Most Significant Contributions - Michael HALLETT

1. The development of de novo methodology to study breast cancer [1922 citations; 54 publications]. My lab has a long standing interest in the development of gene set predictors in breast cancer. Gene set predictors use, for example, mRNA levels for a (small) set of genes in a multivariate fashion to classify or stratify patients relative to a clinical end-point eg prognosis or benefit from a therapy. We have also developed de novo frameworks such as BreSAT (Breast Signatures Analysis Tool), AIMS (Absolute Inference of Molecular Subtype, and AIPS (Absolute Inference of Patient Signatures) supported by funding from Genome Quebec/Canada, NSERC, CQDM and the CIHR. This project will benefit from importing our experiences in developing assays with clinical utility and validity to the fungal setting.

2. Tools to study interactions between tissues and environments [27066 citations]. We are interested in understanding how a tumor influences its microenvironment in order to progress and conversely how the microenvironment influences the tumor. My trainees have first authored papers in high impact journals examining stromal-epithelial interactions (Finak et al. 2009 Nature Medicine), endothelial-epithelial interactions (Pepin et al. 2012 Breast Cancer Research 2012), and epithelial-blood/immune interactions (Dumeaux et al. 2012, 2017). This project will benefit from our experience in generating and analyzing -omic profiles often with small amounts of starting material (inclusive laser capture microdissection and single cell approaches), and our experience with genomic neoplasticity.

3. The development of bioinformatics techniques for chemical genomic profiling, interactions and stress pathway analysis in Yeast and other model organisms [800 citations]. Two of my doctoral students S Gosline and A Lee generated several manuscripts describing novel bioinformatics and experimental methodology in the context of high-throughput genomic screens with model organisms including Yeast and Candida. Of particular note, Lee (2009) presented an approach to predict when two chemical compounds would have synergistic affects to kill fungi. The approach, which appeared in Molecular Systems Biology, is a step towards the rational design of combination therapies. This previous work has largely been done in collaboration with Malcolm Whiteway and directly complements this project.

4. Prediction of subcellular and sub-subcellular localizations [230 citations]. My doctoral student M Scott was the first to use machine learning/probabilistic modelling to predict subcellular location of proteins. This resulted in a program entitled PSLT (Protein Subcellular Localization Tool; PLoS Comp Bio, 118 citations). We showed that PSLT was able to predict the organellar localization of proteins better than existing tools at the time (eg SignalP). The machine learning techniques and probabilistic modelling are of direct relevance to this project.

5. Novel algorithmic approach towards understanding genome evolution [>500 citations]. At the beginning of my academic career, I published ~10 manuscripts with my co-author Jens Lagergren (SciLifeLab, Sweden). Three of my most influential papers, which appeared in the highly ranked RECOMB conference, showed efficient, exact algorithms to reconcile gene and species trees using (1) gene duplications and loss, (2) lateral gene transfers and (3) all three events simultaneously (over 500 citations for our work).