HIDI Monoclonal Antibody Facility

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Radcliffe Department of Medicine

HIDI Monoclonal Antibody Facility

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- Antibodies are critical research tools in many immunological assays
- Therapeutic antibodies are among the most successful modern drugs used to treat human disease
- The global antibody market was reported to top $100 billion in 2017
- We aim to apply our expertise to allow other researchers to find, select, produce, validate and use antibodies successfully in their research
- Our primary focus will be the production, characterisation and validation of novel monoclonal antibodies (mAbs)

Reproducibility crisis: Blame it on the antibodies

Concerns widely raised about the quality of antibodies used for research

Reports that up to 50% of commercially available antibodies fail even basic reactivity and specificity tests

This ‘buyer beware’ culture leads to:

- wasted research time
- wasted money
- errors in the scientific literature

Estimated that the US alone wasted $350 million on ‘bad’ antibodies in 2015

A global standards institute report found almost one third of young scientists did not validate their antibodies in 2016

Nature **521,** 274–276 (21 May 2015)

HIDI Monoclonal Antibody Facility

Professor Alison Banham & Dr Amanda Anderson

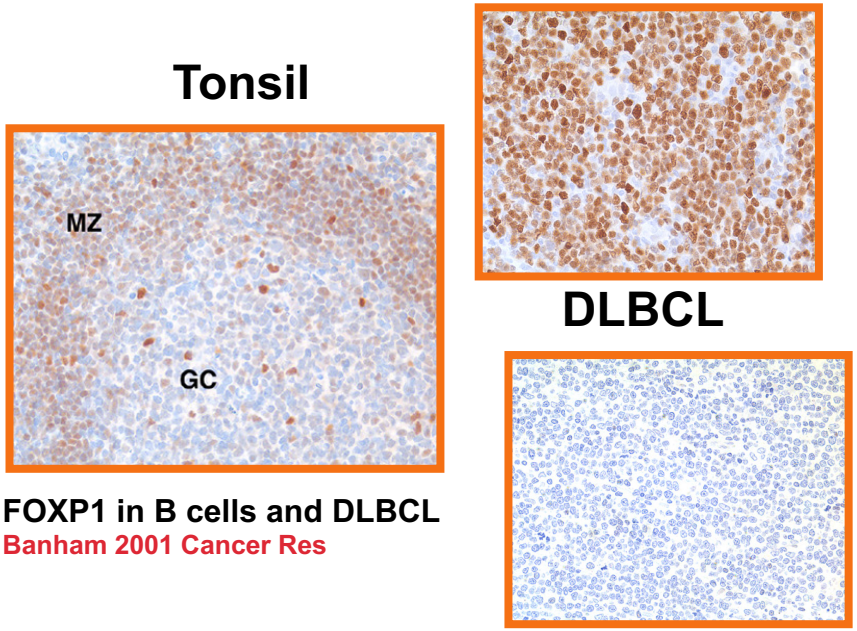
- A combined total of >40 years experience of producing & characterising monoclonal antibodies
- Members of the European Antibody Network (EuroMabNet), Prof Banham, their current Vice President
- Contributed to the EuroMabNet Antibody Validation Guidelines and Antibody Validation Workshops
- Antibodies used as research tools, diagnostic/prognostic biomarkers and therapeutics
- Experience of licensing antibodies for research and *in vitro* diagnostic use to commercial suppliers
- Experience of patenting antibodies, including therapeutics

Examples of Previous mAb Projects

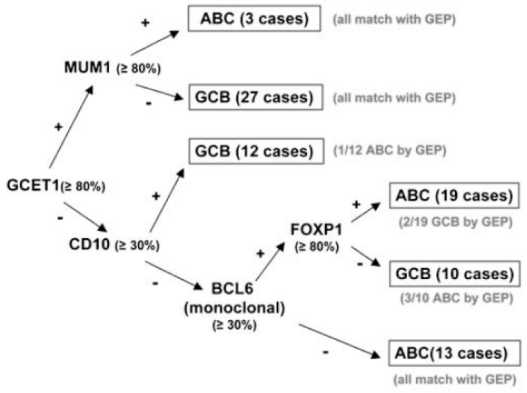
Target	Collaborator(s) outside of NDCLS	
$BCL11A_{XL}$	Prof Martin Dyer	Leicester
ELTD1*	Profs Adrian Harris, Susan Lea, Penny Handford	Oxford
FMIP	Prof Tony Whetton	Manchester
FOXP1		
FOXP2		
FOXP3	Dr Giovanna Roncador	Madrid
FOXP4		
Jagged1*	Profs Adrian Harris, Susan Lea, Penny Handford	Oxford
MORC4		
NFIL3		
Notch1*	Profs Adrian Harris, Susan Lea, Penny Handford	Oxford
p53	Dr Bart Cornelissen	Oxford
P53/HLA-A2*		
PASD1		
Strap	Prof Nick La Thangue	Oxford

*** Therapeutic projects**

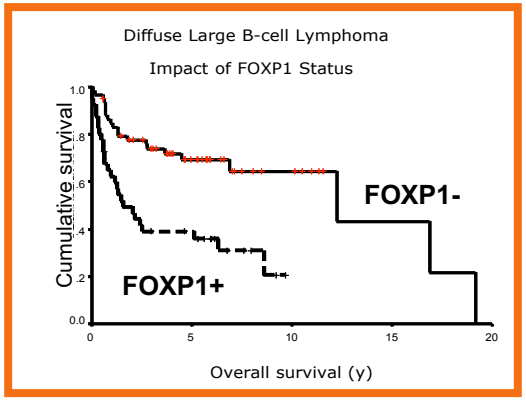
FOXP1 Expression Identifies High-Risk Lymphoma Patients With Smaller Isoform Expression



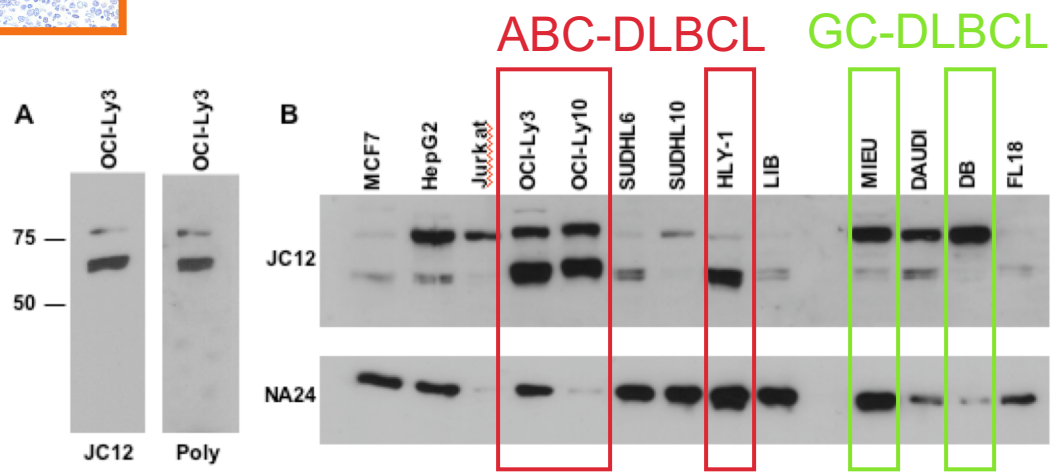
FOXP1 in B cells and DLBCL
Banham 2001 Cancer Res



FOXP1 used for IHC based DLBCL subtyping
Choi 2009 Clin Cancer Res

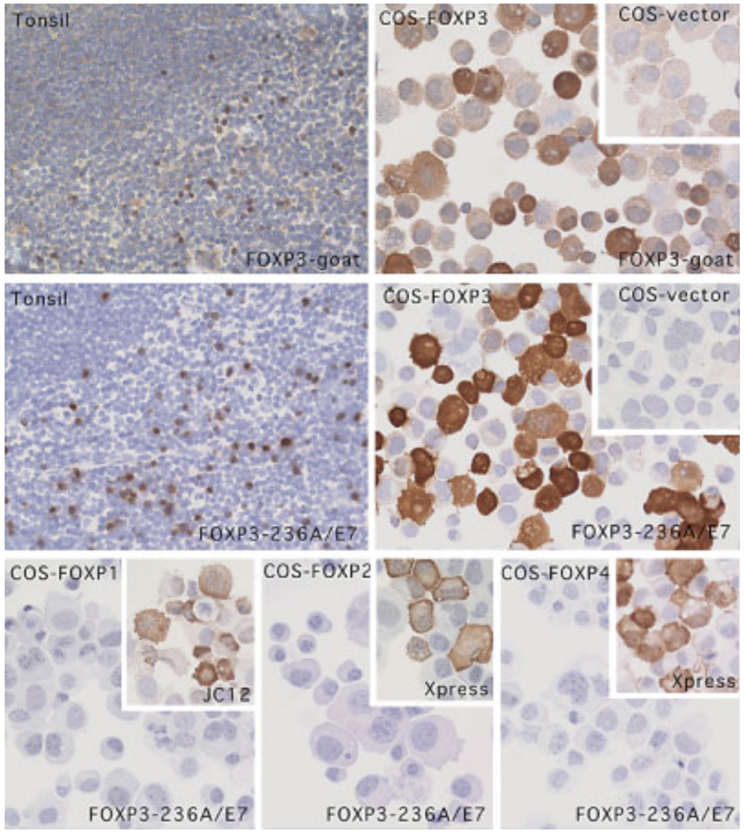


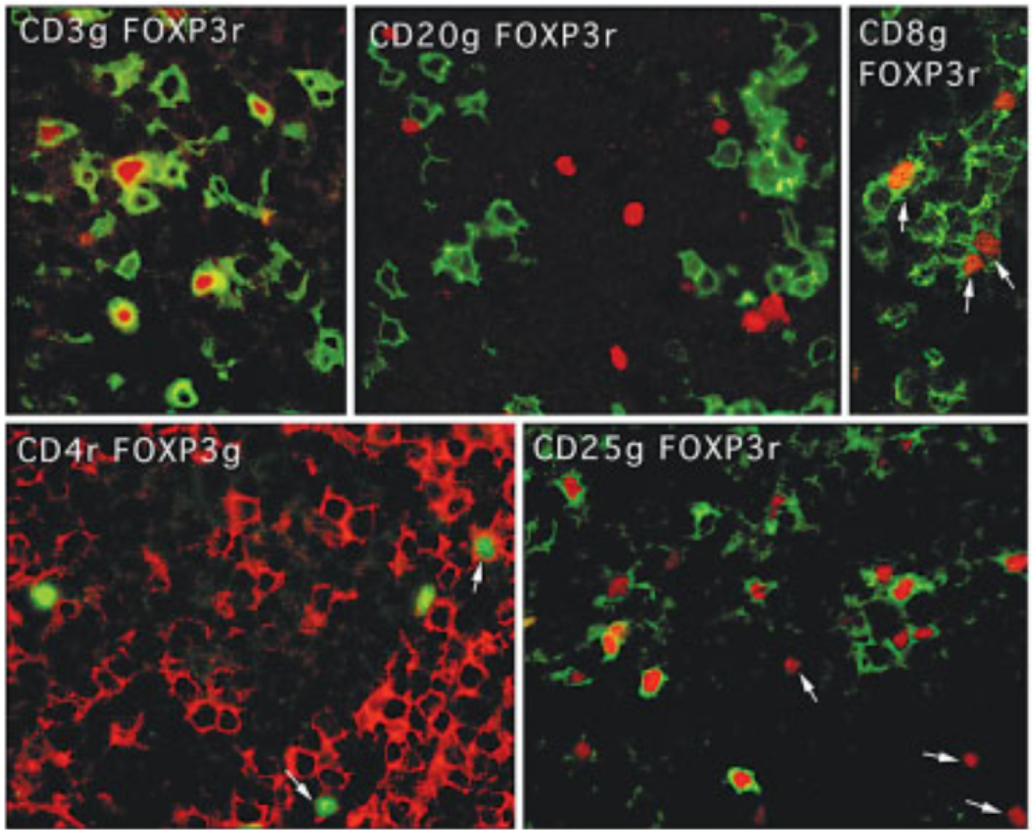
High FOXP1 predicts poor outcome
Banham 2005 Clin Cancer Res



ABC-DLBCL express short FOXP1 isoforms Brown 2008 Blood

FOXP3: A Marker of Regulatory T cells

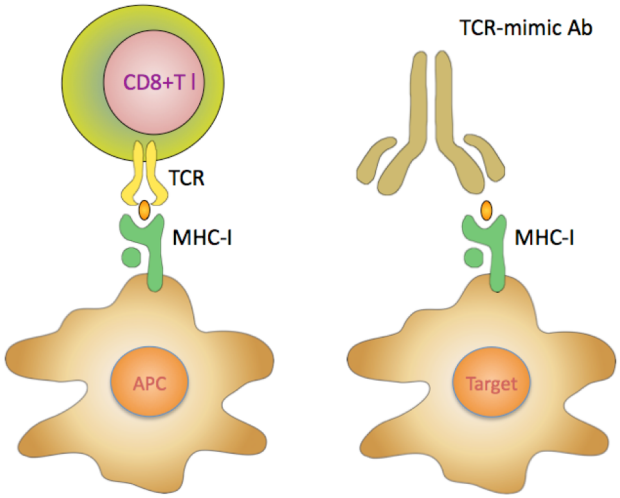


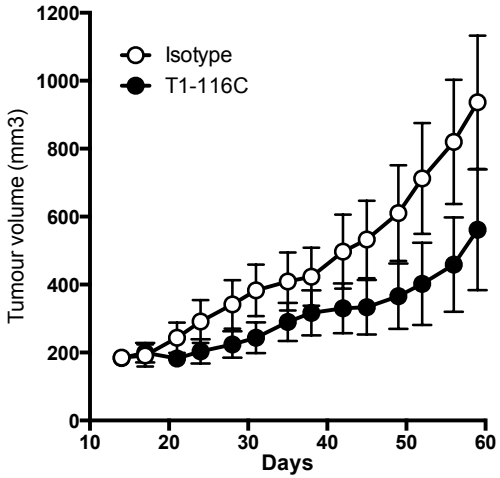


- With Dr Giovanna Roncador (Madrid) we generated the first FOXP3 mAbs
- We characterised the human FOXP3 population, studying both their frequency in the peripheral blood (Prof Fiona Powrie) and their suppressor function (Prof Enzo Cerundolo)

Roncador 2005 Eur J Immunol

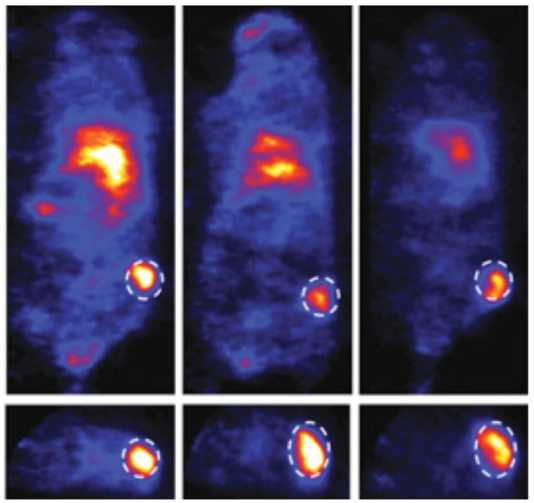
Antibodies Against MHC Class I Presented Peptides to Target the Intracellular Proteome





Li 2017 Cancer Research

Imaging Dr Bart Cornelissen, Oncology



- Intracellular proteins are inaccessible to classical antibodies
- However, peptides derived from intracellular proteins, such as p53, are presented by MHC class I on the cell surface
- T-cell receptor mimic antibodies can be used to therapeutically target such MHC class I presented peptides and to image tumours *in vivo*

HIDI Monoclonal Antibody Facility

- **Identification of existing commercially available antibodies**
- **Antigen design and production:** peptides & recombinant proteins
- **Murine monoclonal antibody production (fusion)**
- **Antibody screening**: reactivity with antigen, typically by ELISA
- **Antibody validation:** positive vs negative cells, transfected cells, siRNA
- **Hybridoma cell line cloning**
- **Hybridoma culture and production of mAb containing supernatant**
- **Antibody purification**
- **Antibody isotyping**
- **Basic training in antibody-based techniques** e.g. WB, IHC, IF, IP

HIDI Monoclonal Antibody Facility

- Resources: a 2 year position supporting an experienced postdoctoral scientist, Dr Amanda Anderson, with both research and industrial experience of antibody production and characterisation who will day-to-day manage and deliver the Facility
- Post funded from existing NDCLS-RDM Antibody Royalty Income
- We have established this activity as a Small Research Facility
- We aim to recover costs by charging users and/or by commercially licensing the antibodies produced for research and *in vitro* diagnostic use
- Our aim is to make the post sustainable in the longer term as it is not currently supported by the NIHR Oxford BRC that supports the other HIDI platforms

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I am happy to take any questions

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