007	SRfluor® 680 alkyne (crystalline Powder)	649 nm/ 673 nm (in DMSO)	Squaraine rotaxane analog that emits in the far-red region of the spectrum and is functionalized with a terminal alkyne group that can readily undergo click chemistry reactions with reagents or biomolecules with an azide group to provide fluorescent conjugates for use in multiple applications.	\$226.00

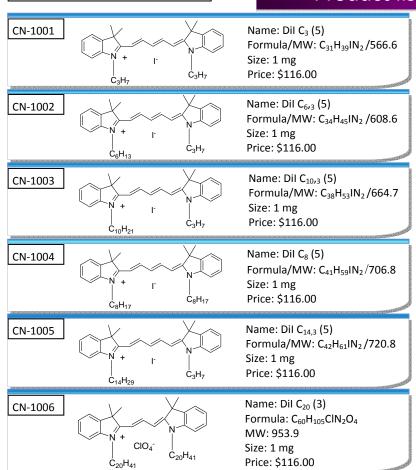
### Cyanine dyes and dye building blocks

Cyanine dyes exhibit large molar absorbtivities (~150,000-250,000 M<sup>-1</sup>cm<sup>-1</sup>) and moderate quantum yields resulting in extremely bright fluorescence signals. Therefore, cyanines have proven useful in several fields including photography, biology, laser technology and analytical chemistry.

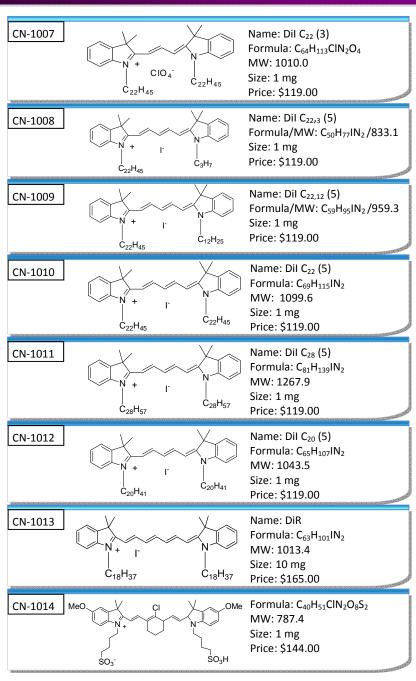
MTTI offers a series of unique lipophilic cyanine dyes which may be useful for biophysical studies of lipid bilayers of cells or other artificial membranes. In particular, these compounds may be useful as molecular probes of membrane potential, for labeling lipid bilayers and for labeling hydrophobic pockets of lipoproteins. MTTI also offers several substituted indole derivatives which can be used as building blocks for the construction of new cyanine dye derivatives for use in the aforementioned fields.

#### **Custom dyes available on request**

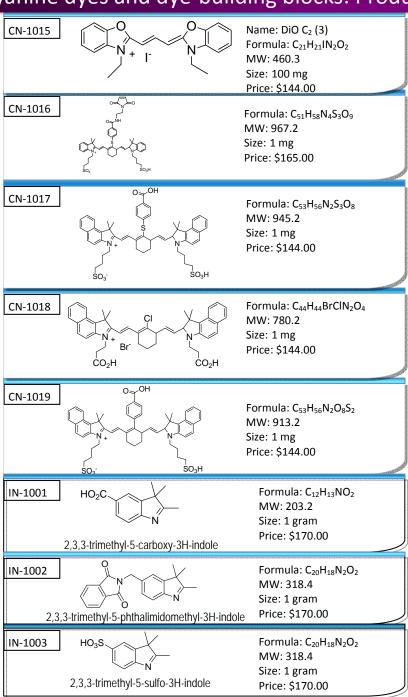
#### **Product list**



### Cyanine dyes and dye-building blocks: Products



### Cyanine dyes and dye-building blocks: Products



### Translating innovative imaging technologies

#### CellVue®

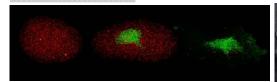


Figure 1: Minimal signal overlap and intercellular dye transfer. Mouse lymphocytes were stained with either 10  $\mu M$  CellVue® Burgundy or CellVue® NIR815 for 5 min at 37°C and imaged using the 700 and 800nm channels of the Odyssey Infrared Imaging System (Li-Cor, NE). Images courtesy of Dr Edward Roy, University of Illinois.



Figure 2: In vivo imaging of CellVue® Maroon Labeled Protein-lipid nanovesicles. Subcutaneous tumor -bearing and control mice were injected via tail vein with tumor-targeted vesicles labeled with CellVue® Maroon and imaged 24 hrs post-injection using the IVIS 200X imaging system (Xenogen, Inc.). Strong fluorescence signals were observed at the tumor site. Images courtesy of Dr Xiaoyang Qi (Children's Hospital of Cincinnati and Medical Center) and Bexion Pharmaceuticals.

#### PSVue®

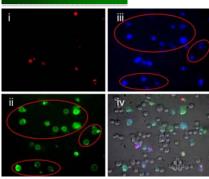


Figure 3: PSVue® staining of apoptotic and necrotic cells. Apoptosis of Jurkat cells was induced by incubation with camptothecin (10 uM) for 4h. The cells were stained simultaneously with (i) 7AAD (250 ng/ml) which binds only to dead cells with permeable membranes, (ii) Annexin-V FITC (10 ul, Pharmingen stock), and (iii) PSS-380 (20 uM). (iv) Overlay of (i-iii) with phase contrast image of cells. Both annexin-V and the Zn-DPA compound (but not 7AAD) were able to bind to cells in early-to-late apoptosis (red ovals), with preserved membrane integrity. (Images courtesy of Dr Bradley Smith, University of Notre Dame).

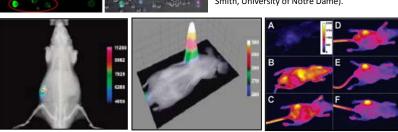


Figure 4: Zn-DPA targets mammary and prostate tumors (From left to right) (a) X-ray and fluorescence overlay image of a rat prostate tumor model at 24 h postinjection of Zn-DPA (4.0 mg/kg) shows clear evidence of selective accumulation in the tumor. (b) Representative overlay image of a nude mouse with an EMT-6 mammary tumor. Brightfield and fluorescence intensity images were acquired 24h following injection of Zn-DPA and show clear evidence of selective accumulation in the tumor. (c) Optical image of a mouse with a *S. aureus* infection in the left rear thigh muscle. Images were acquired before (A), and immediately following (B), iv injection of PSVue® 794 and at 6h (C), 12h (D), 18 h (E) and 21 h (F). (Images courtesy of Dr. Bradley Smith of University of Notre Dame).

### into solutions for research since 2001

#### NeuroVue®

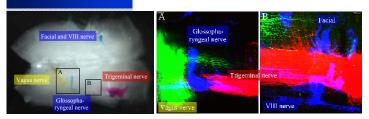


Figure 5: Whole brain mount (left) and central projections (panels A and B) in E12.5 murine embryo. Vagus, trigeminal and facial/VIII/glossopharyngeal nerves were labeled with NeuroVue® Green, NeuroVue® Red and NeuroVue® Maroon, respectively.

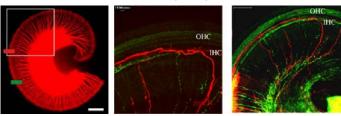
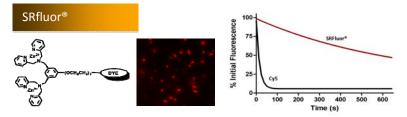
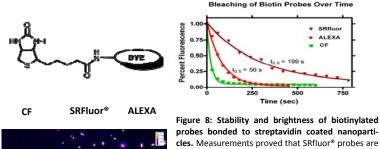


Figure 6. Low, medium and high resolution imaging of afferent and efferent fibers to outer and inner hair cells (OHC, IHC) in murine inner ear after dual labeling with NeuroVue® Red (red pseudocolor) and NeuroVue® Maroon (green pseudocolor). Note that even very thin Type II inner hair cells (IHC), which are normally quite difficult to visualize, are clearly visible at the single fiber level (right panel).



**Figure 7: Relative stability of bacteria-binding probes.** Less photobleaching was obtained with SRfluor® dye than Cy5, during visualization of bacterial cells undergoing continuous irradiation (620 nm ±30) with an X-cite 120 fluorescence illumination system through a Nikon 2000-TE epifluorescence microscope.



at least three times more photostable to Cy5 and

Alexa dye based probes.

### Immobilized steroid beads



#### Description

MTTI's sepharose affinity chromatography beads are covalently linked to steroids (such as estradiol, nortestosterone, androstan or dexamethasone) or other ligands such that ligand binding to receptors is not compromised resulting in high receptor-binding specificity.

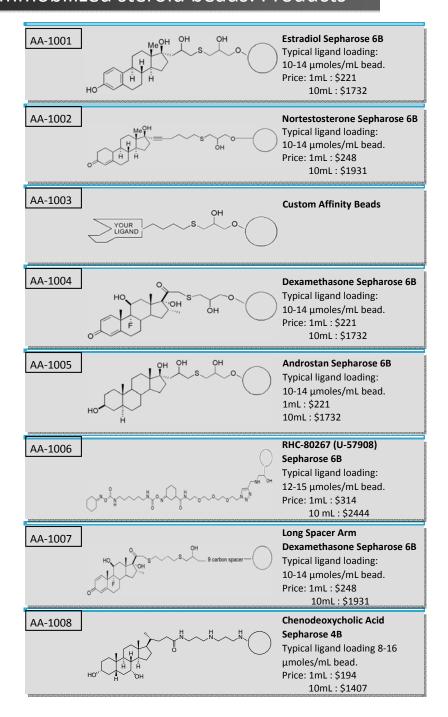
#### Applications include:

- Immobilized ligand affinity chromatography
- Ligand affinity binding studies
- Protein-ligand complexes for crystallography
- Efficient isolation and purification of receptor proteins (nuclear and others)
- Assisting in the structure-based design of receptor selective ligands



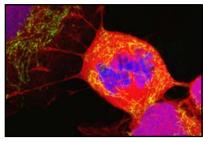
Product volumes are based upon volume of settled beads.
Pricing for larger volumes of all products is available upon request.
Products are sold under license from PTI Research, Inc. Sepharose\* is a trademark of GE Healthcare.

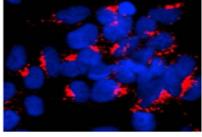
### Immobilized steroid beads: Products



### IRIS™ Dyes

#### Cyanine Technologies





U2-OS osteosarcoma, IRIS™ 2 GAR-IgG, IRIS™ 3 GAM-IgG

Human neuroblastoma Sh-SY5Y cells; primary anti-Lamp1, GaM-lgG Iris3

#### Description

**IRIS**<sup>TM</sup> **Dyes** are proprietary innovative fluorescent dyes belonging to the family of cyanine dyes, characterized by high absorbency and quantum yield, strong photo stability and huge versatility of application: from labeling of antibodies, proteins, nucleic acids, to molecular imaging, *in vivo* optical imaging, cell imaging and click chemistry.

**IRIS™** Dyes Active Esters are succinimidyl derivatives of IRIS™ Dyes. They are suitable for conjugation to any biomolecules carrying free primary amines, such as proteins, peptides, amino-modified antibodies and biopolymers.

The dyes have absorption and emission maxima in the visible and near infrared region of the spectrum. Due to the wide selection of dyes offered with different chemical-physical properties, it is possible to find the right product for any biological application involving fluorescence analysis.

#### Performance

- Solubility: Water soluble or non-water soluble (for NHS active esters)
- Suitable for protein labeling, antibodies labeling, microarrays experiments, RT-PCR, FISH, cell sorting, molecular imaging
- Spectrally similar to FITC, Cy2, Alexa 488 (IRIS™ 2), Cy3, Alexa Fluor 546, Tetramethylrhodhamine (IRIS™ 3), Cy3.5, Rhodhamine, Texas Red, Alexa 594 (IRIS™ 3.5), Cy5, Alexa Fluor 647 (IRIS™ 5), Cy5.5, Alexa 580, IR-Dye 700 (IRIS™ 5.5), Cy7, Alexa 750, IR-Dye 800 (IRIS™ 7), Near infrared dye (IRIS™ 7g)

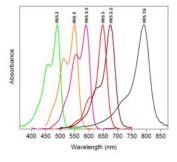
#### **Spectral Properties**

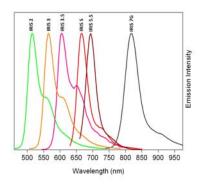
# IRIS™ Dyes

#### IRIS™ Dyes Properties



- Photo Stability
  Brightness
  Near Infrared Emission
  NHS active ester





Dye	Abs	Em	Compatible with filter set for:
IRIS™ 2	490	510	Fluorescein, Alexa 488
IRIS™ 3	550	562	Cy3, Alexa 546, Tetramethylrodhamine
IRIS™ 3.5	590	605	Cy3.5, Rhodamine, Texas red, Alexa 594
IRIS™ 5	648	667	Cy5, Alexa 647
IRIS™ 5.5	675	694	Cy5.5, Alexa 580, IR-Dye 700
IRIS™ 7G	791	818	Alexa 790, IR Dye 800

# IRIS™ Dyes: Products

Product Code	Product Name	Water soluble	Amount	Price
2WS-02	IRIS™ 2 NHS-active ester	Yes	1 mg	\$195
3WS-02	IRIS™ 3 NHS-active ester	Yes	1 mg	\$195
35WS-02	IRIS™ 3.5 NHS-active ester	Yes	1 mg	\$195
5WS-02	IRIS™ 5 NHS-active ester	Yes	1 mg	\$195
55WS-02	IRIS™ 5.5 NHS-active ester	Yes	1 mg	\$208
7GWS-02	IRIS™ 7G NHS-active		1 mg	\$375

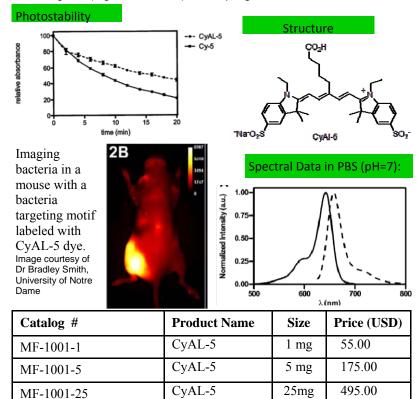
### CyAL-5 Fluorescent Dye

**Product Description:** CyAL-5 is a monofunctional cyanine dye containing a free carboxylic acid group for conjugation with targeting agents containing a free amine group; use for in vivo and in vitro imaging applications

#### **Superior Features of CyAL-5:**

- Excellent water solubility
- Similar ex and em properties to Cy5 and Alexa fluor 647
- Bright fluorescence emission in the near infrared range
- Enhanced photostability cf cy5 and cy5.5
- Useful for a variety of biochemical and in vivo imaging applications
- Very cost effective; allowing scale-up and use in multistep organic synthesis schemes
- Compatible with common filter sets used for imagingActivated with standard

reagents (e.g. HBTU, DSC) for coupling to amines

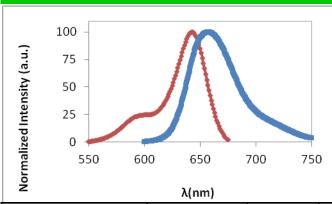


Purity > 95% by HPLC. CyAL-5 is sold under license from Harvard Medical School and Massachusetts General Hospital

### CyAL-5 cyclic RGD Optical Probe

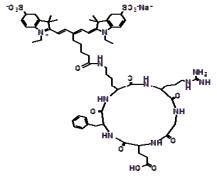
**Product Description:** CyAL-5 cRGD is a fluorescence imaging agent comprising a potent cyclic RGD peptide, c(RGDfK) designed to target integrins and a CyAL-5 dye with emission at 658 nm. This agent has been developed to target  $\alpha_v \beta_3$  expression in the neovasculature as well as tumor cells, to monitor angiogenesis and growth and treatment efficacy. The integrin family is comprised of 25 identified members, which are heterodimers of 19 α- and 8 β-subunits imbedded noncovalently into the cell membrane [1]. Generally, linear RGD peptides, such as GRGDS (Gly-Arg-Gly-Asp-Ser), often have low affinity (IC<sub>50</sub> > 100 nM) and selectivity for  $\alpha_v \beta_3$  and  $\alpha_{\text{IIB}} \beta_3$  [2], and undergo rapid degradation in serum by a variety of proteases [3]. Cyclic RGD (cRGDfk) has shown elevated binding affinity and selectivity for  $\alpha_v \beta_3$  over  $\alpha_{\text{IIB}} \beta_3$  [2,4].

#### Spectral Properties in PBS (abs max=643 nm; Em max=658 nm)



Catalog #	<b>Product Name</b>	Size	Price (USD)
RG-1001	CyAL-5 cRGD	25 nmol	199.00

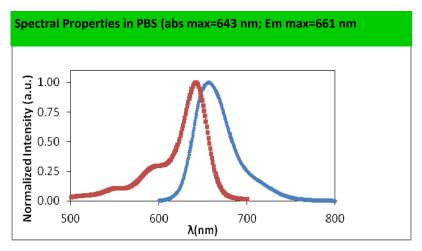
#### Structure of CyAL-5 RGD (mw=1312)



The recommended individual dose per mouse will range from 2-4 nmol, depending upon tumor type, size and location. Each tube contains 25 nmol of CyAL-5 cRGD optical probe

### CyAL-5 2-Deoxyglucose Optical Probe

**Product Description:** CyAL-5 2-deoxyglucose (CyAl-5 2-DG) is a fluorescent imaging agent designed to target a wide spectrum of cancers such as breast, glioblastoma, colon and prostate in vitro as well as in vivo. 2-DG is a glucose analog that utilizes the GLUT transporters for entry into the cell. One of the hallmarks of many cancer cells is an elevated uptake of glucose. Numerous fluorophores, including 800CW [1] and 2-NBDG [2] have been used to label 2-DG for tumor detection. FDG has been used extensively in PET imaging for diagnosis and tumor response monitoring in various types of cancer [3,4].



Catalog #	Product Name	Size	Price
DG-1001	CyAL-5 2DG	125 nmol	199.00

#### Structure of CyAL-5 2-DG (mw=853)

The recommended individual dose per mouse will range from 10-20 nmol, depending upon tumor type, size and location. Each tube contains 125 nmol of CyAL-5 2-DG optical probe.

### **Recent Publications**

#### CellVue®

- **1.** Kaimal V, Chu Z, Mahller YY, Papahadjopoulos-Sternberg B, Cripe TP, Holland SK, Qi X. Saposin C Coupled Lipid Nanovesicles Enable Cancer-Selective Optical and Magnetic Resonance Imaging. *Mol Imaging Biol.*, 2010 [Epub ahead of print].
- **2.** González-Cano P, Mondragón-Flores R, Sánchez-Torres LE, González-Pozos S, Silva-Miranda M, Monroy-Ostria A, Estrada-Parra S, Estrada-García I. Mycobacterium Tuberculosis H37Rv Induces Ectosome Release in Human Polymorphonuclear Neutrophils. *Tuberculosis*, 2010, 90, 125–134.
- **3**. Roy EJ, Sivaguru M, Fried G, Gray BD, Kranz DM. Imaging membrane intercalating near infrared dyes to track multiple cell populations. *J Immunol Methods.*, 2009, 348(1-2), 18-29.
- **4.** Katz SI, Zhou LL, Chao G, Smith CD , Ferrara T, Wang W, Dicker DT , El-Deiry WS. Sorafenib Inhibits ERK1/2 and MCL-1L Phosphorylation Levels Resulting in Caspase-independent Cell Death in Malignant Pleural Mesothelioma. *Cancer Biology & Therapy*, 2009, 8(24), 2406-2416.
- **5.** Bantly AD, Gray BD, Breslin E, Weinstein EG, Muirhead KA, Ohlsson-Wilhelm BM, Moore JS. CellVue® Claret, a new Far-Red Dye, Facilitates Polychromatic Assessment of Immune Cell Proliferation. *Immunol Invest.*, 2007, 36 (5-6), 581-605.
- **6.** Gertner-Dardenne J, Poupot M, Gray B, Fournie JJ. Lipophilic Fluorochrome Trackers of Membrane Transfers between Immune Cells. *Immunol Invest.*, 2007, 36 (5-6), 665-685.
- 7. Tario, JD, Gray BD, Wallace SS, Muirhead KA, Ohlsson-Wilhelm BM, Wallace PK. Novel Lipophilic Tracking Dyes for Monitoring Cell Proliferation. *Immunol Invest.*, 2007, 36(5-6), 861-885.

#### PSVue<sup>®</sup>

- 1. Smith BA, Xiao S, Wolter W, Wheeler J, Suckow M, Smith BD. *In Vivo* Targeting of Cell Death Using a Synthetic Fluorescent Molecular Probe. *Apoptosis*, 2011, 16(7), 722-731.
- **2.** Thakur ML, Zhang K, Paudyal B, Devakumar D, Covarrubias MY, Cheng C, Gray BD, Wickstrom E, Pak KY. Targeting Apoptosis for Optical Imaging of Infection. *Mol Imaging Biol.*, 2011. [Epub ahead of print]
- **3.** Smith BA, Gammon ST, Xiao S, Wang W, Chapman S, McDermott R, Suckow MA, Johnson JR, Piwnica-Worms D, Gokel GW, Smith BD, Leevy WM. *In Vivo* Optical Imaging of Acute Cell Death Using a Near-Infrared Fluorescent Zinc-Dipicolylamine Probe. *Mol Pharm.*, 2011, 8(2), 583-590.
- **4.** Hope-Roberts M, Wainwright M, Horobin R. Real-time imaging of bacteria in living mice using a fluorescent dye. *Biotech Histochem.*, 2011, 86(2), 104-107.
- **5.** White AG, Fu N, Leevy WM, Lee JJ, Blasco MA, Smith BD. Optical imaging of bacterial infection in living mice using deep-red fluorescent squaraine rotaxane probes. *Bioconjug Chem.*, 2010, 21(7), 1297-1304.
- **6.** Smith BA, Akers WJ, Leevy WM, Lampkins AJ, Xiao S, Wolter W, Suckow MA, Achilefu S and Smith BD. Optical imaging of mammary and prostrate tumors in living animals using a synthetic near infrared zinc(II)-dipicolylamine probe for anionic cell surfaces. *J. Am. Chem. Soc.*, 2010, 132(1), 67-69.
- **7.** Hanshaw RG, Lakshmi C, Lambert TN, Johnson JR and Smith BD. Fluorescent detection of apoptotic cells by using zinc coordination complexes with a selective affinity for membranes surfaces enriched with phosphatidylserine. *ChemBioChem*, 2005, 6, 2214-2220.
- **8.** Leevy WM, Lambert TN, Johnson JR, Morris J and Smith BD. Quantum dot probes for bacteria distinguish *Escherichia coli* mutants and permit *in vivo* imaging. *Chem. Commun.*, 2008, 2331-2333.

### Recent Publications (Cont'd)

#### NeuroVue®

- **1.** Duncan J, Kersigo J, Gray BD, Fritzch B. Combining Lipophilic dye, *in situ* Hybridization, Immunohistochemistry, and Histology. http://www.jove.com/details.stp?id=2451 doi: 10.3791/2451. *J. Vis. Exp.*, 2011, 49.
- **2.** Maklad A, Kamel S, Wong E, Fritzsch B. Development and organization of polarity-specific segregation of primary vestibular afferent fibers in mice. *Cell Tissue Res.*, 2010, 340, 303-321.
- **3.** Tonniges J, Hansen M, Duncan J, Bassett MJ, Fritzsch B, Gray BD, Easwaran A, Nichols MG. Photo- and bio-physical characterization of novel violet and near-infrared lipophilic fluorophores for neuronal tracing. *J of Microscopy*, 2010, 239 (2), 117-134.
- **4.** Soukup GA, Fritzsch B, Pierce ML, Weston MD, Jahan I, McManus MT, Harfe BD. Residual microRNA expression dictates the extent of inner ear development in conditional Dicer knockout mice. *Dev Biol.*, 2009, 328, 328-341.
- **5.** Pan N, Jahan I, Lee JE, Fritzsch B. Defects in the cerebella of conditional Neurod1 null mice correlate with effective Tg(Atoh1-cre) recombination and granule cell requirements for Neurod1 for differentiation. *Cell Tissue Res.*, 2009, 337, 407-428.
- **6.** Nichols DH, Pauley S, Jahan I, Beisel KW, Millen KJ and Fritzsch B. Lmx1a is required for segregation of sensory epithelia and normal ear histogenesis and morphogenesis. *Cell Tissue Res.*, 2008, 334(3), 339-358.
- 7. Kikkawa YS, Pawlowski KS. Cochlear neuronal tracing for frequency mapping with Dil, NeuroVue®, and Golgi methods. *Acta Otolaryngol Suppl.*, 2007, 559, 19-23.
- **8.** Jensen-Smith H, Gray B, Muirhead K, Ohlsson-Wilhelm B, Fritzsch B. Long-distance three-color neuronal tracing in fixed tissue using NeuroVue® dyes. *Immunol Invest.*, 2007, 36(5-6), 763-789.

#### SRfluor®

- **1.** White AG, Fu N, Leevy WM, Lee JJ, Blasco MA, Smith BD. Optical imaging of bacterial infection in living mice using deep-red fluorescent squaraine rotaxane probes. *Bioconjug Chem.*, 2010, 21(7), 1297-1304.
- **2.** Gassensmith JJ, Arunkumar E, Barr L, Baumes JM, DiVittorio KM, Johnson JR, Noll BC, Smith BD. Self-assembly of fluorescent inclusion complexes in competitive media including the interior of living cells. *J Am Chem Soc.*, 2007, 129(48), 15054-15059.
- **3.** Johnson JR, Fu N, Arunkumar E, Leevy WM, Gammon ST, Piwnica-Worms D, Smith BD. Squaraine rotaxanes: superior substitutes for Cy-5 in molecular probes for near-infrared fluorescence cell imaging. *Angew Chem Int Ed Engl.*, 2007, 46(29), 5528-5531.

#### Cyanine Dyes

- **1.** Oreopoulos J, Yip CM. Combinatorial microscopy for the study of protein-membrane interactions in supported lipid bilayers: Order parameter measurements by combined polarized TIRFM/AFM. *J. Struct. Biol.*, 2009, 168 (1), 21-36.
- **2.** Bouteiller C, Clavé G, Bernardin A, Chipon B, Massonneau M, Renard PY, Romieu A. Novel Water Soluble Near-Infrared Cyanine Dyes: Synthesis, Spectral Properties, and Use in the Preparation of Internally Quenched Fluorescent Probes. *Bioconjug Chem.*, 2007, 18 (4), 1303-1317.
- **3.** Pham W, Medarova Z, Moore A. Synthesis and Applications of a Water Soluble Near Infrared Dye for Cancer Detection Using Optical Imaging. *Bioconjug Chem.*, 2005, 16 (3), 735-740.

### Recent Publications (Cont'd)

#### Immobilized steroid beads

- **1.** Williams AJ, Norcross AJ, Chandler KA, Bingley PJ. Non-specific binding to protein A Sepharose and protein G Sepharose in insulin autoantibody assays may be reduced by pretreatment with glycine or ethanolamine. *J. Immunol. Methods*, 2006, 314, 170-173.
- **2.** Manas ES, Unwalla RJ, Xu ZB, Malamas MS, Miller CP, Harris HA, Hsiao C, Akopian T, Hum WT, Malakian K, Wolfrom S, Bapat A, Bhat RA, Stahl ML, Somers WS, Alvarez JC. Structure-based Design of Estrogen Receptor- Beta Selective Ligands. *J. Am. Chem. Soc.*, 2004, 126, 15106-15119.
- **3.** Salman M, Ruiz AA, Stotter PL, Chamness GC. A Progesterone Receptor Affinity Chromatography Reagent:  $17\alpha$ -Hexynyl Nortestosterone Sepharose. *J Steroid Biochem.*, 1987, 26 (3), 383-391.

#### CyAL-5 cyclic RGD Optical Probe

- 1. Desgrosellier JS, Cheresh DA (2010). Integrins in cancer: biological implications and therapeutic opportunities. *Nat Rev Cancer*. **10**:9-22.
- **2.** Pfaff M, Tangemann K, Müller B *et al.* (1994). Selective recognition of cyclic RGD peptides of NMR defined conformation by  $\alpha_{\text{IIb}}\beta_3$ ,  $\alpha_v\beta_3$ , and  $\alpha_5\beta_1$  integrins. *J Biol Chem.***269**:20233-8.
- **3.** Gottschalk KE, Kessler H (2002). The structures of integrins and integrin-ligand complexes: Implications for drug design and signal transduction. *Angew Chem Int Ed Engl.* **41**:3767-74
- **4.** Boturyn D, Dumy P (2001). A convenient access to  $\alpha v \beta 3/\alpha v \beta 5$  integrin ligand conjugates: regioselective solid-phase functionalization of an RGD based peptide. *Tetrahedron Lett.* **42**:2787-90

#### CyAL-5 2-Deoxyglucose Optical Probe

- 1. Kovar JL, Volcheck W, Olive DM, Simpson MA (2007). Abstract #5527, Poster presentation, AACR Annual Meeting.
- 2. Lloyd PG, Hardin CD, Sturek M (1999). Physiol Res 48:401-410.
- **3.** Hicks RJ, Wahl RL (2010). PET diagnosis and response monitoring in oncology, Molecular Imaging, Principles and Practice, p875-895.
- **4.** Mankoff DA (2010). PET imaging in cancer clinical trials, Molecular Imaging, Principles and Practice, p1179-1191.

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