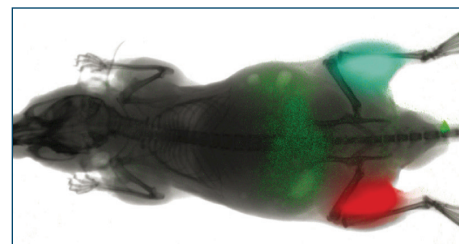


Epistem provides a suite of analytical services which can be utilised as an integrated component of an in-house study package or as a stand-alone service.

SUMMARY

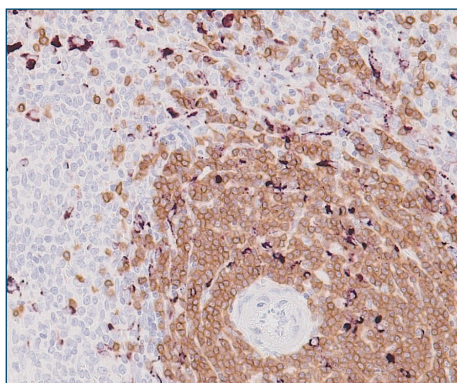
Epistem has provided analytical support to drug discovery and development pipelines for over 20 years. Expert tissue analyses in a suite of preclinical models or patient material (GCLP compliant), forms the basis of our analytical services. This knowledge has been applied to give exceptional support to a portfolio of preclinical models and clinical trials.



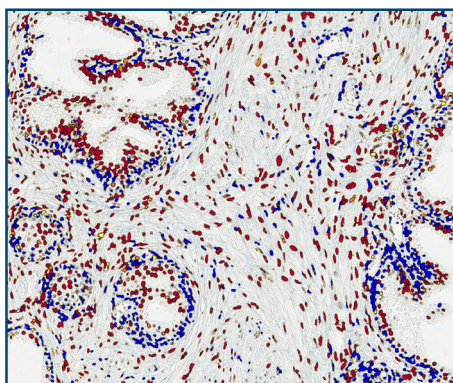
Histology and Immunohistochemistry (IHC)

Epistem provides a tailored histology and immunohistochemistry service to assist with the validation of novel therapeutic targets and biomarkers. Key strengths include:

- Development of new protocols and validating target expression
- Experience with fixed and frozen tissues from a range of species
- GCLP-accredited laboratory and licensed by the Human Tissue Authority
- High quality histology and IHC (manual or fully automated with Ventana Ultra Discovery platform)
- Whole slide scanned images with Aperio ScanScope® slide scanner with quantitative image analysis
- Measurements available include labelled vs unlabelled cell nucleus count, area of labelling, intensity of labelling, plasma membrane labelling, blood vessel count and area, etc.



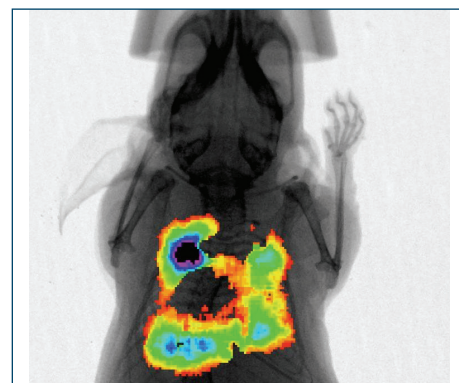
A section of spleen dual-labelled with CD3 (brown) and CD68 (purple)



Aperio generated overlay from nuclear analysis on human prostate tumour labelled with Androgen Receptor (AR)

In-Vivo Imaging

Using this system disease progression can be monitored real-time in living animals. Alongside the luminescent imaging capabilities, there are also in-built X-ray and fluorescent modalities to visualise disease or appropriately labelled agents in both 2D and 3D.



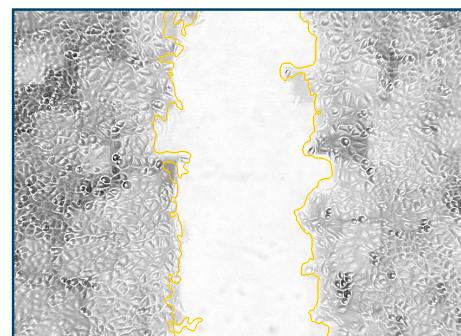
A549 Luc+ cells implanted via intra-thoracic injection in mouse lung cancer orthotopic model

In-Vitro Cell Imaging Multi-Mode Reader

Assessment of cell proliferation and migration is performed using time-lapse live cell imaging (brightfield, phase contrast or fluorescence) via a Cytation 5 Cell Imaging Multi-Mode Reader. Scratch assay wound healing models are also performed using this platform, where the scratch closure can be monitored automatically.

Furthermore, the plate reader capabilities allow detection of fluorescence, luminescence and UV-Vis absorbance.

Automated detection of scratch in A549 monolayer in an *in vitro* model of wound healing



Multiplex Analysis

In addition to traditional ELISA, we offer multiplex cytokine analysis using a bead-based immunoassay platform. Higher sensitivity and throughput than ELISA, multi-parameter readouts are possible using small sample volumes. Secreted proteins in blood products, lysed tissue and cell culture supernatants can all be assessed. Cytokines can be analysed using standard screening panels or custom built panels can be designed to target analytes of interest.

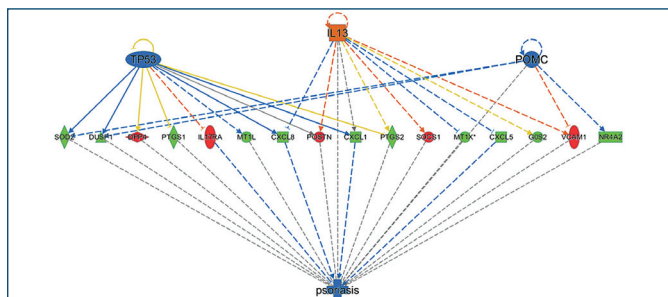
Gene Expression

Epistem's Pharmacogenomics Division provides highly sensitive, GCLP compliant, gene expression (mRNA/miRNA) analysis in both preclinical and clinical settings. We specialise in providing robust and reliable gene expression information from very small starting materials (down to a single cell input). We offer NGS (Illumina platforms), microarray (Affymetrix and Agilent platforms) and RT-qPCR assessments. We also offer single cell assessments (10X Genomics) and provide gene expression information from our proprietary workflows which include plucked scalp hair (to obtain compound mediated biomarker changes) and from discrete cell populations following isolation by Laser Capture Microdissection (LCM).

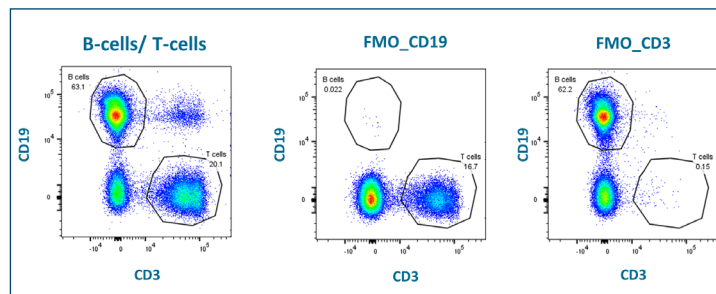
Flow Cytometry Analysis

Epistem's flow cytometry service utilises a three laser multiparametric Agilent Novocyte 3005 platform. This allows for the analysis of up to 15 optical channels, facilitating simple and rapid cellular analysis. Phenotypic analysis is conducted using fluorescent antibodies to the target of interest. In addition to phenotyping, parameters such as cell cycle stage, apoptosis and proliferation can be assessed on a variety of cell types.

Bespoke projects for specific cell population assessment include antibody panels design, FMO control and gating strategy. High throughput analysis is available with automated labelling and a 96-well assay format. Data analysis is highly sensitive with typical inter-sample carry over <0.01%.



Utilising an IL-13 responsive gene list, IPA connected 3 upstream regulators via the expression of 16 genes to psoriasis. One of the regulators predicted is IL-13, showing activation, which is consistent with the IL-13 administration experimental condition from which the list is derived.



Peripheral white blood cells analysed by Flow Cytometry. Left panel, B-cells (CD19+CD3-) and T-cells (CD3+ CD19-) percentages. Middle and right panels, Fluorescence Minus One (FMO) controls.