NHS
Blood and Transplant

PDPU

The Protein Development and Production Unit (PDPU) is part of the International Blood Group Reference Laboratory (IBGRL) and the Bristol Institute for Transfusion Sciences (BITS). The unit works in partnership with the Protein Engineering Group (BITS) to perform a vital role within NHS Blood and Transplant (NHSBT).

PDPU is involved in a range of projects to develop and deliver recombinant proteins (both antibody and antigen) and monoclonal antibodies for research, diagnostic and therapeutic use. These reagents are used within NHSBT, and by external customers and collaborators from the academic, medical and commercial sectors.

We provide a translational route from research to development of diagnostic and therapeutic products, including the custom manufacture of reagents for customers or collaborative partners.

PDPU can generate novel monoclonal antibody specificities using synthetic peptides to produce conventional mouse hybridomas.

Sixty-six monoclonal antibodies are available commercially as

IBGRL RESEARCH PRODUCTS

We have CE marked fluorescently labelled antibodies for diagnosis of Fetomaternal Haemorrhage (FMH).

IBGRL
RESEARCH PRODUCTS

Protein Engineering

The protein engineering group, consisting of antibody (Ab) and antigen (Ag) engineering, has a range of capabilities which complement each other and the monoclonal antibody technology of PDPU. These in-house strengths are available to the whole of NHSBT to produce Abs and Ags identified as important to the service.

Antibody Engineering

The group uses molecular techniques with the potential to isolate novel Ab specificities, to rescue and re-express unstable Abs, and to modify Ab function.

1. **Phage Display Technology:** Phage display libraries have been generated. These are large collections of human Ab heavy and light chain variable regions expressed as single chain fragments (scFv) which can be screened against multiple targets of interest using purified Ag, engineered Ag (generated in-house by the Ag Engineering group), peptides and red blood cells to isolate scFv of interest.
2. **Further Ab engineering:** Isolated scFv can be attached to magnetic beads for use as a diagnostic assay. Alternatively it can be further engineered by isolating the scFv coding sequence and the variable regions re-expressed on an immunoglobulin backbone.
3. **Ab rescue:** DNA can be isolated from unstable Ab-producing cell lines and the Abs re-expressed stably in different mammalian cell lines.
4. **Ab modification**: The same technology can be used to alter existing Abs to give a desired feature such as re-engineering of IgG into IgM. As a polymeric immunoglobulin, the change allows Abs to be used as direct agglutinins.
5. **Ab analysis:** Factors affecting Ab stability and storage, such as protein aggregation, can be assessed.
6. **Computer modelling**: Can be used to study interactions between Ab and Ag.

Antigen Engineering

This group offers a similar range of experience and capabilities to Ab Engineering, using molecular techniques to produce recombinant proteins expressing Ags of interest to NHSBT, in both soluble form and expressed in cells other than blood cells. These soluble recombinant (sr) proteins and proteins expressed in cell lines are primarily erythrocyte, platelet and granulocyte related and are developed primarily for use in antibody screening and identification assays. They are also used in Ab Engineering to aid in the screening and selection of desired specificities from scFv libraries. Expertise in the development, cloning and maintenance of cell lines, and the characterisation and purification of sr proteins complement the capabilities offered by PDPU.

1. **Soluble recombinant proteins** – sr proteins can be used in cell-free assays e.g. ELISA or Luminex for detection/identification of Ab specificity. They can also be used to inhibit Abs in haemagglutination inhibition assays using gel cards or tubes.
2. **sr Ags for reference work:** sr proteins can be used for removal of 'nuisance' Abs from patient samples to enable identification of underlying clinically significant Abs e.g. srCR1 proteins which are used for Knops Ab absorption.
3. **Diagnostic cell lines:**
   a. **Antibody identification:** Transfected cell lines expressing recombinant proteins are available from frozen stocks for platelet and granulocyte antibody identification. This circumvents the need for freshly isolated typed donor cells.
   b. **Confirmation of Ab specificity:** Transfected cell lines expressing blood group proteins with rare/very low frequency mutations can be used to confirm the identity of antibodies in specific patient samples.

Key

Ab	Antibody
Ag	Antigen
BITS	Bristol Institute of Transfusion Sciences
FMH	Fetomaternal Haemorrhage
IBGRL	International Blood Group Reference Laboratory
PDPU	Protein Development and Production Unit (at Filton)
sr	soluble recombinant

Cell lines are available for commercial licensing

Diagnostic Antibodies

Major IgM Blood Grouping	A, B and D
Minor Blood Grouping	A/A1, B, N, D, E, Le, Le^a, Lu, Lu^b, Wr^b
Other	C3c, C3d, IgG, IgG control, IgM control

Research Antibodies

Erythrocytes	A, B RhD, CD173, 175, 233, 235a, 236R, 238, 239, 240
Cytoskeletal	Spectrin, Ankyrin, Protein 4.2, Glut-1
Platelet and granulocytes	CD29, 41, 42b, 49b, 61, 66b
Many cells/tissues	CD44, 47, 55, 58, 59, 239
HLA/stem cells/ Leucocytes/other	Class I A and B, CD34, 45RA, 50, NK, GM-CSF, ENA

IBGRL
RESEARCH PRODUCTS

Contact PDPU for data sheets, prices and further information.

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