

POSTGRADUATE SCHOLARSHIP FINAL REPORT 2014

1	Project Title	Cancer Risks for People with Colorectal Cancer-Predisposing Genetic Mutations						
2	Scholarship Holder	Dr Aung Ko Win						
3	Unit/Institution	Centre for MEGA Epidemiology, University of Melbourne						
4	Years Funded	2011-2014						
5	<p>Lay Abstract: Please provide a short report for a lay audience. <i>(Please refer to the enclosed guide.)</i></p> <p>Bowel cancer is a major public health burden in Victoria and Australia. On average, 1 in 20 people will be diagnosed with colorectal cancer in their lifetime. However, an individual's risk of bowel cancer varies greatly depending on their genetic and environmental factors. One of the strongest risk factors for the disease is inherited mutations in DNA repair genes. Given the availability and effectiveness of bowel cancer screening and interventions, we need precise and accurate risks of cancers to reduce the burden of disease by targeting preventive measures to those at highest risk. The overall aim of my research project was to estimate cancer risks for people with predisposing genetic mutations and their relatives. My research addressed critical clinical questions for people at genetic risk of bowel and other cancers by studying 40,000 people from 12,000 bowel cancer families from the Colon Cancer Family Registry, an international consortium in Australia, New Zealand, Canada and USA, and conducting state-of-the-art statistical analyses. I established the best way to identify people with DNA repair gene mutations, generated the most accurate and precise estimates of their cancer risks, and derived cancer risks for relatives of people with different types of bowel cancer. My work is being used to guide clinical management of cancer families worldwide for targeted and appropriate levels of screening, interventions and genetic testing based on an individual's risk.</p>							
6	<p>Progress: Using the major aims of your scholarship project as a framework, please indicate progress against these aims.</p> <table border="1" style="width: 100%;"> <thead> <tr> <th style="text-align: center;">Aim</th> <th style="text-align: center;">Progress</th> </tr> </thead> <tbody> <tr> <td>1. Literature review of the existing models of colorectal cancer risk prediction</td> <td>This review has been published. Win et al. Risk Prediction Models for Colorectal Cancer: A Review. Cancer Epidemiol Biomarkers Prev. 2012;21(3):398-410.</td> </tr> <tr> <td>2. Literature review of the existing models of mismatch repair gene mutation</td> <td>This review has been published. Win et al. Criteria and prediction models for mismatch repair gene mutations: a review. J Med Genet. 2013;50(12):785-93.</td> </tr> </tbody> </table>		Aim	Progress	1. Literature review of the existing models of colorectal cancer risk prediction	This review has been published. Win et al. Risk Prediction Models for Colorectal Cancer: A Review. Cancer Epidemiol Biomarkers Prev. 2012;21(3):398-410.	2. Literature review of the existing models of mismatch repair gene mutation	This review has been published. Win et al. Criteria and prediction models for mismatch repair gene mutations: a review. J Med Genet. 2013;50(12):785-93.
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2. Literature review of the existing models of mismatch repair gene mutation	This review has been published. Win et al. Criteria and prediction models for mismatch repair gene mutations: a review. J Med Genet. 2013;50(12):785-93.							

3. Estimation of risk of cancers for carriers and non-carriers from mismatch repair gene mutations carrying families	This paper has been published: Win et al. Colorectal and Other Cancer Risks for Carriers and Noncarriers From Families With a DNA Mismatch Repair Gene Mutation: A Prospective Cohort Study. J Clin Oncol. 2012;30(9):958-64.
4. Estimation of risk of cancers following colorectal cancer for carriers of mismatch repair gene mutations	This paper has been published: Win et al. Risks of primary extracolonic cancers following colorectal cancer in lynch syndrome. J Natl Cancer Inst. 2012;104(18):1363-72.
5. Estimation of risk of cancers following endometrial cancer for carriers of mismatch repair gene mutations	This paper has been published: Win et al. Risks of Colorectal and Other Cancers After Endometrial Cancer for Women With Lynch Syndrome. J Natl Cancer Inst. 2013;105(4):274-9.
6. Evidence of breast cancer being part of Lynch syndrome	This paper has been published: Win AK, Lindor NM, Jenkins MA. Breast cancer risk in Lynch syndrome: a systematic review. Breast Cancer Res. 2013;15(2):R27.
7. Investigating genetic modifiers of cancer risks for carriers of mismatch repair gene mutations	This paper has been published: Win et al. Are the common genetic variants known to be associated with colorectal cancer risk in the general population also associated with colorectal cancer risk for DNA mismatch repair gene mutation carriers? Eur J Cancer. 2013;49(7):1578-87.
8. Estimation of risk of cancers for carriers of the <i>MUTYH</i> gene mutations	This paper has been published: Win et al. Risk of Colorectal Cancer for Carriers of Mutations in MUTYH, with and without a Family History of Cancer. Gastroenterology. 2014. PubMed PMID: 24444654.
9. Identifying tumour morphology features that predict an increased risk of colorectal cancer for relatives of onset colorectal cancer cases	This paper has been accepted: Win et al. Role of tumour molecular pathology features to estimate colorectal cancer risk for first-degree relatives. Gut. In Press.

7

Please list all papers arising from your scholarship project that have been published, or accepted for publication, in refereed journals since the commencement of your scholarship.

(Please list in chronological order, include title, sequence of authors, first and last pages, name, volume and date of journal.)

REFEREED RESEARCH PUBLICATIONS

1. **Win AK**, Young JP, Lindor NM, Tucker KM, Ahnen DJ, Young GP, Buchanan DD, Clendenning M, Giles GG, Winship I, Macrae FA, Goldblatt J, Southey MC, Arnold J, Thibodeau SN, Gunawardena SR, Bapat B, Baron JA, Casey G, Gallinger S, Le Marchand L, Newcomb PA, Haile RW, Hopper JL, Jenkins MA. Colorectal and Other Cancer Risks for Carriers and Noncarriers From Families With a DNA Mismatch Repair Gene Mutation: A Prospective Cohort Study. *J Clin Oncol*. 2012 Mar 20;30(9):958-64. PubMed PMID: 22331944.
2. **Win AK**, Lindor NM, Young JP, Macrae FA, Young GP, Williamson E, Parry S, Goldblatt J, Lipton L, Winship I, Leggett B, Tucker KM, Giles GG, Buchanan DD, Clendenning M, Rosty C, Arnold J, Levine AJ, Haile RW, Gallinger S, Marchand LL, Newcomb PA, Hopper JL, Jenkins MA. Risks of primary extracolonic cancers following colorectal cancer in lynch syndrome. *J Natl Cancer Inst*. 2012 Sep 19;104(18):1363-72. PubMed PMID: 22933731.
3. **Win AK**, MacInnis RJ, Hopper JL, Jenkins MA. Risk Prediction Models for Colorectal Cancer: A Review. *Cancer Epidemiol Biomarkers Prev*. 2012 Mar;21(3):398-410. PubMed PMID: 22169185.
4. **Win AK**, Lindor NM, Winship I, Tucker KM, Buchanan DD, Young JP, Rosty C, Leggett B, Giles GG, Goldblatt J, Macrae FA, Parry S, Kalady MF, Baron JA, Ahnen DJ, Marchand LL, Gallinger S, Haile RW, Newcomb PA, Hopper JL, Jenkins MA. Risks of Colorectal and Other Cancers After Endometrial Cancer for Women With Lynch Syndrome. *J Natl Cancer Inst*. 2013 Feb 20;105(4):274-9. doi: 10.1093/jnci/djs525. PubMed PMID: 23385444.
5. **Win AK**, Hopper JL, Buchanan DD, Young JP, Tenesa A, Dowty JG, Giles GG, Goldblatt J, Winship I, Boussioutas A, Young GP, Parry S, Baron JA, Duggan D, Gallinger S, Newcomb PA, Haile RW, Marchand LL, Lindor NM, Jenkins MA. Are the common genetic variants associated with colorectal cancer risk for DNA mismatch repair gene mutation carriers? *Eur J Cancer*. 2013 May;49(7):1578-87. doi: 10.1016/j.ejca.2013.01.029. PubMed PMID: 23434150.
6. **Win AK**, Lindor NM, Jenkins MA. Risk of breast cancer in Lynch syndrome: a systematic review. *Breast Cancer Res*. 2013 Mar 19;15(2):R27. [Epub ahead of print] PubMed PMID: 23510156.
7. **Win AK**, Macinnis RJ, Dowty JG, Jenkins MA. Criteria and prediction models for mismatch repair gene mutations: a review. *J Med Genet*. 2013 Dec;50(12):785-93. doi: 10.1136/jmedgenet-2013-101803. PubMed PMID: 23956446.
8. **Win AK**, Dowty JG, Cleary SP, Kim H, Buchanan DD, Young JP, Clendenning M, Rosty C, Macinnis RJ, Giles GG, Boussioutas A, Macrae FA, Parry S, Goldblatt J, Baron JA, Burnett T, Le Marchand L, Newcomb PA, Haile RW, Hopper JL, Cotterchio M, Gallinger S, Lindor NM, Tucker KM, Winship IM, Jenkins MA. Risk of Colorectal Cancer for Carriers of Mutations in MUTYH, with and without a Family History of Cancer. *Gastroenterology*. 2014 Jan 17. pii: S0016-5085(14)00080-8. doi: 10.1053/j.gastro.2014.01.022. [Epub ahead of print] PubMed PMID: 24444654.
9. **Win AK**, Buchanan DD, Rosty C, MacInnis RJ, Dowty JG, Dite GS, Giles GG, Southey MS, Young JP, Clendenning M, Walsh MD, Walters RJ, Boussioutas A, Smyrk TC, Thibodeau SN, Baron JA, Potter JD, Newcomb PA, Le Marchand L, Haile RW, Gallinger S, Lindor NM, Hopper JL, Ahnen DJ, Jenkins MA. Role of tumour molecular pathology features to estimate colorectal cancer risk for first-degree relatives. *Gut*. In Press.

INVITED EDITORIALS AND REVIEWS

10. Winship I, **Win AK**. The Australasian Colorectal Cancer Family Registry. *Med J Aust*. 2012 Nov 5;197(9):480-1. PubMed PMID: 23121570.
11. **Win AK**. Is prostate cancer a Lynch syndrome cancer? *Asian J Androl*. 2013 Sep;15(5):588-9. doi: 10.1038/aja.2013.87. Epub 2013 Jul 1. PubMed PMID: 23817498.
12. **Win AK**, Ait Ouakrim D, Jenkins MA. Risk profiling: familial colorectal cancer. *Cancer Forum*. 2014 Mar.

LETTER

13. **Win AK**, Jenkins MA. Is the reported modifying effect of 8q23.3 and 11q23.1 on colorectal cancer risk for MLH1 mutation carriers valid? *Int J Cancer*. 2013 Oct 1;133(7):1762-1763. doi: 10.1002/ijc.28179. Epub 2013 Apr 18. PubMed PMID: 23536426.
14. **Win AK**, Jenkins MA. Response: Risks of Colorectal and Other Cancers After Endometrial Cancer for Women With Lynch Syndrome. *J Natl Cancer Inst*. 2013 Dec 4;105(23):1837-8. doi: 10.1093/jnci/djt308. Epub 2013 Oct 29. PubMed PMID: 24168970.

Please provide details of presentations or posters relating to your scholarship project during the tenure of your scholarship.

INVITED PRESENTATIONS

1. Fred Hutchinson Cancer Research Center, University of Washington, Seattle, USA. 30 April 2012. *Early-onset colorectal cancer: what we know in 2012*.
2. Using Risk to Lower the Impact of Cancer. Kingscliff, Australia. 20 Aug 2012. *Recent Clinically-Relevant Findings from the Colon Cancer Family Registry*.
3. National Cancer Center Research Institute, Seoul, Korea. 29 July 2013. *Insights into breast and colorectal cancer genetics from Australian population-based case-control-family studies*.
4. University of Cambridge, Strangeways Research Laboratory, Cambridge, UK. 5 Aug 2013. *Prediction of colorectal cancer risk*.
5. Newcastle University, Institute of Genetic Medicine, Newcastle, UK. 8 Aug 2013. Cancer risks for people with predisposing genetic mutations.
6. University of Leeds, Leeds Institute of Molecular Medicine, Leeds, UK. 12 Aug 2013. *Prediction of colorectal cancer risk*.
7. University of London, Institute of Cancer Research, London, UK. 13 Aug 2013. *Prediction of colorectal cancer risk*.
8. Australian Myanmar Medical Association Annual Meeting, Melbourne, Australia. 13 Oct 2013. *Familial colorectal cancer*.

ORAL PRESENTATIONS

International

9. Breast Cancer Family Registry annual meeting. Salk Lake City, USA. 26 April 2012. *Recent findings in colorectal cancer research*.

10. The 62nd American Society of Human Genetics Annual Meeting. San Francisco, USA. 8 Nov 2012. *Risk of colorectal cancer for monoallelic and biallelic MUTYH mutation carriers.*
11. The 5th Biennial Meeting of International Society for Gastrointestinal Hereditary Tumours (InSiGHT). Cairns, Queensland, Australia. 29 Aug 2013. *Tumour molecular pathology features predict colorectal cancer risk for relatives of people with colorectal cancer.*
12. The 5th Biennial Meeting of International Society for Gastrointestinal Hereditary Tumours (InSiGHT). Cairns, Queensland, Australia. 31 Aug 2013. *Substantial variation in risk of colorectal cancer for monoallelic MUTYH mutation carriers.*

National

13. Work In Progress Seminar. The University of Melbourne. Sep 2011. *Second primary cancers in Lynch syndrome.*
14. Joint Higher Degree Public Health Student Workshop, Australasian Epidemiological Association & Public Health Association of Australia. Melbourne, Australia. Nov 2011. *Colorectal and other cancer risks for carriers and non-carriers of a DNA mismatch repair gene mutation from mutation carrying families: a prospective cohort study.*
15. Australia New Zealand Gynaecological Oncology Group (ANZGOG) Annual Meeting. Gold Coast, Australia. Feb 2012. *Risks of primary cancers following endometrial cancer in Lynch syndrome.*
16. Familial Aspects of Cancer: Research and Practice. Kingscliff, Australia. 22 Aug 2012. *Is breast cancer a Lynch syndrome cancer?*
17. Familial Aspects of Cancer: Research and Practice. Kingscliff, Australia. 24 Aug 2012. *Risk prediction models for mismatch repair gene mutations: a systematic review and a meta-analysis.*
18. Familial Aspects of Cancer: Research and Practice. Cairns, Australia. 27 Aug 2013. *Family history of colorectal cancer and risk of endometrial cancer: a retrospective cohort study.*

POSTER PRESENTATIONS

International


19. The 12th International Congress of Human Genetics and the 61st American Society of Human Genetics Annual Meeting. Montreal, Canada. Oct 2011. *Colorectal and other cancer risks for carriers and non-carriers of a DNA mismatch repair gene mutation from mutation carrying families: a prospective cohort study.*
20. The 15th Annual Meeting of Collaborative Group of the Americas on Inherited Colorectal Cancer (CGA-ICC). Montreal, Canada. Oct 2011. *Risks of second primary extracolonic cancers following colorectal cancer in Lynch syndrome.*
21. The 62nd American Society of Human Genetics Annual Meeting. San Francisco, USA. 9 Nov 2012. *Risks of primary cancers following endometrial cancer in Lynch syndrome.*
22. Post-GWAS Horizons in Molecular Epidemiology: Digging Deeper into the Environment. 12 Nov 2012; Hollywood, Florida, USA. *The Colon Cancer Family Registry: a major resource for Post-GWAS gene-environment studies.*
23. American Association of Cancer Research Annual Meeting. Washington DC, USA. 7 Apr 2013. *Predicting risk of colorectal cancer depending on tumor pathology features for first-degree relatives of persons with colorectal cancer.*

	<p>24. The 63rd American Society of Human Genetics Annual Meeting. Boston, USA. 23 Oct 2013. <i>Combined effect of germline mutations in MUTYH and DNA mismatch repair genes on risk of colorectal cancer.</i></p> <p><u>National</u></p> <p>25. Genetics Society of AustralAsia Annual Conference, Melbourne, Australia. July 2012. <i>Are the common genetic variants known to be associated with colorectal cancer risk in the general population also associated with colorectal cancer risk for DNA mismatch repair gene mutation carriers?</i></p> <p>26. Population Health Congress. Adelaide, Australia. 11 Sep 2012. <i>Second Primary Cancers in Lynch Syndrome.</i></p>
<p>8</p>	<p>Please provide any other information of note, eg awards etc.</p> <p>I am the 2013 Winner of the Premier's Award for Health & Medical Research awarded by the State Government of Victoria.</p>
<p>9</p>	<p>Have you received any other funding for your scholarship project? <i>Please give details (amount, funding source and any other relevant information)</i></p> <ol style="list-style-type: none"> 1. AEA Travel Award from the Australasian Epidemiological Association, 2011: \$2,500 <i>Travel grant for visit to the 12th International Congress of Human Genetics and the 61st American Society of Human Genetics Annual Meeting (Montreal, Canada; Oct 2011).</i> 2. Student Travel Bursary Award from the Australasian Epidemiological Association, 2011: \$400 <i>Travel grant for visit to the Australasian Epidemiological Association Annual Conference (Perth, Australia; Sep 2011).</i> 3. Public Health Initiative for Research Student Training (PHIRST) Award from The University of Melbourne, 2011: \$900 <i>Travel grant for visit to the Australia New Zealand Gynaecological Oncology Group (ANZGOG) Annual Meeting (Gold Coast, Australia; Feb 2012)</i> 4. Melbourne Abroad Travelling Scholarship (MATS) from The University of Melbourne, 2012: \$1,500 5. M.A. Bartlett Research Scholarship Fund Special Travel Grants-In-Aid from The University of Melbourne, 2012: \$200 <i>Travel grants for visits to the USA universities and institutions (Fred Hutchinson Cancer Research Center, Mayo Clinic, University of Southern California) for research presentations and academic collaborations.</i> 6. Population Health Congress Travel Award from the Australasian Epidemiological Association, 2012: \$450 <i>Travel grant for visit to the Population Health Congress (Adelaide, Australia; Sep 2012).</i>

7. Public Health Initiative for Research Student Training (PHIRST) Award from The University of Melbourne, 2012: \$300
Support to attend a short course on analysis of longitudinal and correlated data (Victorian Centre for Biostatistics, Australia; Feb 2013).
8. Picchi Award for Excellence in Cancer Research (Top Applicant in 2012) from the Victorian Comprehensive Cancer Centre, 2012: \$10,000
Travel grant for visits to the American Association of Cancer Research Annual Meeting (Washington DC, USA; Apr 2013) and the 63rd American Society of Human Genetics Annual Meeting (Boston, USA; Oct 2013).
9. Richard Lovell Travelling Scholarship from The University of Melbourne, 2013: \$10,856
Travel grant for visits to Korea (Seoul National University and National Cancer Center) and UK universities (University of Cambridge, Newcastle University, University of Leeds, University of London, and University of Edinburgh) for research presentations and academic collaborations.

10 Certification by Scholarship Holder

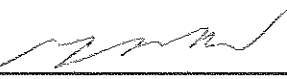
I confirm that the above details are correct.

Signature:  Date: 4/3/2014
Dr Aung Ko Win

11 Certification by Supervisor

I confirm that the above information provided by Dr Aung Ko Win is accurate. His progress is appropriate and I expect that he will submit his thesis by December 2013

Other comments: (optional)

Signature:  Date: 4/3/14
Name of supervisor: Professor Mark Jenkins

If you need to apply for a scholarship extension, please email maria.nuguid@cancervic.org.au for details of the process and what you will need to provide.