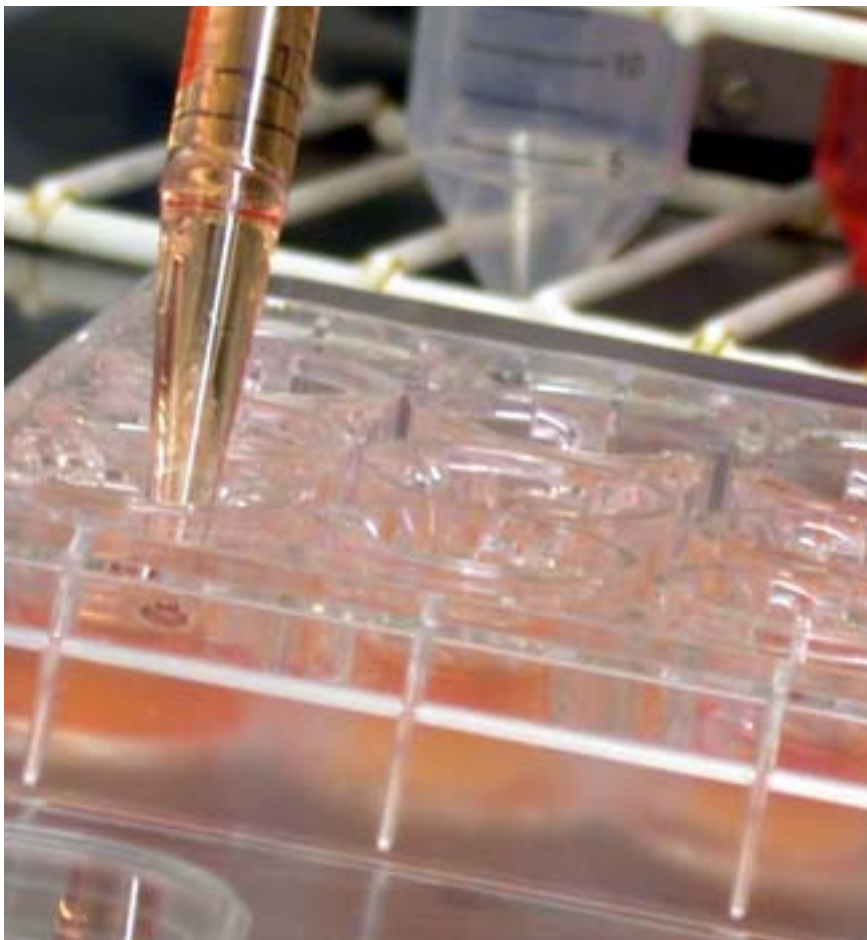


Cell-based *in vitro* models

TNO is a global partner in research for a wide variety of commercial and non-commercial organisations. TNO Pharma is active in co-development projects, collaborative contract research studies, long-term partnerships with universities and in-house strategic research. TNO's researchers employ a range of cell-based *in vitro* models to serve as a platform for target identification and validation, mechanistic research of lead compounds, dose-finding studies and research into potential side effects. The focus in these models is on primary human cells and very often, cells derived from specified patient groups are also included. The cell-based models are therefore uniquely suited to explore truly human targets and pathways.



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At TNO, cell-based *in vitro* models are continuously developed and studied in the context of organ-specific disorders including arthritis and osteoarthritis, neurodegenerative disorders, fibrosis and organ-specific inflammation. In addition a strong science-based focus exists on growth and proteolysis, cell-matrix interactions, vascular remodelling and lipid & cholesterol metabolism. In these areas, drug-affected pathways of gene regulation are extensively analysed. Many unique assays are available that are specialised to provide reliable answers to questions in these particular fields that are supported by an excellent and long-standing scientific position. The unique clinical and scientific network of TNO allows acquisition of a wide range of well-defined human tissue samples and cells, even when not part of the primary focus, and also of a range of tissues and cells from non-human primates. As additional tools, a range of cell lines are available to complement primary cell-based assays. These cell lines include types to represent fibroblasts, mesothelium, hepatocytes, monocytes, oligodendrocytes, and neurons.

Together, the combination of *in vitro* human cell-based models, the strong scientific support and the wide range of specialised and sometimes unique assays offers excellent opportunities for added value in biomedical research. Rather than offering standardised approaches, TNO prefers to discuss research questions with its partners to design tailor-made solutions. Ethical considerations limit TNO's possibilities to provide viable cells and tissues to third parties. In general, collaborative and contract research using TNO's human cell-based *in vitro* models is therefore limited to TNO's research laboratories.

Primary human cells available in TNO's models

Peripheral blood mononuclear cells

- Monocytes
- Dendritic cells
- CD4⁺/CD8⁺ T cells
- B cells

Macrovascular endothelial cells

- Umbilical vein (HUVEC)
- Umbilical artery (HUAEC)
- Aorta (HAEC)
- Iliac vein (HIVEC)

Microvascular endothelial cells

- Foreskin (HFMVEC)
- Endometrium (HEMVEC)
- Brain capillaries (BCEC)

Brain-derived astrocytes

Brain-derived microglia

Brain organotypic cultures

Eye lenses

Synovial fibroblasts (synoviocytes)

Chondrocytes (bovine)

Alginate-recovered chondrocytes (bovine)

Cartilage explant cultures, also as co-cultures with leukocytes

Fat explant cultures

Hepatocytes (limited availability)

Stromal cells of various tissues

Smooth muscle cells

Fibroblasts

Myoblasts

Gastro-intestinal tissues

- Jejunum explants
- Ileum explants
- Colon explants

Specialised assays for TNO's cell-based *in vitro* models

Endothelial cell migration assays

- 2D- and 3D migration assays

Endothelial tube formation (angiogenesis) assays

- 3D assays, incorporating tailor-made fibrin or collagen matrices

Co-culture tube formation assays

- Stromal cells – endothelial cells
- Tumour cells – endothelial cells

Synoviocyte migration and invasion assays

cDNA macro-array-based gene profiling assays

Various types of proliferation assays

A range of –often unique- assays for

- Proteases
- Extracellular matrix composition and -derived components
- Modified proteins
- Mediators in cholesterol uptake and metabolism
- Mediators in lipid uptake and metabolism
- Mediators in cell signalling pathways
- Mediators in fibrinolysis
- Acute phase proteins
- Inflammatory cytokine and chemokine mediators
- Toll-like receptors
- Peroxisome proliferator-activated receptors (PPARs)
- Adhesion molecules

TNO Quality of Life

TNO Quality of Life is a part of TNO; Europe's largest independent research institute for technological and strategic research and consultancy. By translating scientific knowledge into practice we aim to optimise the innovative abilities of the industry and government. As a research partner TNO works for various industries worldwide.

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