GLP Tissue Cross Reactivity Testing

Your needs, our expertise

Tailored Methodology for Biotherapeutic Safety Studies

Asterand Bio's unique combination of research services and tissue procurement capabilities form the pillars of our GLP Tissue Cross Reactivity (TCR) Services.

For more than 20 years, our PhaseZERO® Research Services platform has provided human tissue-based solutions to leading pharmaceutical and biotechnology companies, generating the data they need to support decisions for advancing the best targets and therapeutics.

Asterand Bio also has a heritage of tissue procurement. As a leading global supplier of well characterized human tissue, we are specialists in the procurement, assessment, characterization, and the use of human biospecimens for research. All human tissues recommended for TCR testing by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have been sourced with full consent for commercial research, and pre-assembled 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 preliminary 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 scientists are experts in their fields and this expertise, 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 therapeutic antibody candidate programs.

Key Benefits:

- Prior collection and characterization of 36 human tissue types, providing a quick turnaround for your study without delays awaiting 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 optimization, increasing your 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, resulting in accurate completion of even the most technically challenging assays

Tissue Types are Available from Multiple Male and Female Donors

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

Please contact us regarding availability of other tissues

Meticulously Qualified Specimens for Your TCR Studies

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

Our specimens undergo a four 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. Examination of site audit to ensure compliance with ethical, legal and regulatory requirements
4. Initial confirmation of tissue antigenicity

Confirmation of Tissue Antigenicity

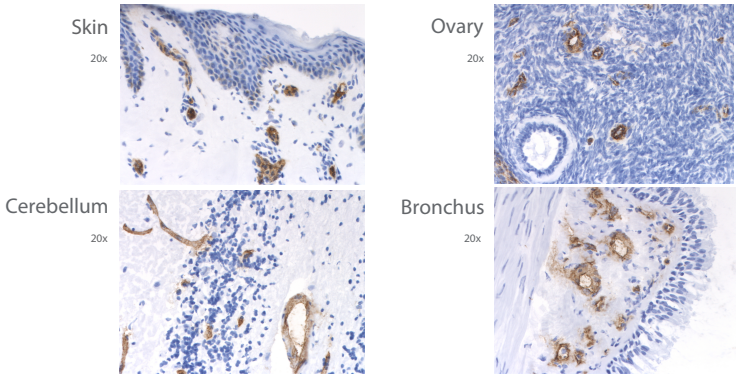


Figure 1. Confirmatory assays are performed to validate the antigenicity of tissues used in TCR studies.

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 in frozen sections of skin, ovary, cerebellum and bronchus.

Complete, Comprehensive GLP Compliant 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.

Asterand Bio's Molecular Pathology team provides a customized service to meet your particular requirements for your biotherapeutic agent. We utilize a two or three phase approach that provides a cost effective solution for making confident decisions regarding the best parameters for your study and minimize 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.

Our 3-Phase Approach Provides Quality Data for Your Study

Phase 1
Assay Optimization

- Control tissues / cell lines
- Matrix of fixation protocols and antibody concentrations (Test Item)
- Assay controls (including Control Item)
- Expert analysis
- Recommendation for IHC assay conditions

Phase 2
GLP Tissue Cross Reactivity

- Pre-clinical candidate
- Full face, frozen tissues validated for use in GLP TCR
- Optimized assay conditions from Phase 1
- Test Items vs Control Item binding
- Board Certified Pathologist review
- Final report suitable for regulatory submission

Phase 1b
TMA screening (non-GLP)

- Triage multiple therapeutic candidates
- Proprietary frozen TMA
- Optimized assay conditions from Phase 1
- Test Items vs Control Item binding
- Board Certified Pathologist review
- Tabular data + digital photomicrograph
- Various reporting options

Phase 1 Assay Optimization Data

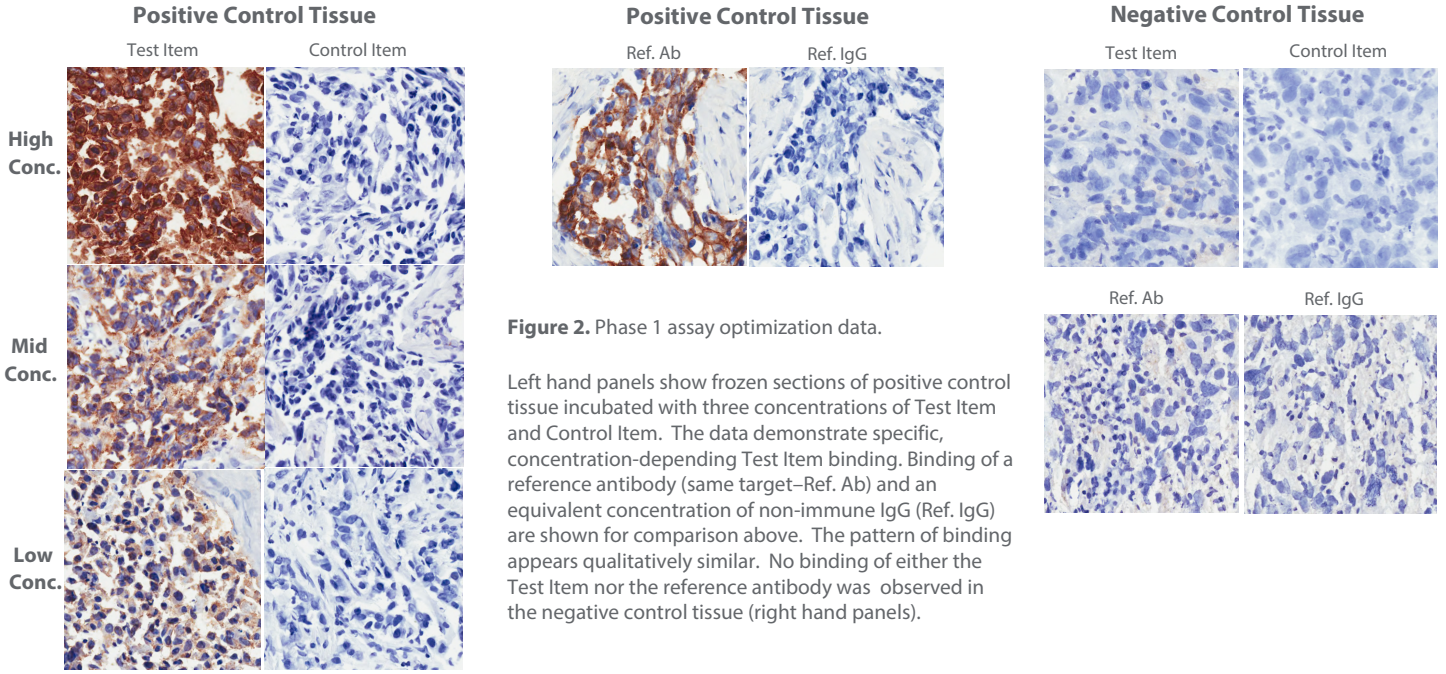


Figure 2. Phase 1 assay optimization data.

Left hand panels show frozen sections of positive control tissue incubated with three concentrations of Test Item and Control Item. The data demonstrate specific, concentration-depending Test Item binding. Binding of a reference antibody (same target–Ref. Ab) and an equivalent concentration of non-immune IgG (Ref. IgG) are shown for comparison above. The pattern of binding appears qualitatively similar. No binding of either the Test Item nor the reference antibody was observed in the negative control tissue (right hand panels).

(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 on 18 December 2008

Phase 2 GLP TCR Data

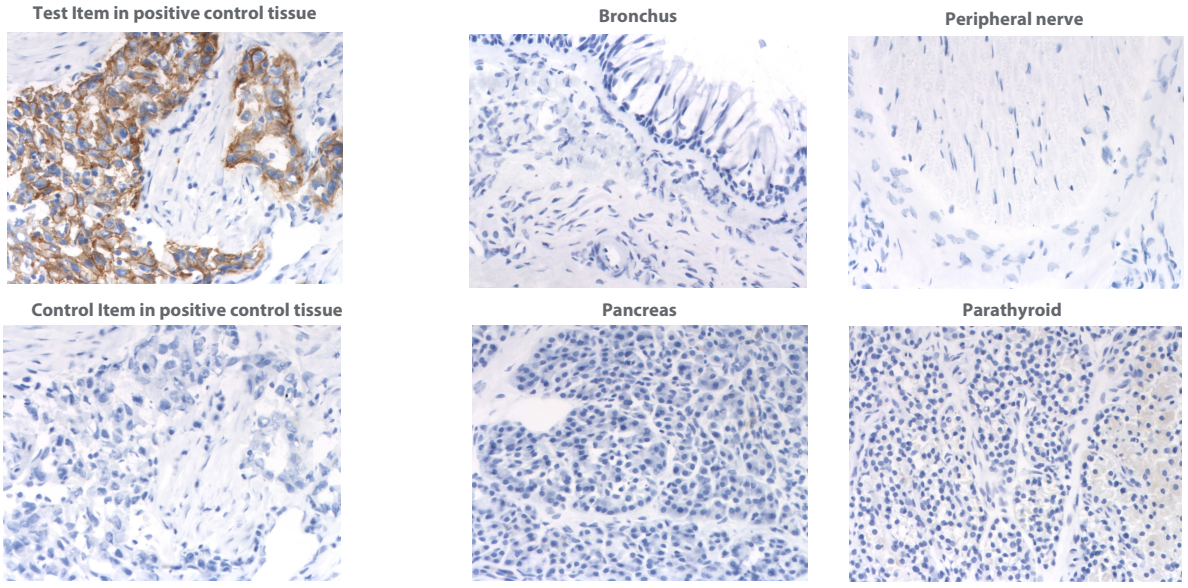


Figure 3. Phase 2 GLP TCR data.
The left hand panels show the binding of Test Item and Control Item to the positive control tissue. The center and right hand panels show absence of Test Item binding to cryosections of bronchus, peripheral nerve, pancreas and parathyroid.

Frozen Tissue Microarray Screening (Phase 1b)

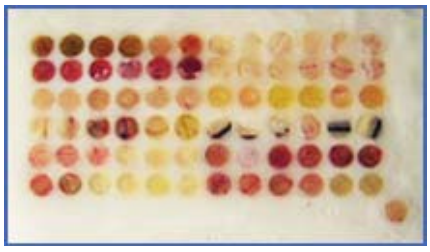
Swift, Accurate Detection

TCR screening using frozen TMAs in place of full face tissue sections offers an economical alternative for rapid feedback on Test Items. Our scientists have developed a panel of TMAs containing the 36 tissues (n=3 donors/tissue) required by the FDA and EMA for assessment of therapeutic antibody binding. Utilization 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, providing actionable feedback on 'off target' effects that can be incorporated into early antibody evaluations
- Single assay format, providing economical alternative to full face sections
- Experiments performed with the same experts, tissues and IHC methods employed for our GLP studies, providing confidence in the results

Frozen TMA for TCR screening



Quality Construction

- Three array set–each block containing 12 tissues from 3 donors each, in duplicate
- Tissue selection 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 mounting process

Excellent Results

- Tabulated data with secure online access to Aperio scanned images–suitible to identify 'off target' effects
- Reporting options available

Asterand Bio has made a significant investment to create a state of the art facility and quality management system for providing GLP compliant immunohistochemical studies. Asterand Bio has been a full member of the Medicines and Healthcare Products Regulatory Agency (MHRA) UK GLP Compliance Monitoring Programme since February 2010, with a track record of successful inspections by the MHRA. These resources allow us to provide our clients with efficient delivery of high quality data to support their IND submission.

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ABOUT ASTERAND BIOSCIENCE®

Asterand Bio is the leading global provider of high-quality, well-characterized human tissue and human tissue-based research solutions to drug discovery scientists. Our mission is to provide human-based solutions to accelerate the identification and validation of drug targets and enhance the selection of drug candidates with an increased likelihood of clinical success.

ETHICAL AND REGULATORY CONTROL

All human tissue samples are obtained with informed donor consent and are de-identified prior to banking and distribution. Asterand Bio acts in strict compliance with the US Health Insurance Portability and Accountability Act (HIPAA) and the United Kingdom Human Tissue Authority (HTA) and is accredited by the College of American Pathologists (CAP) and ISO 9001. Asterand Bio has GLP accreditation according to the requirements of Good Laboratory Practice (GLP)– Directive of the European Commission 2004/9/EEC, and a Good Clinical Laboratory Practice (GCLP) laboratory for clinical assay services.

RESEARCH SERVICES

- Immunohistochemistry
- ISH & FISH
- TMA, FDA & Custom
- Digital Pathology
- Histopathology
- qRT-PCR
- LCM
- siRNA Knockdown
- IHC/ISH Multiplexing
- Western Blotting
- Primary Cell Isolation
- 2D and 3D Culture
- Cell Based Assays
- Assay Development
- OrganDOT™
- Mutation Analysis

BIOMATERIALS AVAILABLE

- Fresh, Frozen & FFPE
- Normal & Diseased Tissue
- OCT Embedded
- Serum, Plasma & Blood
- Synovial Fluid
- RNA, DNA & Protein
- TMA, FFPE & Frozen
- Primary Cells
- Proprietary Cell Lines

THERAPEUTIC AREAS

- Oncology
- Cardiovascular
- Metabolic
- CNS
- Respiratory
- Inflammation
- Genitourinary
- Fibrosis

XpressBANK™ BIOREPOSITORY

The Asterand Bio XpressBANK™ Biorepository is an invaluable source of high-quality, well-characterized and validated tissue, biofluids, cell lines and molecular derivatives, all intended for research use in the drug and diagnostic development process. Our extensive repository contains over 200,000 human tissues and biofluids. This bank includes material that is prospectively obtained in a variety of formats including fresh frozen and FFPE, supported by comprehensive clinical data.

BioSPOKE™ CUSTOM BIOSPECIMEN PROCUREMENT

Through our BioSPOKE™ service, human tissues and clinical data are custom collected to meet unique research requirements within a wide range of disease categories or as normal controls. Samples are provided fresh or in multiple preserved formats. Specialized processing may be tailored to each research request. This service allows Asterand Bio to deliver human tissues, biofluids and accompanying clinical information to our clients that are collected in a manner which is most compatible with their experimental design.

PhaseZERO® RESEARCH SERVICES

For over 20 years, Asterand Bio's trusted scientists have worked collaboratively with clients to facilitate the efficient selection of drug targets and candidate therapeutics with the highest likelihood for clinical success by providing a variety of pre-clinical drug discovery services. From target and biomarker validation, characterization of therapeutic candidates for potency, effect and safety to supporting clinical diagnostic assay development and testing, Asterand Bio provides clients with high-quality experimental design, execution, data interpretation and reporting. Each project is managed by a dedicated scientific project manager and customized to meet each client's specific needs.

Please contact our Business Development Directors in the following regions to discuss your requirements:

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