Final Report – RCPA Foundation Research Fellowship

Cameron Snell 2nd June 2019

Funding from the RCPA Foundation was used to curate a cohort of 229 oestrogen receptor-positive HER2-negative tumours from women who had node-positive breast cancer. From this assembled retrospective cohort, with comprehensive clinical follow-up, we made several tissue microarrays to make critical insights into the role of progesterone receptor signalling in breast cancer and develop new tools which could be used to refine endocrine agent selection in patients to prevent relapse.

The first paper we published demonstrated that assaying hormone receptors in synchronous lymph node metastatic deposits was more prognostic than performing these in the primary tumour (Snell et al., 2017). This adds weight to the idea that axillary nodal tumour deposits display the phenotype of tumour cells which are targeted by systemic adjuvant therapies.

We developed a number of proximity ligation assays which could detect oestrogen-receptor interactions. One of these, which detected interactions between the B-isoform of progesterone receptor (PR-B) and the oestrogen receptor, could effectively predict which patients would relapse on adjuvant aromatase inhibitors (Snell et al., 2018). PR-B levels were also shown to determine prognosis in tamoxifen-treated patients. These are tools which may find clinical utility in selecting for patients that may require additional adjuvant treatments, such as cyclin-dependent kinase 4/6 (CDK4/6) inhibitors. We have filed a patent to allow for clinical development of this assay.

The clinical cohort built using this funding will be important in ongoing studies and is being employed in several other studies. I have applied for ongoing funding to continue this work. Both papers, which are the product of this research funding, have acknowledged the support of the RCPA Foundation.

Snell, C. E., Gough, M., Liu, C., Middleton, K., Pyke, C., Shannon, C., . . . Tilley, W. D. (2018). Improved relapse-free survival on aromatase inhibitors in breast cancer is associated with interaction between oestrogen receptor-alpha and progesterone receptor-b. *Br J Cancer, 119*(11), 1316-1325. doi:10.1038/s41416-018-0331-3

Snell, C. E., Gough, M., Middleton, K., Hsieh, M., Furnas, L., Seidl, B., . . . Armes, J. E. (2017). Absent progesterone receptor expression in the lymph node metastases of ER-positive, HER2-negative breast cancer is associated with relapse on tamoxifen. *J Clin Pathol, 70*(11), 954-960. doi:10.1136/jclinpath-2016-204304