**Annual Research Report, Epworth Dermatology 2013/2014**

Dermatology research at the Epworth has a stellar year in 2013/2014, cementing its position as Australia’s Centre of Excellence for Dermatology Research, Clinical Trials, Education and Patient Care.

Highlights included winning the bid to host the World Congress of the International Society of Dermatology in Melbourne in 2021; Professor Sinclair being invited to deliver the Plenary Lectures at the World Congress of Hair Research in Korea in 2014, the International Hair Restoration Society Meeting in Malaysia in 2014 and to Chair the Symposium on Androgenetic Alopecia and Telogen Effluvium at the World Congress of Dermatology in Vancouver in 2015; research published in 2012 triggering a 2014 Commonwealth House of Representatives Parliamentary inquiry into Skin Cancer in Australia, ground breaking research published in the Proceedings of the National Academy of Science identifying a single molecular pathway in the skin that modulates both hair growth and fat tissue, a review article featured on the cover of the prestigious British Medical Journal; the discovery of the link between skin cancer and internal malignancy; graduation of 2 PhD students and one Master of Medicine Student through the University of Melbourne and graduation of an International Medical Graduate as a Fellow of the Australasian College of Dermatologists.

**Research**

In the past year the team of scientists and clinicians at Epworth Dermatology published 26 original articles in peer reviewed scientific journals as well as 10 book chapters in multi-author dermatology textbooks and a the dermatology textbook *Diseases of the Hair and Scalp*.

Articles were published in leading international and national journals including PNAS, British Medical Journal, Australian Medical Journal, Cancer Epidemiology and Biomarkers, Journal of Investigative Dermatology, British journal of Dermatology, Journal of Clinical Oncology and F1000 research. With a cumulative impact factor over 100 this past year, Epworth Dermatology has the best publication track record in Australia for 2013/2014 and better than all the Victorian Public Hospital Dermatology Departments combined.

Chapters were contributed to the leading international medical textbooks including the Oxford Textbook of Medicine, Dr Groot’s textbook of Endocrinology and Rook’s Textbook of Dermatology.

Epworth Dermatology was the leading centre in Victoria for graduating students with research higher degrees in 2013/14.

Dr Anousha Yazdabadi graduated Doctor of Philosophy (PhD) from the Faculty of Medicine at the University of Melbourne. Her thesis on the androgenetic alopecia identified the mechanism that underlies the pattern of hair loss seen in common baldness and her work is now the cornerstone of early diagnosis of baldness, which is critical to effective treatment.

Dr Juan Lu graduated Doctor of Philosophy (PhD) from the Faculty of Engineering at the University of Melbourne. Her thesis describes a validated automated mechanism for scoring psoriasis severity from digital photographs. Manual scoring is currently used for allocation of approximately $500 million dollars of PBS funded biological therapy for patients with severe
Dr Eshini Perera graduated Master of Medicine form the University of Melbourne (M Med). Dr Perera investigated the prevalence of actinic keratosis in Australia cost of treatment. This was a continuation of the work investigating the prevalence of Skin Cancer in Australia published in The MJA in 2012 that led to a Parliamentary enquiry into skin Cancer in Australia. Dr Perera’s research was presented as evidence to the enquiry in 2014.

Ongoing student projects.

- Dr Niloufar Torkamani is a University of Melbourne research scholar in the second year of her PhD. Her project is an Anatomical study of the arrector pili muscle in normal and diseased hair. The arrector pili muscle links the hair follicle to the surrounding skin, connecting to the follicle at a stem cell compartment known as the bulge. Dr Torkamani is investigating the role of arrector pili muscle degeneration in hair loss disorders. She has found that the muscle degenerates and is replaced by fat tissue in androgenetic alopecia, but not in telogen effluvium, suggesting that arrector pili degeneration may be associated with permanency of hair loss. This novel finding has been published in the British Journal of Dermatology. More recently, Dr Torkamani has obtained evidence that epidermal stem cells are located at the distal end of the arrector pili muscle, suggesting the muscle may help to define a niche for these stem cells, as the proximal end of the muscle does for hair follicle stem cells.

- Dr Jane Li is a University of Melbourne Scholar in the second year of her PhD studies. Dr Li is Victoria’s first student selected in the combined PhD/FACD programme, a pioneering project that aims to graduate future clinical and academic leaders in Dermatology. She is undertaking her research under the co-supervision of Australia Fellow Prof. Frank Carbone (Department of Microbiology and Immunology, Melbourne University). Her project is entitled The role of skin resident memory T cells in alopecia areata. Alopecia areata is an autoimmune hair loss disease. It is the most common autoimmune disease in humans. Dr Li is characterising the role of a recently discovered type of immune cell, tissue resident memory T cells, which provide an immunological ‘memory’ and so may be important in the relapsing character of alopecia areata. Dr Li has found T-cells of the resident memory subtype surrounding the lower hair follicle in alopecia areata skin with active hair loss. These cells were not found around the lower follicle in normal skin, and were rare in from alopecia areata skin that was distant from the site of hair loss, or in which hair had regrown. Thus the presence of resident memory T-cells around the lower follicle correlates with active hair loss. Evaluation of the activation state of these T-cells in alopecia areata skin is underway. Laser capture microdissection will be used to isolate the lower follicle and surrounding cells. A panel of 96 marker genes have been selected, for which expression will be evaluated.

- Dr Agnes Rosarina Prita Sari. M.Phil., is an international scholar at the University of Melbourne. He project is entitled Enhancing expression of hair induction markers in human dermal papilla cells. Dermal papilla cells are able to induce new hair follicles when implanted into the skin. The use of human papilla cells to treat hair loss is limited because they lose this property when grown in culture. In contrast, we have found that papilla cells from sheep robustly retain their hair-inducing activity, and the associated ability to form three-dimensional papilla-like aggregates in culture. Dr Sari is further characterising the aggregation of ovine papilla cells and exploring whether they secrete signalling molecules that enhance the aggregation of human cells. She has shown that ovine cells express a series of molecular markers seen in dermal papillae in vivo, confirming the physiological authenticity of these aggregates. She has found that human cells incorporate into aggregates formed by ovine cells.
when combined in the same culture dish, showing that human cells are able to respond to pro-aggregative signals. She has found that human papilla cells grown in lamb serum exhibit enhanced aggregative behaviour, and has preliminary evidence that aggregation is further enhanced in the presence of molecules secreted by ovine cells. This work is relevant to the field of hair cloning, a proposed alternative to hair transplantation.

- Dr Eugene Ong. Is in the second year of his D. Phil studies in the Department of Public Health at Oxford University in the UK. He is co-supervised by Professor Sinclair who was in Oxford 1991-1993. This primary research project is entitled: Risk of Internal malignancy following skin cancer. Dr Ong has investigated whether people affected by skin cancer are also susceptible to internal malignancy. He analysed the incidence of internal malignancy in 500,000 people affected by skin cancer and found that they were 30% more likely to develop internal malignancy. The main internal malignancies were salivary gland cancer, bowel cancer, bone cancer, nasopharyngeal cancer and leukaemia. The risk of cancer was especially high in people who developed their skin cancer at a young age. The relative risk of cancer in people who developed a skin cancer aged 25 (not uncommon in Australia) was 23. To put this in context, the risk of developing lung cancer after smoking a packet of cigarettes each day for 49 years is 12. His publication in Cancer Epidemiology and Biomarkers has already led to a major change in clinical practice in Australia with respect to patient follow-up post diagnosis of skin cancer and was presented as evidence to the Commonwealth Parliamentary Inquiry into Skin Cancer in Australia.

- Dr Mahsa Rashidi is a University of Melbourne PhD Scholar. She is Investigating the myogenic potential of skin-derived mesenchymal stem cells. After completed her experimental work in the laboratory of Dr Terrence Partridge, at the Children’s National Hospital, Washington DC, USA, Dr Rashidi is now writing her thesis. She investigated the reprogramming of stem cells from the hair follicle dermal papilla to a skeletal muscle phenotype. Several stem cells are capable of muscle differentiation in vitro, incorporating into myotubes when co-cultured with differentiating myoblasts. However similar differentiation is much more difficult to achieve in vivo. Dr Rashidi investigated the possibility of treating papilla cells with bioactive molecules to enhance their myogenic potential. She developed a novel cell tracing method that allowed her to quantify the efficiency of papilla cell incorporation into myotubes. She found that purmorphamine, an agonist of the Sonic hedgehog signalling pathway, appeared to enhance the myogenic differentiation of papilla cells.

- Dr Azar Asgari is an NHMRC scholar. She is in the fourth year of her PhD studies at the University of Melbourne. Her research has investigated Hair follicle cells and regenerative medicine. Dr Asgari has completed her experimental work and is now writing her thesis part-time. She investigated the potential of follicle stem cells to be reprogrammed to cardiac muscle, and also to contribute to skin wound healing. She found that these cells can adopt a skeletal muscle phenotype in culture, but not cardiac muscle. She also showed that cells migrate up to 1 mm from follicles to contribute to wound healing. The presence of follicles near a wound accelerated wound closure and facilitated innervation of the healing tissue.

- Dr Niyati Sharma. M.Med., University of Melbourne. Non-melanoma skin cancer in Australia. Dr Sharma investigated the prevalence and cost of non-melanoma skin cancer in Australia, and the trends in incidence. She demonstrated that while skin cancer is still increasing in those over the age of 60, the incidence and prevalence are reducing in younger Australians. This coincides with the introduction of the Sun Smart campaign by the Cancer Council of Victoria. She correctly predicted that in 2014 there would be nearly 1 million skin cancers treated in Australia among a population of 23 million people, at a cost to the Commonwealth
Government of almost $1 billion annually. Her publication in the MJA in December 2012 triggered a Parliamentary enquiry into Skin Cancer in Australia that is ongoing.

**Clinical Trials**

Epworth Dermatology has one of the largest centres for sponsored clinical trials in Australia, with over 80 patients currently participating on phase II and III clinical trials. Phase I clinical trials are conducted in collaboration with Nucleus Network. Epworth Dermatology has extensive experience in clinical trials in psoriasis, atopic dermatitis, skin cancer, actinic keratosis, cellulitis and infection of the skin, alopecia and nail infections (onychomycosis).

**Ongoing Clinical trials include:**

- **Merck Sharp & Dohme, Protocol No. MK-3222-010.** A 64-Week, Phase 3, randomized, placebo-controlled, parallel design study to evaluate the efficacy and safety/tolerability of subcutaneous SCH 900222/MK-3222, followed by an optional long-term safety extension study, in subjects with moderate-to-severe chronic plaque psoriasis.

- **Astellas, Protocol No. 7163-CL-0107.** A Phase 2a, randomized, double blind, placebo-controlled, sequential, multiple-dose escalation study to evaluate the safety, efficacy, pharmacokinetics and pharmacodynamics of ASKP1240 in subjects with moderate to severe plaque psoriasis.

- **Amgen, Protocol No. 20120263.** A Phase 3, multicenter, randomized, double-blind study evaluating the efficacy and safety of ABP 501 compared with adalimumab in subjects with moderate to severe plaque psoriasis.

- **Celgene, Protocol No. CC-10004-PSOR-010.** A Phase 3B, multicenter, randomized, placebo-controlled, double-blind, double-dummy, study of the efficacy and safety of Apremilast (CC-10004), Etanercept, and placebo, in subjects with moderate to severe plaque psoriasis.


**Education**

In addition to being Victoria’s leading centre for Dermatology research higher degrees, Epworth Dermatology participates in Dermatology registrar training, Medical Student Teaching, General Practitioner Education, as well as patient education.

Epworth Dermatology was accredited by the Australasian College of Dermatologists in 2013 as a centre for specialist training in Dermatology. In 2014 Dr Samantha Eisman was awarded her Fellowship of the Australasian College of Dermatologists. Dermatology trainees due to complete in 2014 are Dr Deepani Rathnayake and Dr Ilsphi Browne.

Epworth Dermatology has acquired a multi-headed microscope for dermatology registrar pathology teaching. Dermato-pathology is complex subspecialty of pathology and dermatology
registrars are examined in pathology as part of their Fellowship exams. Weekly teaching in pathology is available at the Epworth Dermatology Centre.

Having been the lead author in the Versions 1, 2 and 3 of Therapeutic Guidelines Dermatology, Professor Sinclair stood down from the committee that will develop Version 4 in 2014. He is replaced by Dr Leona Yip, FACD form Epworth Dermatology.

Epworth Dermatology runs numerous GP education evening events throughout the year as well as the GP education days 3 times a year. Dermatologists form Epworth Dermatology are also regular contributors of review articles in Dermatology to Australian Family Physician, Medical Observer and Australian Doctor.

Epworth Dermatology are a content partner to the Victorian Government Better Health Channel. This provides Victorians with relevant and reliable information on a range of skin diseases. With over 180,000 hits to the Epworth Dermatology content pages each month, the Epworth is a major contributor to patient education.

**Patient Care**

With a new, state of the art Dermatology Centre opening at 2 Wellington Parade in early 2014, Dermatologists affiliated with the Epworth are able to provide 24 hour support to patients admitted to the Epworth with skin disease or with skin complications of surgery or other medical illness. The Epworth is the only private Hospital in Victoria that offers this cover.

Epworth Dermatology offers sentinel lymph node biopsy for patients diagnosed with melanoma and participates in the Melanoma Multidisciplinary Clinic at Epworth Box Hill.

With 7 consultant dermatologists, 2 Fellows and Plastic Surgeon Miki Pohl, Epworth Dermatology provides rapid access to specialist care for patients with suspected skin cancer and screening for high risk patients.

Patient needs drive our teaching and research at the Epworth Dermatology Centre for Research and Clinical Trials. We are grateful for the support we receive form The Epworth Hospital Research Endowment, The NHMRC, Aus Aid, The University of Melbourne, Australasian College of Dermatologists Research Fund, The F and E Bauer Research Fund, the Margaret Walkom endowment, , the Ross Foundation, the Alopecia Areata Australia Foundation and Sinclair Dermatology.

We are also pleased to announce the recent award of over $120,000 for Perpetual trusts to trial a new intervention to prevent chemotherapy induced hair loss. Many patients find chemotherapy induced hair loss stigmatizing and humiliation and we are striving for ways to alleviate the distress experienced by patients undergoing chemotherapy for cancer.

Professor Rodney Sinclair

Director of Dermatology

Epworth Healthcare