

Metabolic Disease Research & Drug Discovery



Metabolic Disease Research & Drug Discovery at Evotec

A leading platform for rapid progress and increased probability of success

- **Over 2 decades of expertise in metabolic disorders**

- Diabetes, obesity, kidney diseases, liver diseases (MASLD, MASH), cardiovascular, and muscle diseases
- Wide range of target classes, e.g. GPCRs, ion channels, transporters, and enzymes

- **Comprehensive platform of translational models and readouts maximizing the chances of therapeutic success**

- Disease-relevant *in vitro* assays in immortalized cell lines compatible with high throughput screening, primary cells from human patients, and *ex vivo* tissues derived from animal disease models
- Covering all relevant target tissues such as pancreatic islets, adipose, skeletal muscle, kidney, heart, and liver
- *In vivo* animal models (diet-induced, surgical, or disease-specific genetic strains) complement the cellular assay cascade during lead optimisation

- **Our expertise in metabolic drug discovery is integrated into Evotec's drug discovery processes and technology platforms, making us the preferred partner for pharmaceutical and biotech companies**

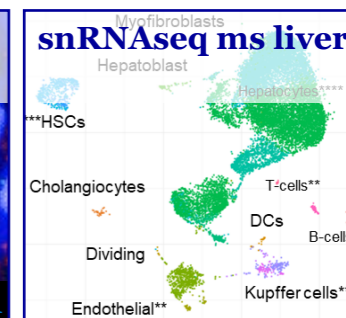
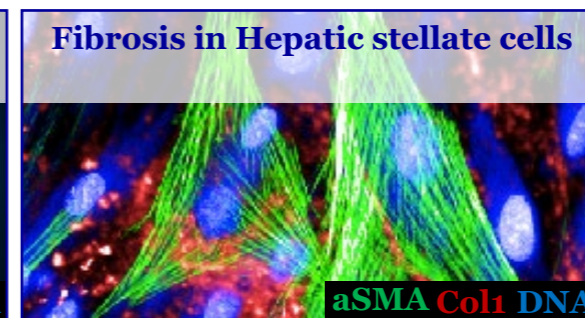
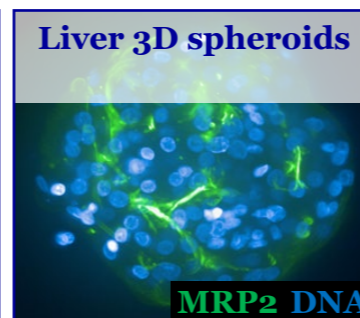
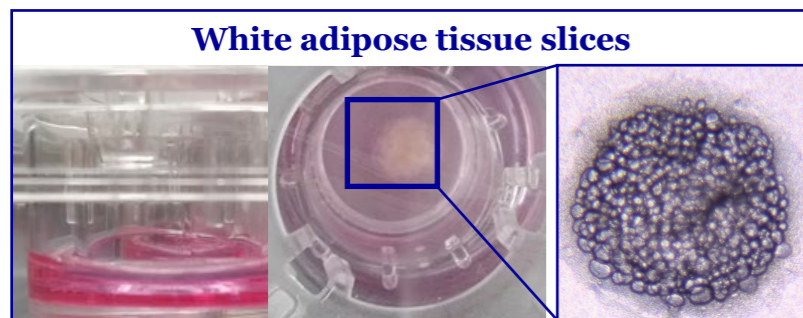
- **We deep-dive into the science of your target or therapeutic focus area, to provide you with support, solutions, and innovative ideas for project, whether that's focused tasks or more complex multiyear collaborations**



Translational Biology in Metabolic Disease Research

Covering metabolic syndrome, diabetes, obesity, and liver diseases

| | <i>In vitro</i> Biology | <i>In vivo</i> Biology |
|------------------------|---|--|
| β-cells Islets | <ul style="list-style-type: none"> Primary hu and rodent islets, hu EndoC-βH5, rat Ins-1 β-cell lines Glucose stimulated insulin secretion, cell composition, proliferation and differentiation | <ul style="list-style-type: none"> Type 1 diabetes STZ and genetic models (NOD, AKITA) Islet transplantation |
| Adipose | <ul style="list-style-type: none"> Primary & immortal hu adipocytes, hu SGBS, 3T3-L1, <i>ex vivo</i> adipose slices Metabolic assays in white & beige adipocytes, including Seahorse | <ul style="list-style-type: none"> HFD-induced obesity and pre-diabetic mouse models Genetic models of obesity and diabetes: db/db, ob/ob mice, ZDF rats |
| Skeletal Muscle | <ul style="list-style-type: none"> Primary & immortal hu myoblasts and myocyte cell lines Myogenic differentiation, morphology, and metabolic assays | <ul style="list-style-type: none"> Muscle xenotransplant regeneration models Muscle strengths and endurance tests |
| Liver | <ul style="list-style-type: none"> Primary hu & rodent hepatocytes and cell lines; iPSC-derived hepatocytes & organoids Primary and immortal hu hepatic stellate cells Primary hu PBMC derived immune cells incl. macrophages, monocytes; hu Kupffer cells, mouse BMDMs; cell lines 3D hu primary liver spheroids, mouse precision cut liver slices Metabolic, inflammation, fibrosis assays | <ul style="list-style-type: none"> Diet and genetic induced MASLD and MASH models covering steatosis, inflammation and mild to-moderate-to severe fibrosis: modified-amylin diet, choline-deficient diet, ob/ob GAN diet CCL4 toxin-induced liver fibrosis model |





Platforms for Metabolic Disease Research

Diverse downstream analyses for cellular assays and animal studies established

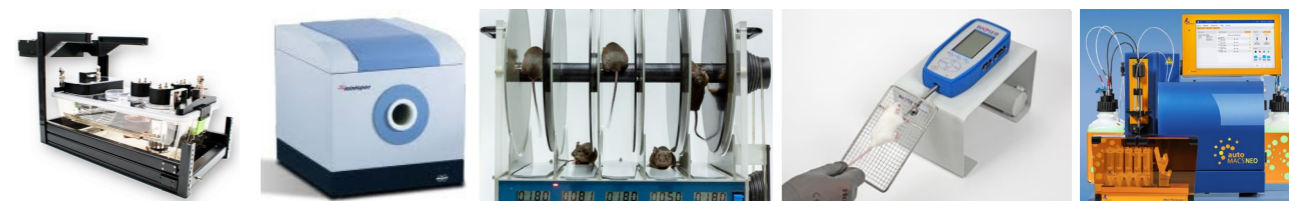
Live Cellular Phenotyping and Imaging

- High content / high throughput imaging (PE Operetta, Opera Phenix)
- Live cell imaging (IncuCyte)
- Cellular respiration (Seahorse)
- Electrophysiology (Manual patch, Qpatch, SynchronPatch)



Comprehensive *In vivo* Phenotyping

- Body composition & PhenoMaster system for indirect gas calorimetry, tolerance tests
- Muscle function
- Clinical chemistry, MSD, and FACS



Longstanding **Histology & Pathology** expertise

- Automated processes for staining and image analysis
- AI-based pathology – Veterinarian Pathologist validated



E.MPD, PanOmics & PanHunter based **TargetID & Validation**

- Evotec Molecular Patient Database (E.MPD): Proprietary collection of human biosamples from large disease cohorts
- PanOmics: Industrialized transcriptomics and proteomics data
- PanHunter: User friendly AI/ML driven multi-omics analysis platform

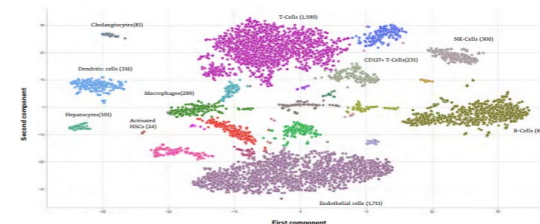


Figure 5: Illustration of automated AI-driven cell type annotation for clusters of liver scRNAseq cells



Metabolic Disease Research at Evotec

Partner of Choice for Increased Probability of Success

- 1 Proven track record in metabolic disease discovery on a wide variety of target classes using multiple state-of-the-art technology platforms**

- 2 Dedicated metabolic biology research team** with extensive drug discovery expertise and in-depth disease knowledge

- 3 An expanding platform of *in vitro*, *ex vivo*, and *in vivo* translational models** to execute integrated projects to treat a wide range of metabolic disease indications

- 4 Molecular Patient Databases for **target identification, patient stratification**, and an internal **portfolio of targets and projects**** for the treatment of Metabolic Diseases

- 5 Fully integrated drug discovery and development** platform with project management expertise to accelerate our partner's projects from **target ID to IND**

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