

# True precision medicine through single-cell science

Scailyte's artificial intelligence-powered platform, ScaiVision, identifies disease signatures that predict drug efficacy and describe drug mode of action to improve clinical outcomes for patients with complex diseases.

Despite recent advances in molecular diagnostics and genetic testing, failure to capture disease complexity and patient heterogeneity means that even the most successful treatments are ineffective or cause unpredictable toxic effects in a high proportion of patients. To address this problem and advance precision medicine, Scailyte, an ETH Zürich spin-off, has built a unique end-to-end artificial intelligence (AI)-powered platform named ScaiVision.

ScaiVision is proven to successfully integrate single-cell and multi-modal datasets from patient tissue with clinical endpoints to identify novel ultra-sensitive biological signatures and cell functionality states. The predictive capability of the platform—including forecasting drug efficacy, toxicity and mode of action discovery—has multiple applications across the drug development value chain, including improving clinical trial design and differentiating drug candidates from competitor products.

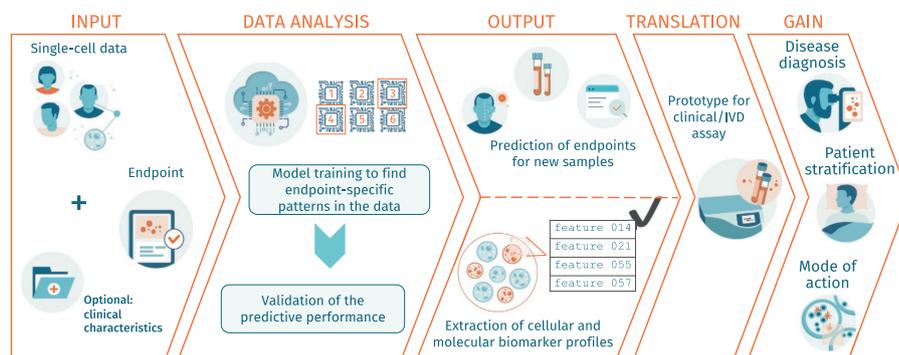
“Our algorithm out-performs common analytical approaches and has discovered new, sensitive biomarkers which have unlocked new mechanistic insights about disease and drugs for the global medical community,” said Corinne Solier, COO.

## ScaiVision: a novel and versatile platform

The unique architecture of ScaiVision enables flexible correlation of different multimodal single-cell data sets (including RNA-/TCR-/BCR-seq and CyTOF) with clinical endpoints, such as disease diagnosis, progression, severity, and treatment/toxicity response. Using a neural network, the platform automatically learns molecular patterns associated with relevant clinical outcomes (Fig. 1). This way, the system can find biosignatures without requiring upfront clustering, thus reducing potential bias. Moreover, it applies an intelligent pooling technique that only regards relevant cells (independent of the proportion of such cells in the sample), while data augmentation enables signature identification from a low number of patient samples. Novel biomarkers can be discovered in as little as eight weeks from only a few dozen samples.

“Single-cell datasets represent biological heterogeneity from diseased tissue and organs in the best possible way,” explained Lena Toska, data scientist. “Unraveling the hidden secrets of complex single-cell multi-omics data provides unprecedented resolution and insight into a disease and patients' biology, enabling us to capture novel cellular states, elucidate complex biological processes, and discover new clinically relevant biological signatures.”

Once validated in independent patient cohorts, these signatures can be used to develop routine clinical assays for predicting endpoints for new samples/patients by simplifying these signatures into limited-panel biomarkers.



**Fig. 1 | End-to-end pipeline.** Single-cell data and clinical-endpoint outcomes collected by Scailyte or its partner (INPUT) are pre-processed and analysed by ScaiVision. The model performance is then validated (DATA ANALYSIS), resulting in (i) a network that can predict endpoints of new samples and (ii) biomarker profiles (OUTPUT). The number of molecular biomarkers is reduced and used to develop a prototype clinical assay (TRANSLATION). The assay can then be applied at various stages of drug development, such as diagnosing disease, stratifying patients, or identifying drug mode of action (GAIN). IVD, in vitro diagnostic.

## Numerous applications

Scailyte has an outstanding discovery track record, including nine biomarker discovery projects in multiple immunology and oncology indications, a success rate of over 90%, and single-cell signatures translated into clinical/in vitro diagnostic (IVD) prototype assays; these include a nine-marker clinical flow-cytometry assay that outperforms all existing assays to diagnose cutaneous T cell lymphoma. Scailyte is also pursuing IVD development of signatures discovered in endometriosis, and has multiple projects in which validation of signatures in independent cohorts is underway.

The company's platform is particularly suited to addressing drug development challenges in immunology, cell- and gene-therapy. For example, ScaiVision successfully identified a patient T cell signature predicting neurotoxicity in CAR-T cell therapy directed against diffuse large B cell lymphoma, and a signature predicting complete remission in the same cohort.

## Improving immunotherapies

In 2021, ScaiVision has been used to find better predictive biomarkers for patients with metastatic non-small cell lung cancer requiring treatment with one of two common checkpoint inhibitors: a PD-L1 inhibitor or a PD-1 inhibitor. These therapies only work in about 30% of patients, and the sole biomarker available to guide therapy choice—tumor PD-L1 expression level scoring—is often unreliable and inaccurate.

Using easily accessible peripheral blood mononuclear cell samples, ScaiVision was trained to predict treatment response in patients receiving either a PD-L1 inhibitor or a PD-1 inhibitor. In the PD-L1

inhibitor-treated patients, ScaiVision identified cell populations and an associated novel single-cell gene signature predicting response to PD-L1 therapy with 87% accuracy. The predictive performance of this signature was then evaluated in the PD-1 inhibitor-treated patients. “Interestingly, this signature performed even better, reaching 100% accuracy in predicting therapy response,” said Benjamin Essigman, data scientist. “Additionally, our algorithm prediction significantly outperformed PD-L1 scoring.”

Based on the identified cell population and gene signature genes, Scailyte is currently planning an expanded validation in a new cohort, as well as testing its gene signature prototype in bulk RNA sequencing data to translate it into a prototype assay for clinical implementation.

Scailyte is open to partnering with companies interested in accelerating development of their products and improving clinical outcomes. “Using multi-omics single-cell data in combination with AI to discover and develop biomarkers fully exploits the power of these cutting-edge technologies in translational research,” said Martijn van Attekum, technical lead. “With our game-changing platform we are enabling the development of next-generation therapeutics for the benefit of patients with complex diseases.”

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