Enabling Technologies

OMICS

The OMICS approach applies cutting-edge analytical methods to comprehensively profile biological molecules in the body such as proteins and metabolites. These molecules (biomarkers) unmask dynamic biological processes within the body. Using such tools, the WCIT programme aims to discover biomarkers that provide unprecendented insight into wound healing processes, specifically in hard-to-heal wounds for which our knowledge remains limited. These biomarkers will in turn be translated into candidates for diagnostic, prognostic, or therapeutic applications to improve monitoring and management of such wounds.

Guided by findings from an earlier Caucasian clinical cohort in Australia, WCIT aims to investigate chronic wounds in an Asian, multi-ethnic Singaporean cohort using our established OMICS technologies. The programme currently focuses on two main chronic wound etiologies, diabetic foot ulcer (DFU) and venous leg ulcers (VLU). The key distinguishing feature of WCIT is its longitudinal design which monitors chronic wounds over 12 weeks. This allows us to closely track the changes in biomarker levels and relate them to changes in wound healing. Our OMICS analyses currently focus on the following biological molecules:

Proteins (Proteomics)

- Proteomic profiles are obtained from untargeted data-independent acquisition using high-resolution and high-sensitivity mass spectrometers
- Quantification of protein abundances reveal dynamic changes during wound healing, with high translational outcome due to the longitudinal study design

Small molecules/metabolites (Metabolomics)

- Broad range of metabolites (e.g. amino acids, lipids) are quantified with high throughput and multiplexed liquid chromatography-tandem mass spectrometry
- Cross-mapping of metabolite changes with biological pathways provide a window into wound healing biology
- Profiling of microbial and human-microbial metabolites will assist investigation of complex host-microorganism interactions

Wound microbes (Metagenomics)

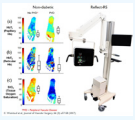
- Microbial communities in wound fluid and biofilm will be analysed via whole genome shotgun using Illumina® NextSeq® platform for unparalled throughput
- Taxonomical (e.g. species and strains) and functional (e.g. antimicrobial resistance genes) correlations to wound healing will guide future clinicians in wound antimicrobial management

Photoacoustic (PA) and Diffuse Optics Based Imaging and Raman Spectroscopy Platform for Wound Care Management

Novel non-invasive photonics technologies developed by Professor Malini Olivo and team at Singapore Bioimaging Consortium (SBIC), A*STAR, for accurate imaging and analysis of wounds include:

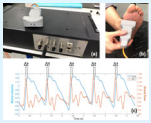
Multispectral Optoacoustic Tomography (MSOT)

- Contact based imaging system which uses multiple wavelengths of light (660-1300 nm) to provide anatomical, functional and molecular information
- Capable of detecting various endogenous chromopores, including haemoglobin, lipids and melanin
- Provides detailed images of skin and wound architecture as it can image up to a depth of 1-2 cm, depending on transducer



Spatial Frequency Domain Imaging (SFDI)

- A contactless portable imaging system that utilizes multiple wavelengths of light to image large areas (20 cm x 15 cm)
- Short exposure time (5-60 ms) and acquisition time (1 s or 25 s)
- Provides functional information, including oxygen perfusion up to a depth of 3 mm,

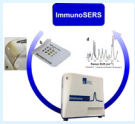


Diffuse Speckle Pulsatile Flowmetry (DSPF) System (Haloflow)

- Deep penetration: 1 – 20 mm underneath the skin
- Simultaneous measurement of blood flow and blood volume
- Fast measurement rate: >300 Hz, remove the 'heart-beating noise'
- Portable device with a flexible hand-held probe

Advantages

- Accurate and non-invasive
- Ability to analyse oxygenation and other important parameters that cannot be visualized via the naked eye
- Validated technology in clinics



Surface Enhanced Raman Spectroscopy (SERS) Sensor (ImmunoSERS)

- *In-vitro* biosensing platform of wound biomarkers
- State-of-the-art flexible elastomeric film based SERS sensor, 5x5 mm active area with randomly arranged Ag nanoparticles for the detection of biomarkers
- Portable Raman reader that can provide multiple biomarker concentration from a single flexible film sensor

Advantages

- Sensitive *ex vivo* analysis of wound exudates
- Ability to detect multiple biomarkes
- Potential to incorporate into wound dressings