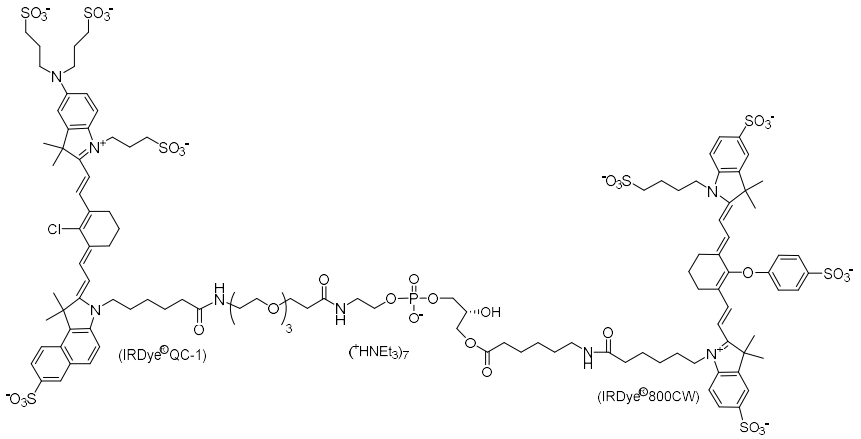
ATXRed AR-2

Catalog number: L-2010



Molecular Formula: $C_{159}H_{263}ClN_{15}O_{39}PS_8$

MW: 3331.81

CAS#: n/a

Excitation/Emission: 775/800 nm

Solubility: Water, MeOH (>5 mg/mL)

Storage and Handling: ATXRed AR-2 is best stored as a solid at -20 °C and protected from light. Storage in basic (pH>9) or acidic (pH<4) solutions may result in decomposition. Stock solutions should be stored at -20 °C and protected from light.

Background: ATX-Red AR-2 is an analog of the autotaxin substrate lysophosphatidyl choline (LPC) and contains a near-infrared fluor (LI-COR IRDye® 800CW) and quencher (LI-COR IRDye® QC-1). The design is modeled after FS-3, a fluorescent ATX substrate that has been validated as an ATX substrate and is predictive of ATX inhibitor activity [1-4]. In the parent compound, the quencher interferes with fluorescence, but when autotaxin cleaves ATX-Red AR-2, fluorescence increases. This activation mechanism is specific to autotaxin in vitro and in vivo.

Suggested Protocol: ATX-Red AR-2 is designed for imaging autotaxin activity in living organisms. This compound was validated using a mouse model bearing orthotopic MDA-MB-231 breast and MDA-MB-435 melanoma tumors and is expected to be effective in numerous other animal models. Different models may require modification to the dosing and administration route.

Add PBS to ATX-Red AR-2 to a final concentration of 0.2 mg/ml and mix well by vortexing. Sterile filter through a 0.2 μm filter membrane and store frozen or on ice if solution will be used within two hours. Inject by lateral tail vein injection at a final dose of 0.5 mg/kg. Image animals on appropriate imager. The timing of animal imaging will depend on the research question being addressed. The parent compound does possess background fluorescence in vivo so background levels may be high at early timepoints. The parent compound displays typical bi-exponential kinetics in blood, suggesting rapid distribution followed by slow elimination with half-lives of 0.3 hr and 8.5 hr, respectively. The signal to background optimum in orthotopic tumor model was reached at 48 hours (Figure 1).

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For additional information see: Madan, D., C.G. Ferguson, et al. (2013) "Non-Invasive Imaging of Tumors by Monitoring Autotaxin Activity Using an Enzyme-Activated Near-Infrared Fluorogenic Substrate" PLoS One 8(11): e79065

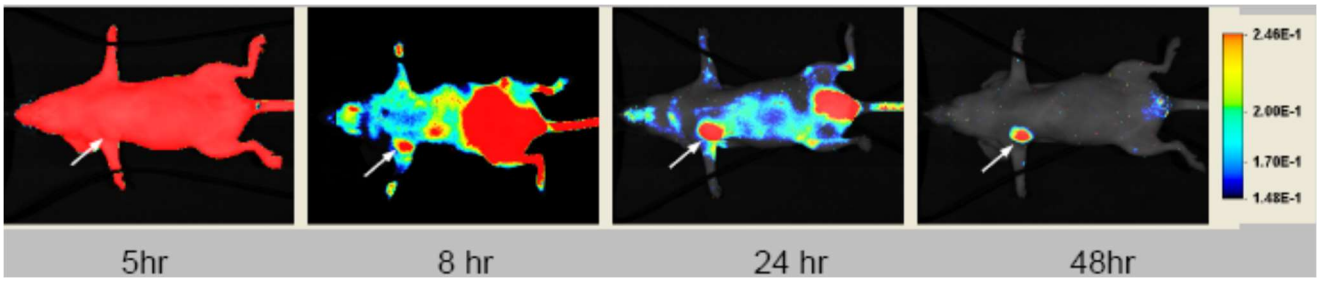

Figure 1. A mouse bearing an MDA-MB-231 orthotopic tumor (arrow) was injected i.v. with ATX-Red AR2 at 0.5 mg/kg. The mouse was imaged on a Pearl Impulse imager (Licor) at the indicated times.

References:

1) Baker DL, *et al.* (2006) Carba analogs of cyclic phosphatidic acid are selective inhibitors of autotaxin and cancer cell invasion and metastasis. *J Biol Chem* 281(32):22786-22793.
2) Ferguson CG, *et al.* (2006) Fluorogenic phospholipid substrate to detect lysophospholipase D/autotaxin activity. *Org Lett* 8(10):2023-2026.
3) Hoeglund AB, *et al.* (2010) Optimization of a pipemidic acid autotaxin inhibitor. *J Med Chem* 53(3):1056-1066.
4) Parrill AL, *et al.* (2008) Virtual screening approaches for the identification of non-lipid autotaxin inhibitors. *Bioorg Med Chem* 16(4):1784-1795.

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Hazardous Properties and Cautions: The toxicological and pharmacological properties of this compound are not fully known. For further information see the MSDS on request. This product is manufactured and shipped only in small quantities, intended for research and development in a laboratory utilizing prudent procedures for handling chemicals of unknown toxicity, under the supervision of persons technically qualified to evaluate potential risks and authorized to enforce appropriate health and safety measures. As with all research chemicals, precautions should be taken to avoid unnecessary exposures or risks.

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