

Protocol #1007

Use of Visistar®-Integrin for Imaging Tumors in Small Animals

v. 1.1

Materials Needed

1. Visistar-Integrin ultrasound contrast agents (VS-101)
2. Sterile 0.5 or 1.0 mL syringe with attached 28 G needle

Summary

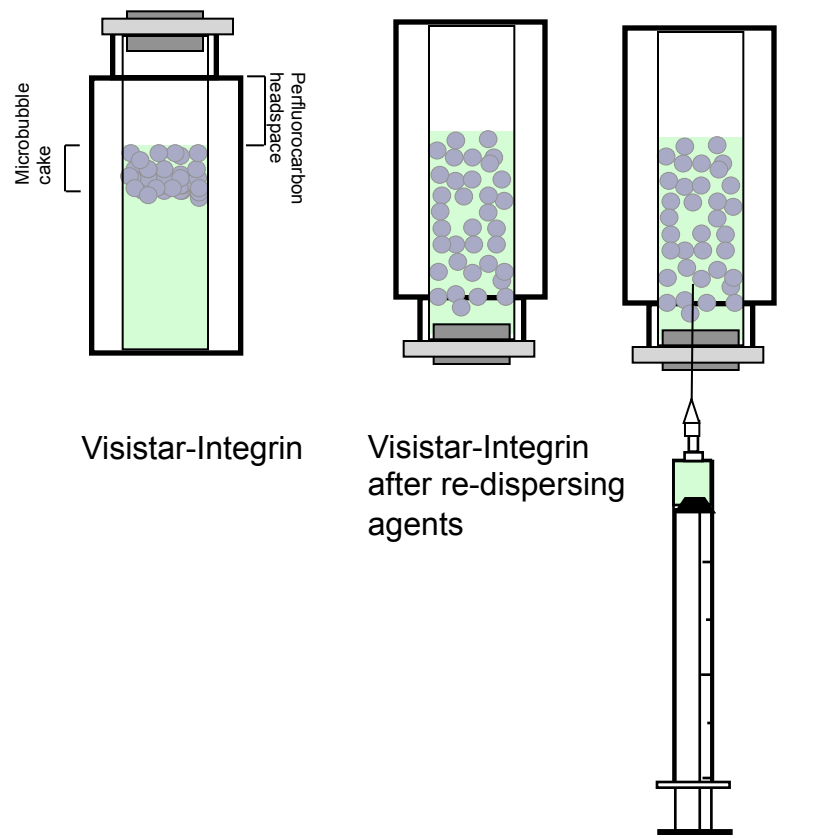
Visistar-Integrin is an microbubble ultrasound contrast agent containing a cyclic RGD targeting ligand. Visistar-Integrin is known to bind to alpha-v beta-3 integrin found on angiogenic vascular endothelium. The agent is useful for imaging angiogenesis in small animal models of tumor development. Agents are administered as an intravenous bolus injection, via retro-orbital, tail vein, or jugular injection in mice.

1. Disperse the Visistar-Integrin agents by gently shaking the vial end-to-end for 10 seconds. The dispersion should appear uniformly opaque.

2. Remove and discard the center of the aluminum crimp. Carefully insert a sterile 28-G syringe needle through the elastomeric septum, and withdraw the desired volume of Visistar-Integrin. Do not open the Visistar-Integrin vial.

4. After sampling the vial, store vial upright at 4-8 degrees C.

5. Although dilution is not necessary for administration, Visistar-Integrin agents may be diluted with Targestar® Buffer, sterile saline or other aqueous buffer immediately prior to administration.



Withdraw with a sterile syringe

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Dosage and Administration

Optimal dosage of Visistar-Integrin depends upon the tissue to be imaged, route of administration, and scanner settings. Dose optimization should be performed for each application. In mice (25 g), a dose of 30 uL administered by jugular or retro-orbital injection generally results in sufficient contrast enhancement for subcutaneous tumors. Higher doses may be required for administration via tail vein. Higher doses are generally required for ultra-high frequency (>20 MHz) imaging.

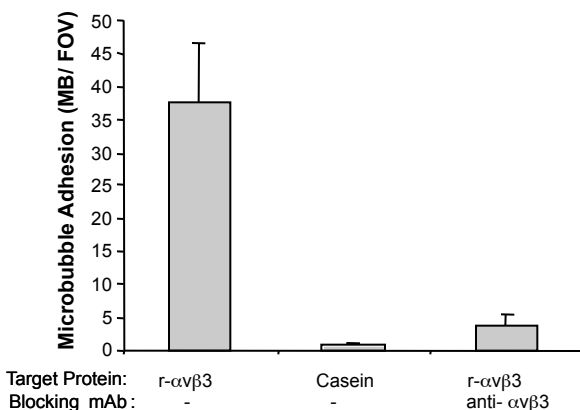
Contrast imaging settings (such as pulse inversion, sub-harmonic filtering, or CPS) must be enabled on the ultrasound scanner for optimal contrast sensitivity. Agents remain acoustically active *in vivo* for 5-15 minutes, depending on the administered dose and scanner settings. Please contact Targeson technical support for protocol assistance.

Precautions

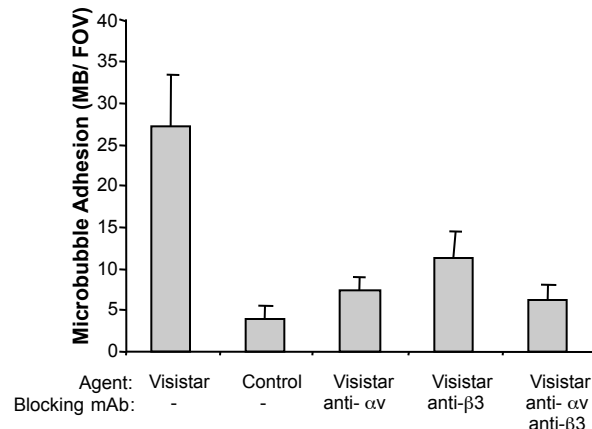
Visistar-Integrin should appear as a milky white dispersion after re-dispersion by gentle shaking. Do not use if liquid in vial appears clear, as this indicates that the contrast agents have been damaged or destroyed. Unused portions of Visistar-Integrin may be stored at 4-8 degrees C for up to 3 months after first use. Visistar-Integrin does not contain preservatives or bacteriostatic agents. Do not freeze.

Examples

Functional Adhesion of Visistar-Integrin *in vitro*



The figure demonstrates adhesion of Visistar-Integrin agents to recombinant mouse α v β 3 integrin in a parallel plate flow chamber adhesion assay². The Visistar-Integrin agents exhibit little non-specific adhesion to casein-blocked control surfaces. Incubation of α v β 3 flow chambers with an anti- α v β 3 blocking antibody abolishes of >95% of Visistar Integrin adhesion.



The figure demonstrates adhesion of Visistar-Integrin agents to α v β 3 -expressing murine endothelial cells (bEND3) in a parallel plate flow chamber adhesion assay². Non-targeted control agents show little non-specific adhesion to endothelial cells. Blocking antibodies against α v and β 3 subunits block adhesion of Visistar Integrin agents by >80%. Courtesy Dr. Michael Lawrence, University of Virginia.

References

1. Rychak JJ, J Graba, AM Cheung, BS Mystry, JR Lindner, RS Kerbel, FS Foster. 2007. Mol Imaging 6(5): 289-96
2. Takalkar AM, AL Klihanov, JJ Rychak, JR Lindner, K Ley. 2004. J. Control Release 96(3): 473-82

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