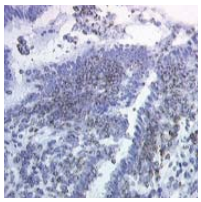
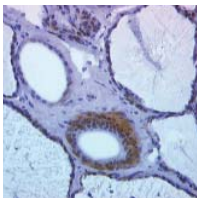
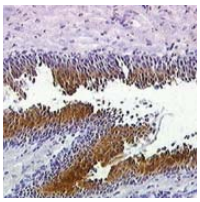




charles river
accelerating drug development. exactly.

Tissue Cross-Reactivity

When manufacturing and testing monoclonal antibody products for human use, it is important to be aware of any possible nontarget tissue binding that may occur. Nontarget tissue binding could have serious consequences, particularly when using pharmacologically active antibodies or cytotoxic immunoconjugates. Cross-reactivity studies with human tissues or cells should always be conducted prior to a Phase I clinical trial to search for cross-reactions or nontarget tissue binding.

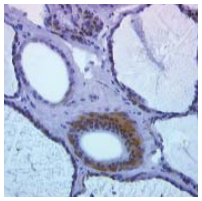
Charles River can support your monoclonal antibody research with our extensive expertise in the initial stages of safety assessment for therapeutic antibodies targeted for use in humans. We have experience with nearly every type of therapeutic antibody, including unconjugated antibodies, antibodies conjugated to a variety of substances, and Fab fragments.

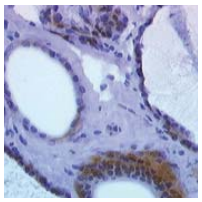
We hold a full range of tissues from various animal species. As outlined in FDA guidelines, we store an array of human tissues from multiple donors sourced from ethically approved tissue banks with full patient consent.

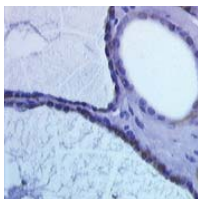
Our commitment to new and improved pathology techniques has led to the generation of highly specific mechanistic drug action/tissue response data critical to worldwide regulatory filings. For immunohistochemical detection of monoclonal antibody cross-reactivity studies, we provide efficiency of scale in full compliance with Good Laboratory Practice (GLP) regulations and can represent you in presenting and interpreting findings to the applicable regulatory agencies.

Services

- Preliminary studies
- Definitive study
  - Three antibody concentrations
  - 37 tissues
  - Three different human subjects
- Extensive controls
- Slide evaluation and interpretation
- Internal peer review
- *In vitro* cross-reactivity
- *In vivo* binding of test articles
- Analysis of potential treatment-related effects
- Potential immune complex deposition in kidneys
- Immunophenotyping
- Monoclonal preclinical safety
  - Human
  - Humanized
  - Chimeric
  - Murine
- Clinical trial support
  - Entry criteria
  - Biomarker
  - Proof-of-principle
- Final report







Capabilities

- Assist with protocol design and regulatory considerations
- Preliminary staining to optimize conditions
- Study tissues stained with individual controls
- Ability to stain hundreds of slides in a single staining run
- Positive and negative controls
- Slides interpreted and graded semiquantitatively by experienced pathologists
- Internal peer review
- Semiquantitative assessment of immunostaining in context of histomorphologic and histopathologic changes
- Representative digital images
- Comprehensive report
  - Materials and methods
  - Tabulated data
  - Interpretation of results with literature review
  - Photomicrographs
  - QA statement

charles river | preclinical services

NORTH AMERICA Tel: +1 (877) CRIVER-1 (877-274-8371)
Email: askcharlesriver@crl.com
EUROPE Tel: +44 (0) 1875 614545 Email: info@eur.crl.com
CHINA Tel: +86 (0) 21-51320370 Email: info_cn@crl.com
JAPAN Tel: +81 (0) 45 474 474 1 Email: infopcc@jp.crl.com