**Cancer Research Division**

**PhD STUDENT COMMITTEE REPORT**

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| **STUDENT NAME: Kenneth Doig** | |
| **MEETING DATE: 5 Dec 2014** | **VENUE: Surgical Oncology Meeting Rm** |
| **COMMITTEE:** | |
| **SUPERVISORS: Prof. Stephen Fox and A/Prof. Tony Papenfuss** | |
| **MENTOR: Dr Ricky Johnston** | |
| **LENGTH OF CANDIDATURE TO DATE: 10 months** | |
| **PROJECT TITLE: Addressing the barriers to translating genetic sequencing into a clinical oncology setting.** | |
| **COMMITTEE MEMBERS PRESENT:** | |

**For the 1st (6 month) Committee review meeting**

* 1. Provide key background information (and references as appropriate) that has led to the definition of your project’s aims.

*Researchers are increasingly using Genomics, but its uptake into the clinical environment has been slow, mainly because of the complexities of bioinformatic analysis. It is in hospitals that the high diagnostic and discriminative ability of genomics could have positive health impacts for individual patients and for infection control programs. Hospital pathologists and microbiologists have been reluctant to embrace genomic approaches because of issues of sequencing costs and the complexity of data analysis. The former issue is being addressed by rapid technology improvements in NGS equipment. However, data complexity and problems associated with data analysis remain a serious impediment to the wider use of genomics in clinical pathology.*

*Over the last few years, the commodisation of genetic sequencing platforms has brought nucleotide level genetic analysis within the economic reach of most hospitals and pathology labs. This has allowed these institutions to have unprecedented access to genetic diagnostic information about their patients and diseases. But the volume of data has left a gap between the availability of genetic information and the institute’s ability to process and interpret the data. This PhD proposes to address this gap and address the barriers to clinical adoption of high throughput sequencing diagnostics.*

* 1. Are the topic and aims now well defined? What are the aims?

*Aim1: To identify and articulate the technical, logistical and organisational barriers to entry for the adoption of high throughput sequencing (HTS) in a clinical oncology setting.*

*Aim2: To develop the methodologies and software engineering systems necessary for the processing of HTS data from sequencer through to a clinical report.*

*Aim3: To anticipate the possible technology directions for molecular diagnostics in cancer and develop software architectures and systems that can address future sequencing needs in a scalable manner.*

* 1. Are the appropriate methods for your project established?

*The primary method of addressing the studies aim(s) will be through the implementation of software systems and variant databases that will be actively used by clinicians, molecular scientists and pathologists in a Cancer hospital.*

* 1. Do you have a good understanding of the literature relevant to your project?

*I have been developing a large set of papers relevant to this PhD over the last two years which covers the past and cotemporary literature in clinical sequencing and variant databases.*

* 1. How good are you at finding help (technical or academic) when your project calls for it?

*I have built a number of relationships with the Peter Mac researchers and have a number of collaborations with colleagues at RCPA, VLSCI, University of Melbourne (Translation Pathology and Microbiology and Physics), MCRI as well and colleagues in the software engineering industry.*

* 1. Have any problems been encountered which need to be resolved?

*There is an ongoing tension between the effort required to implement an operational system and the research required for a PhD of this nature.*

* 1. Do you have any plans for publications or conference presentations related to your project ? (present a plan if you think it would be helpful)

***Proposed first author papers:***

* *The Clinical Bottleneck of Next Generation Cancer Diagnostics. Review paper for clinical oncologists.*
* *PipeCleaner: A framework for the testing and evaluation of bioinformatics pipelines. Technical Note.*
* *Path-OS: A variant curation system for high throughput clinical sequencing. Technical Note.*
* *A federated variant database for clinical sequencing curation*
* *Variant Viewer: A light weight web application for managing VCF files. Technical Note.*

***Published and submitted papers and books:***

*Massively-parallel sequencing assists the diagnosis and guided treatment of cancers of unknown primary,* Richard W Tothill, Jason Li, Linda Mileshkin, **Ken Doig**, Terence Siganakis, Prue Cowin, Andrew Fellowes, Timothy Semple, Stephen Fox, Keith Byron, Adam Kowalczyk, David Thomas, Penelope Schofield, David D Bowtell, J Pathol. 2013 Dec;231(4):413-23. doi: 10.1002/path.4251.

*Bioinformatics Pipelines for Targeted Resequencing and Whole-Exome Sequencing of Human and Mouse Genomes: A Virtual Appliance Approach for Instant Deployment.*

Jason Li, Maria A. Doyle, Isaam Saeed, Stephen Q. Wong, Victoria Mar, David L. Goode, Franco Caramia, **Ken Doig**, Georgina L. Ryland, Ella R. Thompson, Sally M. Hunter, Saman K. Halgamuge, Jason Ellul, Alexander Dobrovic, Ian G. Campbell, Anthony T. Papenfuss, Grant A. McArthur, Richard W. Tothill *PLoS ONE 9(4): e95217. doi:10.1371/journal.pone.009521*

*Sequence artefacts in a prospective series of formalin-fixed tumours tested for mutations in hotspot regions by massively parallel sequencing.*

Stephen Q Wong, Jason Li, Angela Y-C Tan, Ravikiran Vedururu, Jia-Min B Pang, Hongdo Do, Jason Ellul, **Ken Doig**, Anthony Bell, Grant A MacArthur, Stephen B Fox, David M Thomas, Andrew Fellowes, John Parisot and Alexander Dobrovic*. BMC Medical Genomics*

*Assessing the clinical value of targeted massively parallel sequencing in a longitudinal, prospective population-based study of cancer patients. Submitted for publication.*

Stephen Q. Wong1,2, Andrew Fellowes1, **Ken Doig3**,4, Jason Ellul3, Trent Bosma1, Darryl Irwin5, Ravikiran Vedururu1, Angela Y-C Tan1, Jonathan Weiss6, Kian Sing Chan7, Mark Lucas8, David M. Thomas2,4,9, Alexander Dobrovic1,2,4,6,10, John P Parisot2,4, Stephen B Fox

*The CANCER 2015 Cohort: A Unique Prospective and Longitudinal, Population-based Cancer Genomics Cohort - Clinical and Economic Rationale for Personalized Medicine. Submitted for publication.*

John P Parisot, Heather Thorne, Andrew Fellowes, **Ken Doig**, Mark Lucas, John McNeil, Brett Doble, Alexander Dobrovic, Paul James, Lara Lipton, David Ashley, Theresa Hayes, Paul McMurrick, Gary Richardson, Paula Lorgelly, Stephen B Fox, David M Thomas.

*Clinical Bioinformatics 2nd edition, Book Chapter*

Maria A. Doyle, Jason Li, **Ken Doig**, Andrew Fellowes and Stephen Q. Wong

***Previous conferences and seminars:***

* Oral presentation. WEHI bioinformatics seminar, May 2014
* Oral presentation and Poster. Human Variome Project 5th Biennial meeting Paris, May 2014
* Oral presentation. VLSCI
* Oral presentation. Laby Foundation November/December 2014
* Oral presentation. Garvan Institute Sydney, November 2014.
* Oral presentation. 10th Australasian Mutation Detection Meeting, August 2014
* Invited participant. RCPA workshop - Standards for Clinical Databases of Genetic Variants.
* Invited participant. Melbourne Genomics Health Alliance.
  1. Are there any issues you wish to discuss with your committee?

*The appropriate allocation of effort by a team of contributors for a thesis by publication.*

* 1. Are the short and long term experiments clearly mapped out?

*The current web pages for Path-OS and Variant Viewer outline the development plans. The Jira issue management site has a detailed list of pending and completed features.*

*See:*

[*PathOS Jira Issues*](https://115.146.86.118/jira/browse/PATHOS)

[*PathOS Confluence Page*](https://115.146.86.118/confluence/display/PVS/Path-OS+Variant+System)

[*Variant Viewer Confluence Page*](https://115.146.86.118/confluence/display/VV/Variant+Viewer)

* 1. Do you have a time line to show?

*See 9 above.*

* 1. Overall, do you think you are on track with your project?

*The implementation of Path-OS while well advanced still needs a large amount of work to be robust and suitable for wider use in the Australian environment. I was hoping to have a least one first author publication completed this year.*

* 1. **Committee Comments/Report (to be completed by Mentor after the meeting):**

**Research Training in past year**

Attach a summary sheet for the research training activities highlighting the activities you participated in since commencing, including details of any of the following:

* Induction and Orientation program
* Specialist laboratory skills training
* Hub, Lab meetings and Journal clubs
* Seminar and workshop programs
* Annual Student Retreat
* Topics in Cancer program
* Research Seminar program
* Research lunches attended
* Research Governance program
* Research reporting (Presentations, written reports submitted etc)
* Technical seminars

