

Angene™

angiogenesis drug discovery platform

Target Identification

Unique *in vitro* model of human angiogenesis

DNA microarray

Bioinformatics and genomics tools

In Vitro Validation

Medium throughput capillary tube formation assays

RNAi and antisense technologies

Fluorescent imaging of capillary networks and image analysis

Expression screening:
• tumour samples
• inflammation samples

In Vivo Validation

Angiogenesis *in vivo* assays and animal models under development

Human antibodies in mice

Tumour models

Validated Targets

Assay Development for Drug Discovery

Compound Profiling

Angene™ is a powerful platform for angiogenesis target and drug discovery

- Powerful and unique models of human angiogenesis
- Over 140 novel angiogenesis genes
- Medium throughput assays for target validation and compound profiling
- Angiogenesis *in vivo* assays and models under development

Target Identification

Unique *in vitro* model of human angiogenesis

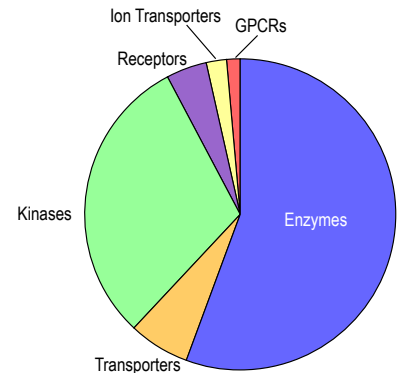
DNA microarray

Bioinformatics and genomics tools

Combining DNA microarray with a unique *in vitro* model of human angiogenesis, Bionomics has identified over 480 genes not previously associated with angiogenesis. Of these, over 160 are novel genes. As an indication of the quality of Angene™ for target identification and to provide proof of concept, Bionomics has identified a further 130 known angiogenesis genes from Angene™.

Using advanced bioinformatics, Bionomics is identifying those novel angiogenesis genes that are the best candidates for validation as diagnostic markers and therapeutic targets.

Bionomics' portfolio of novel angiogenesis genes includes small-molecule drug targets, antibody targets and targets appropriate for gene therapy.



Representation of Angene™ genes (excluding novel genes) by function of gene

Target Validation

Medium throughput capillary tube formation assays

RNAi and antisense technologies

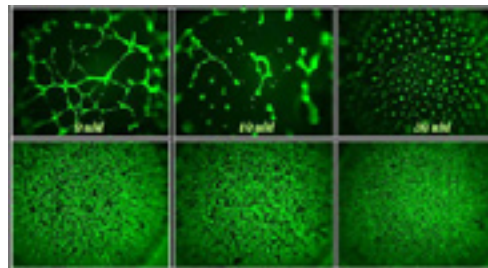
Fluorescent imaging of capillary networks and image analysis

Expression screening:
• tumour samples
• inflammation samples

Bionomics validates its novel angiogenesis genes using a range of assays of endothelial cell function including cell proliferation and migration assays and a medium throughput capillary tube formation assay operating in a 96-well format.

Bionomics incorporates a range of technologies to regulate the expression of target genes and proteins, including antisense and RNAi approaches.

Combined with the expression analysis for Angene™ targets in human tissue samples and cell lines, Bionomics' *in vitro* functional validation operates as a strong predictor of Angene™ genes as targets for cancer and inflammatory disease treatments.



Capillary tube formation assay incorporating fluorescent staining of endothelial cells in 96-well format

Capillaries at varying doses of inhibitor compound

Monolayer at varying doses of inhibitor compound

Proprietary Target BNO69

Novel target, suitable for small molecule therapy

Knock-down inhibits capillary tube formation

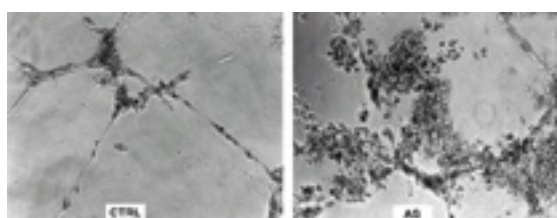
Endothelial cell specific

One example of Bionomics' proprietary angiogenesis targets is BNO69 - a novel gene not previously cloned in humans.

BNO69 is highly upregulated in expression at the 3 hour time point of the *in vitro* model of angiogenesis. Functional experiments have indicated that the knock-down of BNO69 expression markedly inhibits capillary tube formation.

Sequence analysis of BNO69 indicates the presence of a functional domain implicating the gene in cell signalling events involving cytoskeletal structure.

BNO69 is differentially and specifically expressed in endothelial cells, rendering BNO69 an important therapeutic target for angiogenesis-directed applications.



Functional experiments showing effect of knock-down of BNO69 on capillary tube formation in Matrigel.

CTRL: Empty vector control.
AS: Antisense BNO69.