

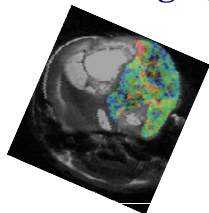
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www.molecularimaging.com

Anti-Cancer Efficacy Testing

Anatomical & Functional Imaging

Imaging of Molecular Events



Metabolic Imaging

Pharmacokinetics

Histology

Pharmacodynamics

In Vitro Services



Contrast Agent Testing

Rheumatoid and Arthritis

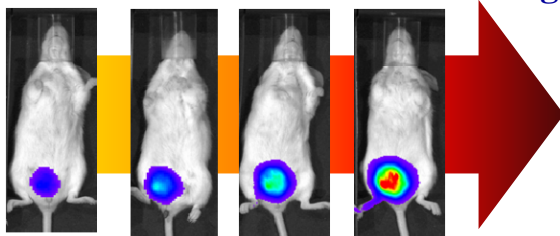
Delayed Type Hypersensitivity (DTH)

Carageenan Footpad Edema (CFE)

Models of Chronic Inflammation

Sample Generation

Consulting



# MIR Preclinical Services

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*Innovation in Drug Evaluation*

# MIR Preclinical Services

## Angiogenesis

Your Source For Preclinical In Vivo Anti-Cancer/Inflammation Drug Evaluation & Preclinical Imaging Services

Conventional Tumor Xenografts

Inflammation and Arthritis

PD and PK Studies

Histology & Immunohistochemistry

Small Animal MRI

Preclinical PET/CT

High Resolution CT

Bioluminescence and Fluorescence



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## Angiogenesis Studies

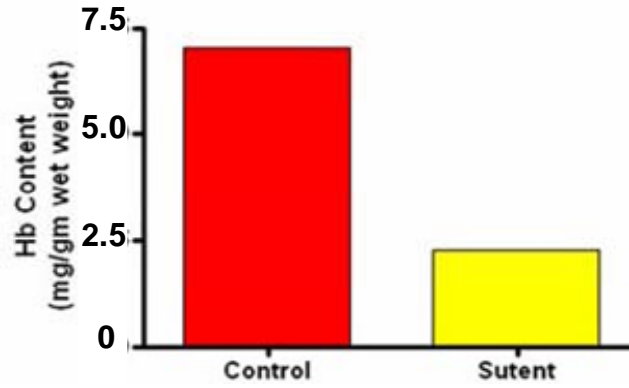
Angiogenesis plays a major role in supplying nutrients and oxygen in embryogenesis, wound healing and placental implantation for the delivery of nutrients and the removal of waste products. In pathologic conditions, such as tumor growth, diabetic retinopathy, psoriasis and rheumatoid arthritis this response plays a key role in disease progression. Because of this, angiogenesis has become a prime target for novel therapies in a variety of conditions.

While therapeutic targeting of angiogenesis is important, the development of suitable methods for the assessment of this process in vivo has been problematic. Traditionally, the use of Matrigel plugs impregnated with angiogenic factors has provided a measure of new vessel formation. A major limitation of this approach has been the ability to reliably recover the implanted plugs.

## Histology, Immunohistochemistry

MIR offers histology and immunohistochemistry services to determine vessel formation in tumors using endothelial cell markers such as CD31 or Factor VIII. Blood vessels can then be quantified by counting the number of vessels present within a defined frame of view over a number of different slices throughout the depth of the tumor. Other methods are also under development. MIR can also supply fixed, frozen or powdered samples to clients for their analysis.

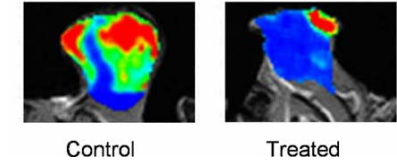
## Improved Matrigel Assay



Matrigel is a gelatinous material derived from mouse tumor cells that is commonly used in vitro and in vivo as a substrate for cells. When pro-angiogenic agents are also added to the matrigel and it is injected into the subcutaneous space of an animal, new blood vessels invade the matrigel, similar to vessel formation in tumors. This is the basis of an assay referred to as the “matrigel plug” assay. The matrigel can be harvested and the new vessel formation in the plug can be assessed. The difficulty with the traditional matrigel plug assay is that the matrigel disperses easily in the subcutaneous tissue and does not form a tight solid mass. MIR has developed methods that minimize this dispersion.

## Dynamic Contrast-Enhanced (DCE) MRI

DCE preclinical MRI is a clinically proven method for the quantification of the effect of anti-angiogenic or vascular targeted therapies. DCE utilizes the imaging of gadolinium uptake into the interstitial space for the quantification of vascular permeability, vascular surface area and blood flow. This quantitative technology can be applied to both clinical and preclinical studies.



## Important Biomarkers & Targets in Angiogenesis

**FGF:** endothelial cell proliferation and differentiation

**VEGF:** vascular growth factor

**VEGFR & NRP-1:** survival signals

**Ang1 & Tie2:** Stabilize vessels

**PDGF & PDGFR:** recruit smooth muscle

**TGF-β & TGFβR:** extracellular matrix production

**avb3, avb5 & a5b1:** Bind matrix macromolecules and proteinases

**VE-Cadherin & CD31:** endothelial junctional molecule

**AC133:** regulates angioblast differentiation

**Id1 & Id3:** regulates endothelial transdifferentiation