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Wound Management Innovation Cooperative Research Centre – a new model for inter-disciplinary wound research

Wound research is a complex multidimensional activity most effectively conducted by inter-disciplinary teams that connect studies in basic wound biology, devices and biomaterials with clinical practice. These complexities have been recognised in a new initiative through the establishment of an inter-disciplinary wound research centre in Australia; the Wound Management Innovation Cooperative Research Centre (WMI CRC). The Centre is funded by the Australian Government's Cooperative Research Centre Program and a consortium of 22 participants and has a resource of US\$108 million over 8 years.

The principle under which the centre is funded is that Government funds are matched by cash and in-kind resources from participants in the research centre. Participants include universities and research centres (Queensland University of Technology, Curtin University, University of South Australia, University of Western Australia, Southern Cross University, University of Queensland, Womens and Childrens Health Research Institute and Flinders University), health departments (South Australia, Victoria, Queensland, Western Australia including Wounds West), nursing agencies (Silverchain, Bluecare, Royal District Nursing Services in Victoria and South Australia), companies with an interest in wound care and skin integrity (Tissue Therapies, Smith & Nephew, Ego Pharmaceuticals) and Hospitals (Wesley Centre for Hyperbaric Medicine, Gallipoli Medical Research Foundation). The Australian Wound Management Association is also a Participant.

The Centre is established under an agreement between Participants and is managed by an independent Board (Chaired by Dr Peter Riddles) and a management company. Intellectual property generated within CRC projects is owned by the project participants who also have responsibility for its development. Advice is provided to the Board and management team by a Scientific Advisory Committee (Chaired by Professor Keith Harding) and an Education Advisory Committee (Chaired by the CEO).

The philosophical approach is to develop cross-organisational and inter-disciplinary projects, particularly connecting researchers and end-users. The research tends to be more at the application oriented end of the research spectrum and a critical element is to identify a path to impact early in the life of projects. However, there are some smaller projects exploring the more esoteric areas of wound research.

The Centre commenced activity in mid-2010 and is now moving from the establishment phase into full operations. The research is conducted in Participant organisations in 5 Australian cities involving approximately 150 people comprising 65 effective full time researchers. As at the start of 2012, there are 30 projects in place in three research programs; Enabling Technologies (Program Leaders, Professor Zee Upton and Dr Gary Shooter), Tools and Therapies (Program Leader, Dr Sherry Kothari) and Clinical Application (Program Leader, Professor Helen Edwards). Project outcomes flow from wound biology studies into tools and therapies, then into clinical practice; giving strong links

between the clinic and the laboratory. Prototype products from the research will be taken through proof of concept clinical trials in the Participants' wound care clinical environments. There is also a strong focus on post-graduate training with the current projects involving 25 postgraduate students.

The research in Program One, 'Enabling Technologies', aims to improve the understanding of how various genes, proteins, peptides, microorganisms and metabolites are involved in tissue repair and change and influence wound healing and recurrence. The key outputs from this program include: a world-first dataset that identifies key protein and genetic components in acute and chronic wound healing; and novel preclinical models for assessing wound therapies. This research will underpin wound diagnostic development and the identification of candidate targets for new therapies and bioactive compounds. The program has 4 major project streams:

Proteomic and Metabolic Analysis of the Wound Environment: A complete analysis of the dynamic changes in wound environments based on state-of-the-art proteomic and metabolomic measurements of sequential wound fluid and tissue biopsy samples (with associated clinical data) is being undertaken. This will create a world-first database of changes in the molecular physiology associated with wound healing in many different wound types. The key objective is to identify biochemical indicators of healing status and potential therapeutic targets - these will be validated using robust molecular, biochemical and cellular approaches.

Analysis of Microbial Load in Wounds: Advanced molecular tools are being used to identify key indicators of delayed wound healing caused by bacterial infections, particularly those involving biofilms. In particular, novel DNA genotyping methods are being applied to determine the relationship between microbe strain types and the wound healing process, and to monitor any changes that might occur in the microbial populations before, during and after treatment.

Genetic studies to identify new therapeutic targets and biomarkers: Susceptibility to chronic wounds and poor healing outcomes of all wounds is influenced by genetic factors. This study is the first in the world to apply genome-wide association studies to analyse variations in an extensive library of DNA samples (collected from venous ulcer and burns patients with defined clinical outcomes and controls). This will lead to new diagnostics, tailored interventions, improved decision making paradigms and treatments for wounds and prevention of scarring.

Development of improved models for pre-clinical testing: Numerous difficulties are associated with conducting pre-clinical studies on skin products and therapies. Use of small animal models such as rodents, is not optimal due to their physiological differences to human skin and mode of wound healing. Pigs have previously been used due to their human-like mode of healing, but the expense and logistics related to their use also renders them sub-optimal. This project is employing state-of-the-art techniques to develop improved models for pre-clinical testing of new therapies and skin integrity products, including the further development of 3D human skin equivalent models constructed in the laboratory using human skin discarded from surgical procedures.

The outputs from Research Program 2, 'Tools and Therapies' are directed at the development of advanced dressings and delivery systems as well as providing clinicians and healthcare personnel with safe, reliable and easy-to-use, point-of-care diagnostic and prognostic tools. These will help to better inform treatment modalities and consequently, dramatically improve healing outcomes. There are three major directions in this Research Program.

The development of novel dressings and scaffolds: Advanced biomaterials engineering is being used to develop new technologies which can be incorporated into dressings to indicate the healing status of a wound or to deliver bioactive molecules or cells to the wound. The aim is to release of the bioactives in a controlled and sustained manner, perhaps even responding to changes in the wound environment. These 'smart dressings' will enable administration of the appropriate bioactive, at the most appropriate dose, at the right time and directly to the wound.

Diagnostic platforms: In this project tools are being fabricated incorporating "biological recognition", whereby it is possible to detect, at extraordinary low levels, biomolecules that are indicative of a deteriorating wound or of the early signs of infection. This "recognition event" will be converted (transduced) into a change that can be read by patient, clinician or healthcare provider.

New Bioactives: A search for new bioactive molecules that promote wound healing is being conducted based on a novel ethnographic approach using Australia's unique flora.

The above advances will have a significant impact on the ability of patients to manage their own wounds and improving healing in long-established wounds. The diagnostic/prognostic tools will also help clinicians and healthcare providers to make quick and better-informed decisions, while these bandages will provide a new class of therapies for the treatment of wounds.

The Tools and Therapies research program provides a bridge between the fundamental discoveries of wound pathways and new biomolecules in Program 1 (Enabling Technologies) and Program 3 (Clinical Applications) which will improve the quality and consistency of care provided to patients.

Research Program 3 is focussed on the generation of evidence relating to processes, methodologies and technologies that lead to the early healing of wounds, reduce scarring and to prevent the occurrence and recurrence of wounds, particularly in the community setting. The key outputs from this Research Program include proof-of-concept clinical studies of new therapies, dressings and diagnostic tools; assessment tools to identify those at a high risk of developing wounds or hypertrophic scarring; validated prevention strategies; and the validation of the efficacy of new technologies and care pathways in clinical settings.

Diagnostic and prognostic tools and therapies developed in Programs 1 and 2 will be incorporated into the best practice models developed and evaluated in Program 3. This will add cutting-edge innovations to models that capture the best of existing practices, enabling clinicians and health professionals to provide vastly improved patient care.

The three streams of activity in Program 3 are as follows:

Proof-of-Concept trials and Clinical Trials: Approaches to wound management that have demonstrated an impact on wound healing/scar reduction in preclinical evaluations are being evaluated in randomised, placebo-controlled clinical trials to determine the extent of their influence on wounds. Strategies being evaluated include hyperbaric oxygen therapy for venous ulcers, modulating proteins that are associated with wound/hypertrophic scar susceptibility; reducing the dressing-wound interface pressure; modifying psychosocial risk factors; exercise and positioning programs using remote monitoring; modifying tissues beneath the skin with strategies such as electrical stimulation; and modifying pressure delivered by compression bandages using sensors.

Development of Risk Assessment Tools for Wound Occurrence/Recurrence and Scarring: Ground breaking wound risk-assessment tools are being developed from longitudinal (months to years) studies evaluating combinations of factors including genetics, dermal thickness/condition, skin oxygenation, interface pressures and psychosocial variables. Identifying individuals at high risk of developing wounds, hypertrophic scarring, or wound recurrence will enable appropriate, targeted and cost effective use of preventative strategies.

Education, Training and Awareness: An education program that strengthens consumer engagement through building awareness of wounds and empowering patients and their families to make informed decisions about their care is an integral part of the proposed CRC. Research outputs will be incorporated into short-course training to enhance the competencies of community nurses, GPs, care workers in residential aged care facilities and those health professionals that service remote communities. Materials (including guidelines) will be developed to assist patients and their families to understand and perform best practice self-managed care. CRC participants Wounds West and the peak body for the industry, the Australian Wound Management Association will assist in developing and delivering education and training.

The research is truly inter-disciplinary including proteomics, molecular biology, genetics, wound biology, cell biology, microbiology, biomaterials, sensor technology, wound management, health economics, clinical trials and risk assessment.

The WMI CRC works closely with the Australian Wound Management Association in initiatives to enhance wound awareness at the political, professional and community level. The Centre also supports the Joanna Briggs Institute Wound Healing and Management node at Curtin University.

With the major projects established and operational the Centre is now planning longer term outcomes and legacies. These include products under development, spinoff companies, best practice wound management systems, heightened political awareness and an increased wound R&D capability and capacity. The establishment of a sustainable National Australian Wound Research Centre remains an aspirational goal.

This is a novel and exciting approach to wound management research that has the potential to deliver substantial benefits to the wound care community through new products and enhanced patient care.

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