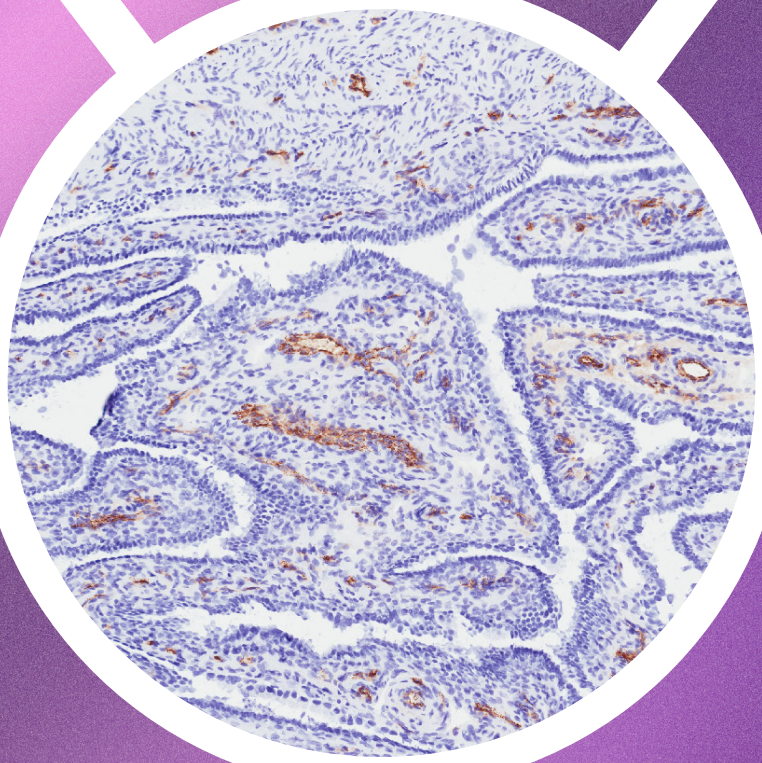
PHARMAGENE
discovery services

GLP Tissue Cross-Reactivity Services

Your needs, our expertise



Tailored methodology for biotherapeutic safety studies

Our unique combination of research services and high quality human tissue samples form the pillars of our GLP Tissue Cross-Reactivity (TCR) Services.

Pharmagene Discovery Services has developed, and maintains, a well-curated, dedicated panel of high-quality frozen human tissues to deliver TCR studies. All human tissues recommended for TCR testing by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) are fully consented for commercial research, and available from at least 3 male and 3 female donors.

Clients may elect to have their TCR studies conducted in compliance with Good Laboratory Practice (GLP) or under non-GLP conditions. For TCR studies, our service provides clients with an accurate assessment of the on and off-target binding of their therapeutic antibody candidates, or related products, in human tissues. Our expertise in IHC assay development, combined with a tailored scientific approach, enables us to deliver high quality data to our clients in a defined time to accelerate the development of their biotherapeutic candidate programs.

Key benefits:

- Established inventory of the 36 human tissue types required, providing a quick turnaround for your study without delays sourcing scarce tissues
- Robust qualification of tissues from procurement to assay use, resulting in superior data quality and reduced time lost due to experimental failure
- Expert assay optimisation, providing confidence in the scientific integrity of the results
- Flexible study design: either non-GLP tissue microarray (TMA) screening to provide an initial assessment or GLP study using full-face sections
- Fully automated immunohistochemical (IHC) assays, offering consistent and reproducible results
- State-of-the-art MHRA-certified, GLP-compliant facility
- Experienced scientific and pathology staff, enabling delivery of even the most technically challenging assays

Tissue types are available from multiple male and female donors		
Adrenal gland	Ileum	Prostate
Bladder	Kidney – glomerulus and tubule	Skeletal muscle
Blood cells	Liver	Skin
Blood vessel endothelium	Lung – bronchus and parenchyma	Spinal cord
Bone marrow	Lymph node	Spleen
Breast	Ovary	Stomach
Cerebellum	Pancreas	Testis
Cerebral cortex	Parathyroid gland	Thymus
Colon	Parotid salivary gland	Thyroid gland
Eye	Peripheral nerve	Tonsil
Fallopian tube	Pituitary gland	Ureter
Heart	Placenta	Uterus – cervix and endometrium

Please contact us regarding availability of other tissues.

Complete, comprehensive, compliant GLP TCR Services

Guidelines issued by the FDA and EMA for the development of therapeutic antibodies and related products recommend their testing for TCR on a range of human tissues.[1,2] Given that such testing is performed in the pre-clinical phase of drug development prior to submission of Investigational New Drug (IND) applications to the FDA in the United States or Regulatory Authorities elsewhere, it is recommended that the data are generated to GLP standards.

Pharmagene's scientific team provides a customised service to meet your specific requirements for your biotherapeutic agent. We utilise a 2- or 3-phase approach that provides a flexible and cost-effective solution for making confident decisions regarding the best parameters for your study and minimise the risk of GLP study failure. We deliver a final report that is suitable for submission as part of an IND application to the FDA or other Regulatory Authorities.

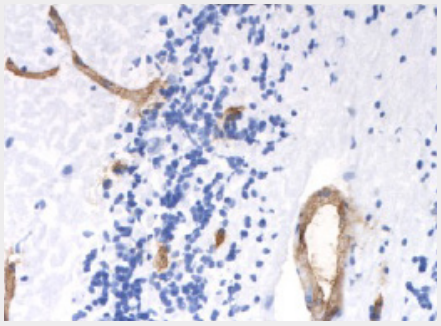
Meticulously qualified specimens for your TCR studies

Each of our TCR studies begins with well characterised human specimens that have been rigorously qualified to meet the exacting requirements of this research.

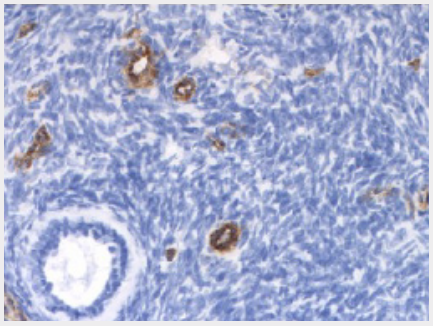
Our specimens undergo a 4-point inspection to qualify for GLP TCR studies:

1. Donor clinical history evaluation to ensure experimental suitability
2. Specimen review by board certified pathologists to validate normal morphology
3. Confirmation of compliance with ethical, legal and regulatory requirements
4. Initial confirmation of tissue antigenicity

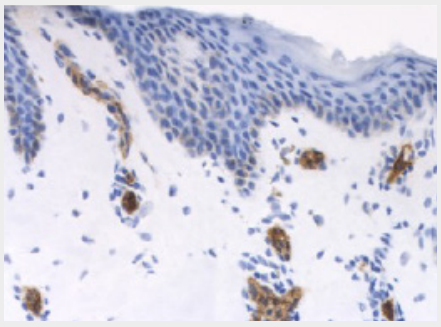
Confirmation of tissue antigenicity



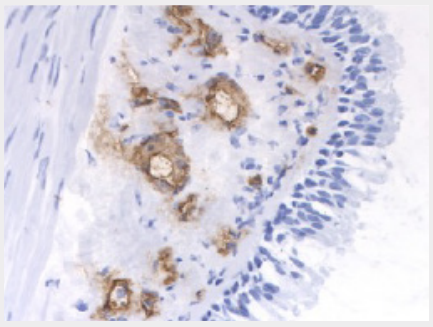
Cerebellum



Ovary



Skin



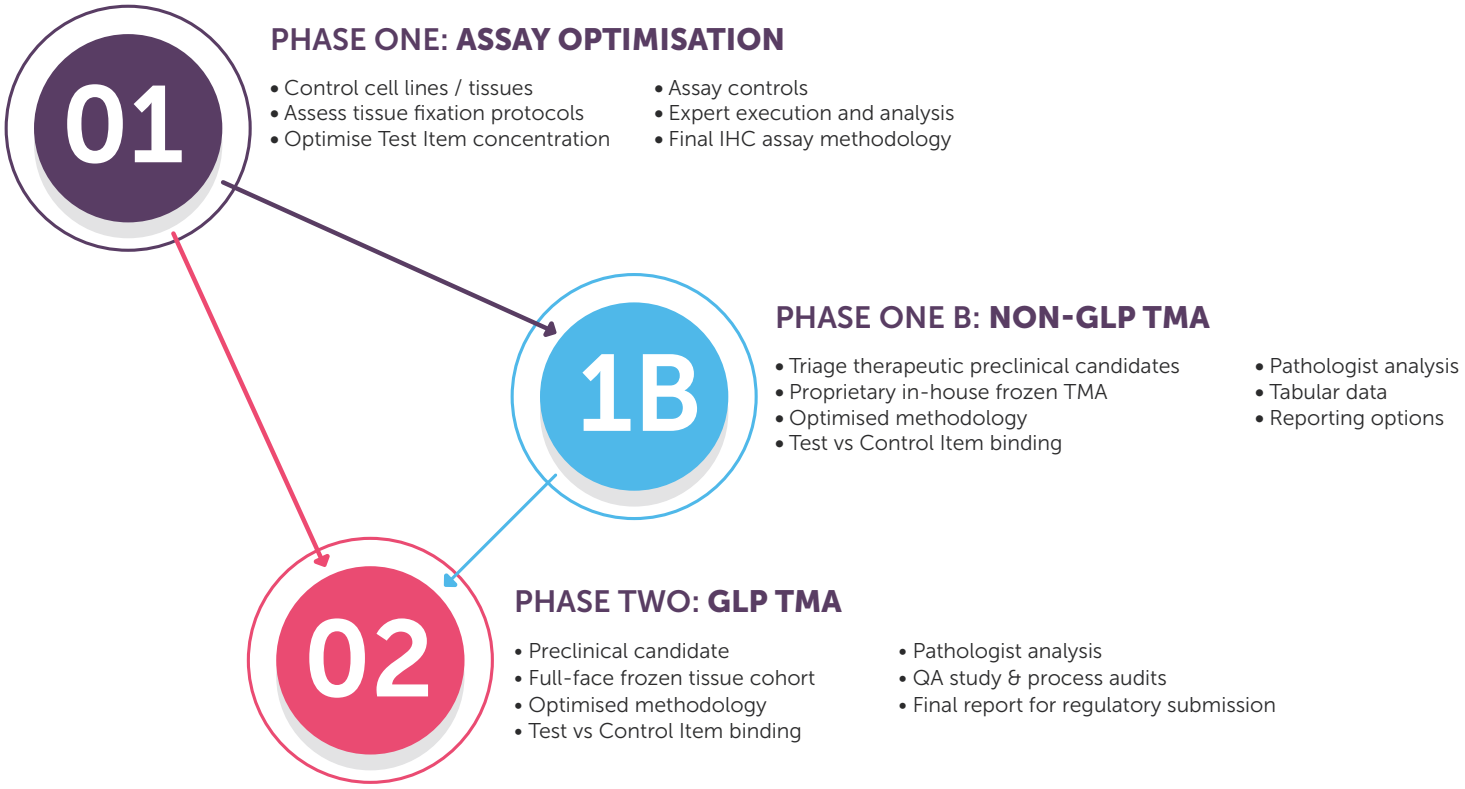
Bronchus

Figure 1. Confirmatory assays are performed to validate the antigenicity of all tissues used in TCR studies. One such test involves the immunostaining of tissues with von Willebrand Factor (vWF) antibodies. Images show the binding of vWF antibodies to the microvascular endothelium proteins in frozen sections of cerebellum, ovary, skin and bronchus.

References

1. Points to Consider in the Manufacture and Testing of Monoclonal Antibody Products for Human Use, Docket No. 94d-0259. February 28, 1997.
2. Guideline on Development, Production, Characterisation and Specifications for Monoclonal Antibodies and Related Products, EMEA/CHMP/BWP/157653/2007. Adopted December 18, 2008.

Our 3-phase approach provides quality data for your study



Phase 1 assay optimisation

For Phase 1, typically we assess 2 different tissue fixation techniques in positive and negative control cell lines and/or positive and negative control tissues. We evaluate the Test Item at 3 concentrations with matched Control Item (isotype control) concentrations to demonstrate specificity of Test Item binding. Several rounds of optimsation may be required depending on the target(s) and individual biotherapeutic molecule, for example to introduce various blocking steps to reduce any non-specific binding.

Phase 1 assay optimisation data

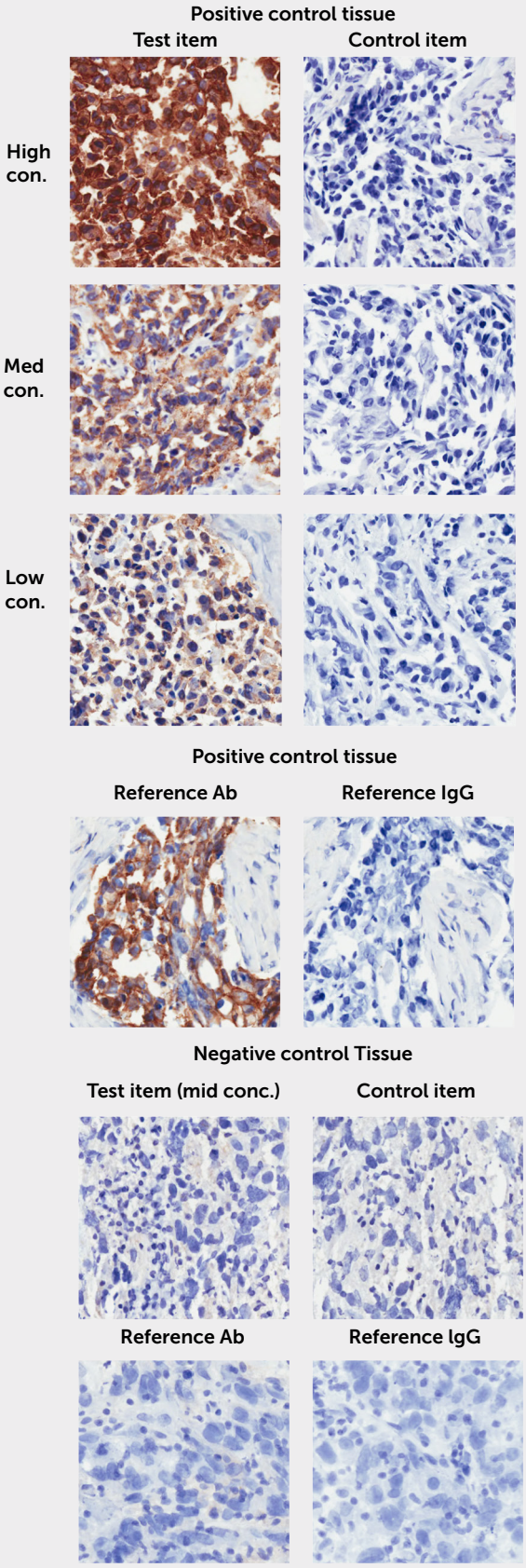


Figure 2. Left hand panels show frozen sections of positive control tissue incubated with 3 concentrations of Test Item and Control Item. The panels demonstrate specific, concentration-dependent Test Item binding. Binding of a reference antibody (same target - reference. Ab.) and an equivalent concentration of non-immune IgG are shown for comparison. The pattern of binding is similar. No binding of either the Test Item nor the reference antibody was observed in the negative control tissue.

Phase 1b frozen tissue microarray screening

Swift and accurate detection for triaging candidates

TCR screening using frozen TMAs offers a non-GLP option as an economical alternative to full face sections for a rapid turnaround on screening candidate molecules.

Our scientists have developed a panel of TMAs containing the 36 tissues required by the FDA and EMA for assessment of therapeutic antibody candidates. Utilisation of this approach is designed to accelerate the de-selection of antibody candidates which exhibit significant 'off-target' immunoreactive profiles.

Advantages of this service include:

- Assessment of all 36 FDA and EMA tissues; provides actionable feedback on 'off-target' effects that can be incorporated into early antibody evaluations
- Single assay format; provides economical alternative to full face sections
- Experiments performed with the same experts, tissues, and IHC methods employed for our GLP studies; provides confidence in the results

Frozen TMA for TCR screening

Figure 3a. Frozen, normal tissue TMA for TCR screening.

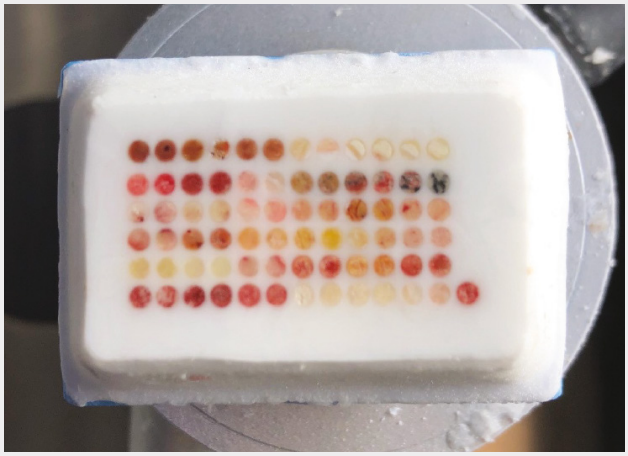
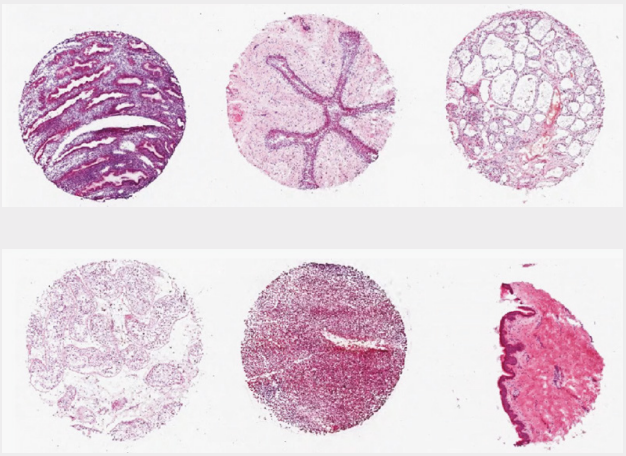


Figure 3b. H&E images of selected cores from our frozen TMA.



Top left to bottom right: uterus endometrium, ureter, thyroid, testis, spleen & skin

Quality construction

- Three TMA set—each block containing 12 tissues from 3 donors, each in duplicate
- TMA tissues selected using the same stringent criteria as for our GLP studies using the same parameters as our GLP level studies
- Pathology review to ensure all cores are representative of the full tissue section
- Tissue remains frozen throughout the coring and TMA construction process

Excellent results

- Tabulated data with access to Aperio scanned images—suitable to identify 'off-target' effects
- Reporting options available

Phase 2 GLP TCR

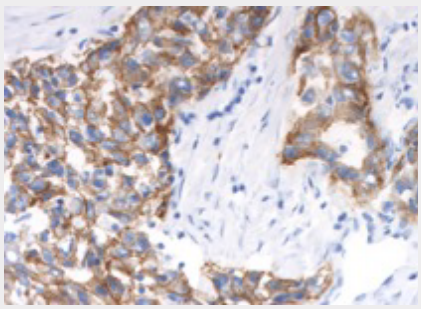
High-quality, compliant data to support IND

The appointed Study Director will generate a GLP Study Plan based on the final IHC methodology, and execute the GLP TCR study using our cohort of full-face, frozen human tissues.

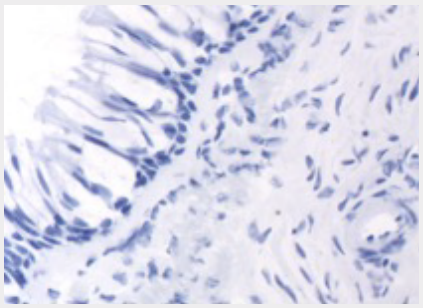
Our specialist pathologists review and report on the resulting staining, and our QA team audit throughout the planning, execution and delivery of each study, including audit of the final GLP Study Report.

Advantages of this service include:

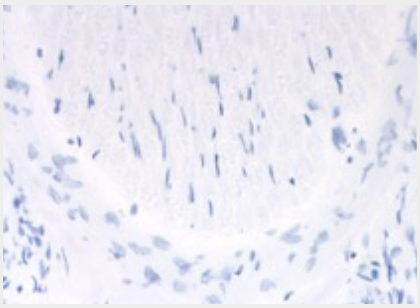
- Fully compliant GLP Study execution
- Established process and timeline for delivery
- Expert scientific, pathology and QA teams provide confidence in the data



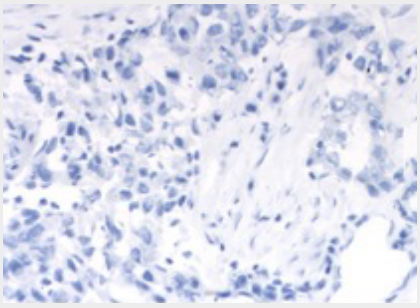
Test item in positive control tissue



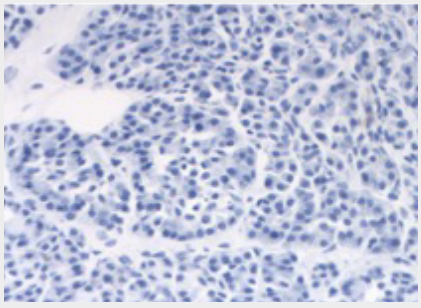
Bronchus



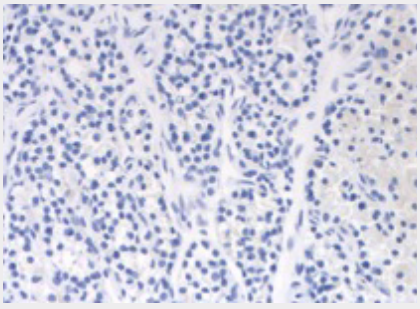
Peripheral nerve



Control item in positive control tissue



Pancreas



Parathyroid

Figure 4. The left hand panels show the optimised IHC assay binding of Test Item and Control Item to the positive control tissue.
The right hand panels show absence of Test Item binding to cryosections of bronchus, peripheral nerve, pancreas and parathyroid.

About Pharmagene Discovery Services

Originally founded in 1996 and operating from laboratories near Cambridge, UK, Pharmagene Discovery Services is built upon the scientific knowledge, expertise and reputation of its legacy, and remains one of the earliest established companies to focus on human tissue-based research. Leveraging these skills and experience, it specialises in tailored assay design and development, with range of research services encompassing target expression, interrogation of spatial biology, functional cellular biology and bioassays, and biotherapeutic safety testing human tissues and primary human cells. The facility operates to GLP and is licenced by the UK Human Tissue Authority.

Pharmagene has created and curates an in-house human tissue biorepository to support research for its clients, and in addition offers sample processing and biostorage services. With a wealth of knowledge of the human tissue research sector, and having conducted hundreds of studies for life science researchers around the world over the past three decades, the business is uniquely placed to support its clients to develop safe and efficacious new therapies and associated biomarkers more rapidly and with greater confidence.

PHARMAGENE
discovery services

PHARMAGENE DISCOVERY SERVICES LIMITED
2a Orchard Road, Royston, Herts SG8 5HA

pharmagene.com

Contact: info@pharmagene.com

BR_TCR_28.01.26