THE UNIVERSITY OF QUEENSLAND
AUSTRALIA
CREATE CHANGE

Honours project

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Project 1: Development of intracellular delivery strategies for antibody therapeutics (Supervision: Dr Christian Fercher)

Monoclonal antibodies (mAb) have been utilised widely in clinical and basic research settings for the treatment of various diseases. Whilst all therapeutically approved monoclonal antibodies or fragments thereof are directed against cell surface receptors or proteins of the human secretome, intracellular antigen targeting strategies still await translation into the clinic. Despite significant advances in protein delivery technologies, reports of highly efficient transport vehicles are still sparse when systemically delivered *in vivo*. According to recent estimations, only several hundred proteins of the human proteome are suitable targets for small molecule drugs, providing an excellent opportunity for intracellular antibody therapeutics.

This project aims to develop suitable delivery strategies to translocate mAbs and various antibody fragments across the mammalian cell membrane. Potential strategies include the use of virus-like particles (VLPs), proteolipid and synthetic nanoparticles, liposomes and an in-house developed bispecific antibody platform. Cargo encapsulation will be tested using a variety of methods such as analytical HPLC-SEC, UV-Vis, DLS, BLI, SPR, immunostaining, flow cytometry etc. Intracellular delivery will be assessed using *in vitro* cell culture models. The successful applicant will be further trained in all aspects of recombinant mammalian and bacterial protein expression and purification techniques to enable in-house production of required antigens and antibodies.

To discuss further details of this project please contact **Dr Christian Fercher** (Phone: +61 7 334 64280; Email: c.fercher@uq.edu.au; https://researchers.uq.edu.au/researcher/17020)

Enrolling school: School of Chemistry & Molecular Biosciences (SCMB)

Suitable academic background: BSc in Molecular Biology, Biotechnology, Biochemistry etc.

Skills obtained in project: molecular cloning methods, protein expression and purification, protein analysis, biomaterial science, mammalian cell culture

Publication & postgraduate career potential: All our projects will lead to refereed publications and will provide a solid foundation for postgraduate studies.

Contact: Christian Fercher – c.fercher@uq.edu.au

Website: http://www.arccbi.org/

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Project 2: Discovery of novel functional antibodies against a human transcription factor cancer target (Supervision: Dr Christian Fercher)

Transcription factors (TFs) are DNA binding proteins responsible for regulating gene expression in all forms of life. In embryonic development of complex eukaryotes, some TFs are expressed in a spatiotemporal manner, giving rise to cell differentiation and proliferation, tissue specification and directional growth and remodelling. Their biological functions oversee the biological specification and cellular differentiation in a wide range of cell embryonic cell lines in development. Mutations can have potentially severe phenotypic consequences and can be embryonically lethal. This is indicative of their crucial roles in organogenesis throughout embryonic development. The TF Sox18 is involved in lymphangiogenesis and is upregulated in certain cancers, contributing to metastatic tumour transition. Its redundant roles in fully developed humans makes for an attractive therapeutic target. Consequently, the discovery of functional antibodies against Sox18 and related TFs (e.g. Sox2, Sox9) presents an opportunity to develop a potential therapeutic modality for preclinical *in vitro* and *in vivo* animal studies.

Methodologies in this project include recombinant bacterial expression and affinity purification of truncated TF variants. Successful isolation of these proteins will be assessed via SDS-Page and immunoblotting, and their structural integrity will be analysed by analytical HPLC-SEC and ELISA. The purified proteins will be used as antigens in a phage display biopanning campaign using an in-house human single-chain variable fragment (scFv) antibody library. Isolated phage pools will be assessed by phage ELISA and screened for high affinity binders to the corresponding TF. The most promising candidates will be reformatted into full length monoclonal antibodies via in-fusion cloning methods. Functional testing of antibodies expressed and purified from CHO cells will be carried out using *in vitro* binding and cell culture assays.

To discuss further details of this project please contact **Dr Christian Fercher** (Phone: +61 7 334 64280; Email: c.fercher@uq.edu.au; https://researchers.uq.edu.au/researcher/17020)

Enrolling school: School of Chemistry & Molecular Biosciences (SCMB)

Suitable academic background: BSc in Molecular Biology, Biotechnology, Biochemistry, immunology

Skills obtained in project: protein expression and purification, protein analysis, antibody discovery, functional antibody screening

Publication & postgraduate career potential: All our projects will lead to refereed publications and will provide a solid foundation for postgraduate studies.

Contact: Christian Fercher – c.fercher@uq.edu.au

Website: http://www.arccbi.org/