Stabilised peptides that specifically inhibit activity of the Grb7 adaptor protein, a potential oncology drug target for tumours driven by epidermal growth factor receptor and/or ephrin receptors. The target and peptides offer a basis for developing novel, safe and effective anti-cancer drug compositions.

- Potential to develop ‘First in Class’ anti-cancer drugs targeting Grb7 adaptor protein in epidermal growth factor receptor (EGFR) and/or ephrin receptor driven tumours
- Differentiated Mechanism of Action that inhibits the direct intra-cellular link to the Ras/proto-oncogene pathway
- In vitro ‘Proof of mechanism’ with efficacy for stabilised peptide molecule inhibitors
- Potential as a single agent and in combination therapies

THE CHALLENGE

Growth factor receptor-bound protein 7 (Grb7) belongs to a small family of SH2-domain adaptor proteins that interact with a number of receptor tyrosine kinases and signalling molecules.

Grb7 interacts with EGFR and ephrin receptors, providing a direct intra-cellular link to the Ras proto-oncogene. This links the function to proliferation of EGFR or ephrin driven tumours.

Grb7 also plays a role in the integrin signalling pathway by binding with focal adhesion kinase (FAK), and support its role in cell migration/tumour metastasis.

Grb7 is validated as a prognostic marker of HER2+ve breast cancers and was identified as a therapeutic target in this and other cancers, including triple negative breast cancers for which there are no current effective treatments.

THE TECHNOLOGY

A first generation of our cyclic peptide-based inhibitors enhance activity of other anticancer agents, reduce breast cancer cell migration in vitro and reduce tumour size as a single agent in a mouse model of pancreatic cancer.

Augmented treatment efficacy is expected from a combinatorial approach with reduced resistance to first line therapies. There is a need to identify improved compounds that can specifically inhibit Grb7 without inhibiting other SH2 domain proteins.

Monash Researchers have created a library of stabilised peptides that specifically inhibit the activity of Grb7 in vitro with Kd in the mM to nM range. There remains a need to make more potent drug-like novel inhibitors for drug development.

THE OPPORTUNITY

Monash University seeks a partner to create and test novel compositions (peptide and/or small molecule) against this exciting target. The Monash team has extensive experience in all aspects of preclinical development from peptide chemistry, structural biology and cellular biology with in vitro analysis and in vivo integrative function.

The team has gained valuable structure/activity know-how of the target and test compounds. This knowledge forms the basis for creating novel, safe and effective anti-cancer drug compositions based on small molecules or stabilised peptides.

References
