

## TRANSFORMING CRITICAL CARE THROUGH RESEARCH



550+

Manuscripts and publications



400+

International collaborating sites



\$40M+

Competitive Grants

- Largest critical care research group in Australasia with largest preclinical ICU in the Southern Hemisphere
- Unique location within the grounds of Australia's leading cardiothoracic hospital
- Holistic and multi-disciplinary approach to translational research: Clinicians, Scientists, Engineers, and Data Scientists with admin support team
- Strong industry partnerships across education, private and notfor-profit sectors

"We founded the Critical Care Research Group in 2004. The purpose behind the group has not changed—we're about changing patient outcomes through a better understanding of the disease process, of the technology and of the treatment."

Clinicians

Improved treatment outcomes

Scientists & Engineers

**Patients** 



**John Fraser**Founder & Director

## CCRG FELLOWSHIP PROGRAMME FAST FACTS

- CCRG accepts expressions of interest to join the Fellowship Programme year-round.
- Applications are considered by our Senior Leadership Group based on academic merit in conjunction with the current vacancies and research priorities of the Group.
- Following the initial interview, if the applicant is deemed appropriate, applicants will be introduced to CCRG Fellows and will be required to demonstrate writing skills by completing a task such as a systemic literature review of the agreed research priority.
- The CCRG Fellowship is a nonremunerated position. Candidates
  will be supported in applying for funding through various grants
  and initiatives, however it is the responsibility of the Fellow to
  proactively seek funding to cover costs, including living and
  relocation costs, as required.
- The primary responsibility of Research Fellows is to conduct research in collaboration with the wider CCRG team and contribute to the advancement of the Group's shared research goals. It is expected that Fellows contribute to grant writing, review and develop manuscripts, and give presentations on the Group's research.
- The minimum term of a CCRG Fellowship is one year, although a two-year term is preferred. During this time the CCRG Fellow will work on the predetermined research project/s as identified during the recruitment process.
- CCRG is based at The Prince Charles Hospital (TPCH), a major teaching and tertiary referral hospital in Chermside, a northern suburb of Brisbane, Australia. TPCH is a public hospital operated by Metro North Health, the largest health service provider in Queensland Health. CCRG Fellows are expected to have a minimum 40 hours of contact in the CCRG offices/labs at TPCH per week.
- Fellows must provide written confirmation from their home institution showing they are authorised to complete their Fellowship in Australia. It is also the responsibility of the incoming Fellow to apply for and receive all necessary documentation, including visas, and comply with the requirements of enter Australia and the right to undertake the predetermined work.



## TODAY'S RESEARCH TOMORROW'S TREATMENTS

CCRG is a springboard to some of the most sought after research positions in the world. From world renowned universities to cutting edge science institutes, CCRG Alumni go on to hold senior positions and reach incredible advancements in many fields of medical research all while improving the lives of critically ill patients.

#### As a CCRG Research Fellow you will:

- Participate in clinical trials and preclinical studies
- Contribute to life-changing translational research that increases clinicians understanding of critical illnesses
- Have access to state-of-the-art facilities, world-renowned mentors and a supportive admin and management team
- Have a streamlined pathway to a career in academia and research
- Have access to world-leading tertiary education providers including The University of Queensland, Queensland University of Technology, Monash University, Bond University, and Griffith University



#### ORGAN SPECIFIC BIOMARKERS FOR MULTI-ORGAN FAILURE

Use new discoveries of genetic biomarkers to detect organ-specific injury in preclinical and clinical cohorts.

#### The Living Heart Project - THE USE OF HMP IN HEART TRANSPLANTATION

Revolutionising heart transplantation through hypothermic machine perfusion (HMP). The next phase of The Living Heart Project will investigate the use hearts donated after circulatory death.

#### **PULSATILE ECMO**

Work on a novel ECMO machine to examine the interaction and consequences of various blood flow conditions in a preclinical model of cardiogenic shock and with a world-renowned mock circulation loop.

#### SHOCK STATES

Use novel models of septic, cardiogenic and hemorrhagic shock to investigate the impact of resuscitative therapies - volume expansion, resuscitation fluids and vasopressors - on endothelial dysfunction and end-organ injury.

#### **NOVEL THERAPEUTICS FOR SEVERE ARDS**

Examine the effect of an innovative therapeutic strategy, in which hydrogen gas is systematically administered through ECMO, for severe ARDS requiring VV-ECMO in a clinically relevant ovine model of sepsis-induced severe ARDS.

#### ROTARY BLOOD PUMPS (RBP)

Examine traditional RBP designs and test the efficacy of novel designs using accurate CFD models providing critical insights into the flow patterns within RBPs, complimented with experimental benchtop testing.



### **STARLab**

#### <u>Scientific & TrA</u>nslational <u>R</u>esearch Laboratory

#### **MISSION**

Focusing on Heart, Lungs, ECMO & Circulation, STARLab works to further our understand of the most serious health conditions facing critically ill patients.



"From its world-class laboratories, multidisciplinary team and extensive global reach, CCRG offers the perfect springboard into a research career."

#### **Dr Silver Heinsar**

EuroELSO Young Investigator 2022 Former CCRG PhD Research Fellow (Estonia)





#### **Heart Failure:**

- Cell Free DNA
- LV EF vs Strain
- RV EF vs Strain
- Acute Kidney Injury

#### **Cardiogenic Shock:**

- Biobank
- Biomarker

#### **Heart Transplant:**

- Cell Free DNA
- Drug discovery
- Mitochondria
- HEVP/BSD
- HEVP/DCD
- Metabolic/Vascular
   Biomarker
  - Kidney injury



#### **CIRCULATION**

- F Endotheliopathy
- Stem cell therapies
- Ex vivo | in vitro endothelial model
- Acute Lung Injury
- Haemorrhagic shock
- Septic shock



#### **ECMO**

- ► Novel pump design
- E-CPR/Cardiac arrest
- Differential hypoxia
- Immune response
- Fibrinolysis / Coagulopathy
- Small animal models
- Blood trauma



#### **LUNGS**

- Ex-vivo lung perfusion (EVLP)
- ARDS Subphenotypes
- Coagulation
- Fluid Imaging





- Heart Transplantation
- · Brain Stem Death
- Cardiopulmonary bypass
- Traumatic Brain Injury
- Cardiogenic Shock
- Septic Shock
- Haemorrhagic shock
- Transfusion-related acute lung injury
- Acute Respiratory Distress Syndrome
- VV/VA ECMO
- Invasive Mechanical Ventilation
- High Flow Nasal Cannula
- Chronic Heart Failure
- Ex Vivo Organ Perfusion

#### **ASSESSMENTS**

- Electron microscopy SEM and TEM
- Bioinformatics
  - Transcriptomics
  - Proteomics
  - Spatial transcriptomics
- Droplet Digital PCR
- Flow cytometry
- High-resolution Respirometry
- Sidestream Dark Field imaging (SDF)
- Electroanatomic mapping
- Cardiac MRI
- CT
- PFT
- Electrical Impedance Tomography
- Pressure-Volume Loop

- Echocardiography
- Speckle-tracking echocardiography
- Blood gases
- Microdialysis
- Haemodynamics



## PRIMELab PReclinical Innovative Medical Engineering Laboratory

#### **MISSION**

To develop and test the efficacy and safety of novel medical and surgical interventions.

#### **SPECIALIST TEAM**

- Intensivists
- Cardiologists & cardiothoracic surgeons
- Angesthetists
- Pneumologists
- Nurses & Respiratory Therapists

#### **FOCUS AREAS**

- Severe Cardiac Failure
- Heart Transplantation (HTx)
- Shock States
  - Novel models of septic and hemorrhagic shock
- Acute Respiratory Distress Syndrome (ARDS)
  - o Hydro-Rescue
- ECMO
  - Pulsatile ECMO
- Pulmonary Diseases and Imaging



This **international collaboration** aims to increase the number and quality of hearts available for transplant using **hypothermic ex vivo perfusion (HEVP).** 

Heart transplantation is the most effective therapy for end-stage heart failure but is severely limited by the chronic shortage of donor hearts. In 2021 only 26% of donated hearts were transplanted.\*

HEVP increases the "allowable" ischemic time for donor hearts by up to 9 hours - more than double the previous average.

Translated to clinical study in less than 5 years, including **36 HEVP HTx with 100% success rate.** 

**PHASE 2:** Investigate the use of HEVP for organ donations after circulatory death (DCD), to find a new source for organ donation and increase the 'pool' of available hearts, ultimately to save more lives.

# Recent HTx using HEVP: 8 hrs 47 mins ex-vivo



#### **2015-2016**

Developed advanced preclinical HTx model

#### **= 2017-2020**

4 years of preclinical programme (funded by NHMRC)

#### 2021-2022

Phase I: Clinical trial (Australia and New Zealand)

- 36 HTxs completed
- 100% success rate

#### Feb 2022

CCRG data used in the first ever xenotransplantation

#### Oct 2022

Successful HTx performed with ischemic time of 8hrs 47mins - longest found on record

#### 2022-2025

Phase 2 Clinical trial

#### 2023-2026

Second Preclinical programme: DCD



Alex Moroianu received a new heart through **The Living Heart Project**. Scan to learn more about her HTx journey.



## ICETLab Innovative Cardiovascular Engineering & Technology Laboratory

#### **MISSION**

To expedite the development of novel cardiovascular technologies while investigating challenges with existing devices

#### WHY

Mortality from cardiovascular disease is expected to rise exponentially over the next 20 years. Cardiovascular devices play an important role in managing these conditions, yet the pathway to clinical implementation for novel devices is convoluted and their subsequent uptake is often slow.

#### **FACILITIES & CAPABILITIES**

- Computational Fluid Dynamics (CFD)
- Custom Pump Controllers
- Particle Image Velocimetry (PIV)
- Rotary Moulding
  - Blood Circulatory Loop
- 3D Printing
- Left Ventricular Assist Device (LVAD)



## The IN-SYNC trial Bench to bedside translation timeline

#### 2018-2019

Model development

#### 2019-2023

Preclinical programme funded by Fresenius



#### 2024-2026

Australian clinical trial

#### **2023-2026**

Preclinical programme for device optimisation

#### \_ 2026 and beyond

International trial for efficacy





Scan or click on the image above to learn more



**IN-SYNC Chief Investigator** Dr Silver Heinsar was named as one of 12 ELSO Young Investigators in 2022, one of only a few researchers ever to receive the award twice.

The EuroELSO Young Investigator Award supports young research fellows to attend congresses of the various Extracorporeal Life Support Organisation (ELSO) chapters and present their scientific abstracts to the world's top ECMO leaders.

Silver Heinsar, MD

Heinsar et al. Intensive Care Medicine Experimental https://doi.org/10.1186/s40635-020-00303-5 (2020) 8:16

Intensive Care Medicine Experimental

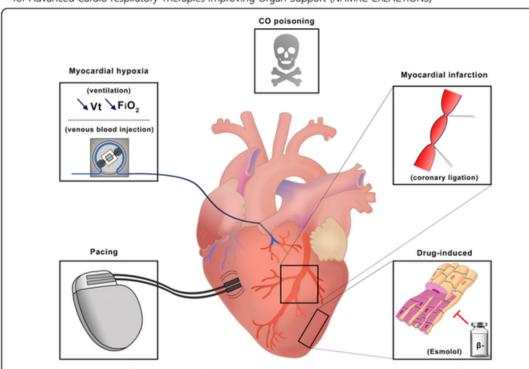
REVIEW Open Access

# Heart failure supported by veno-arterial extracorporeal membrane oxygenation (ECMO): a systematic review of pre-clinical models



**READ MORE** 

Silver Heinsar<sup>1,2†</sup>, Sacha Rozencwajg<sup>1,3\*†</sup>, Jacky Suen<sup>1\*</sup>, Gianluigi Li Bassi<sup>1</sup>, Maximilian Malfertheiner<sup>1,4</sup>, Leen Vercaemst<sup>5</sup>, Lars Mikael Broman<sup>6,7</sup>, Matthieu Schmidt<sup>2</sup>, Alain Combes<sup>2</sup>, Indrek Rätsep<sup>3</sup>, John F. Fraser<sup>1</sup>, Jonathan E. Millar<sup>1,8</sup> and on behalf of the European Extracorporeal Life Support Organisation (EuroELSO) Innovations Workgroup & the National Health Medical Research Council Australia Centre of Research Excellence for Advanced Cardio-respiratory Therapies Improving Organ Support (NHMRC CREACTIONS)



**Fig. 2** Representation of the five heart failure models that were used in our review. From left to right: ventricular pacing, myocardial hypoxia (through lowering of mechanical ventilation *or* perfusion of desaturated blood in the coronary arteries), CO poisoning, myocardial infarction, and drug-induced heart failure. CO, carbon monoxide; FiO2, inspired fraction of oxygen; Vt, tidal volume. Images were obtained from <a href="https://smart.servier.com">https://smart.servier.com</a> and are available under a creative commons license

# COVID-19 Critical Care Consortium



#### A GLOBAL COLLABORATION BORN FROM A GLOBAL CRISIS

Founded by **Professor John Fraser**, **A/Professor Gianluigi Li Bassi** and **Dr Jacky Suen**, the COVID-19 Critical Care Consortium brings together a global alliance of researchers and clinical personnel from **400+** hospitals and sites in over **60** countries.

Through data modelling, COVID Critical has been able to generate clinical insights about COVID-19, a disease that was completely unknown before January 2020.

**COVID Critical** has revolutionised the way data can be safely and securely shared across the world. This is health care without borders, without politics, and without financial gain.





#### **GLOBAL CONNECTIONS**

- World Health Organization
- Bill and Melinda Gates Foundation
- University of Oxford
- IBM & Aridhia Informatics
- Asia-Pacific, North American and European Chapters of the Extracorporeal Life Support Organisation

"During the pandemic, CCRG single-handedly assembled a global alliance of health care professionals to support those at the coalface. This will have an impact on the way medical research operates for generations to come."

#### Dr Leticia Helms MD

PGY1 Internal Medicine, Columbia Medicine Residency (Brazil/USA)



## ICU of the **FUTURE**



In partnership with medical research charity, The Common Good, the CCRG recently unveiled the world-first ICU of the Future, a project redesigning the Intensive Care Unit environment to be more patient-centric and recovery focused.

ICUs can be daunting places for patients and their families with up to 75 per cent of ICU patients globally experiencing anxiety, depression, or other physical, cognitive, or psychological problems. While the quality of care provided and survival rates in Australian ICUs are exceptional, the quality of a patient's life post-discharge can be suboptimal.

This ends now with new bed spaces unveiled at The Prince Charles Hospital, in a world-first model that is hoped will change the way ICUs operate and care for critically ill patients.

Silent







### CRIKEY: <u>Critical care Research International:</u> <u>K</u>nowledge, <u>E</u>vidence and be<u>Y</u>ond

March 8-10, 2023 | Gold Coast, Australia



CCRG hosted the inaugural **Critical care Research International: Knowledge, Evidence and beYond** (CRIKEY) Summit in 2023. The event saw international delegates come together in Australia for four days of tours, workshops, panel discussions and special events.

A first for the critical care community, CRIKEY was designed as a platform for robust conversations and a "Think Tank" for future research plans and new partnerships. We aim to encourage new, young leaders to emerge and through their growth, we can ensure the patients of tomorrow will benefit from experts that are borne through such collaborations.



86

Delegates



Countries represented



Stipends for early career researchers



Quality of speakers out of 5\*



Quality of content out of 5\*

\*based on feedback survey

"...I would like to commend you on organizing an **excellent scientific program** for the CRIKEY Summit. The event was highly informative and stimulating, fostering a productive atmosphere of collaboration and knowledge exchange."

- Delegate feedback

"Amazing congress. Thank you. Please keep involving EMCR to expose them to such expert opinions and help them form new ideas and build a support network."

- Delegate feedback

















CRIKEY was made possible with thanks to our sponsors:











"CCRG offers unique research possibilities found in a combination of engineering, biology lab, preclinical models and patients, all on one campus."

Professor Maximilian Malfertheiner Medical Director Lung Centre Donaustauf (Germany)

"CCRG has provided me so many opportunities to progress my research career...The work we do has the potential to make a real difference to the lives of critically ill patients and their families. And for that I am truly grateful."

**Dr Nchafatso Obonyo**CCRG Postdoctoral
Research Fellow (Kenya)

"Research is about solving problems through innovation. CCRG provided me with the opportunity to do just that, and more, while working alongside a highly skilled and motivated team."

## **Dr Lucia Gandini**Department of Pathophysiology and Transplantation University of Milan (Italy)

"The space where engineering meets healthcare is a very interesting field to be a part of... CCRG is the perfect place to



Simon Crilly
Queensland Brain Institute
University of Queensland
(Australia)

"This is true science to me... That's why I get excited..!"

Dr Mark Ogino MD
International President (2020)
Extracorporeal Life Support Organization
COVID Critical Steering Committee (USA)

"It is no exaggeration to say that working with CCRG profoundly changed my career... consider CCRG if you want to learn how to conduct your own research in an immersive and supportive environment."

Dr Kei Sato CCRG Postdoctoral Research Fellow (Japan)







Scan QR code or visit <u>ccrg.org.au</u> to read our **2023-24 Research Prospectus**.

Submit your expression of interest, including CV and cover letter, via our website <a href="mailto:ccrg.org.au/fellowships">ccrg.org.au/fellowships</a>.

All enquiries should be directed via email to <a href="mailto:tpch-ccrg@health.qld.gov.au">tpch-ccrg@health.qld.gov.au</a> or call +61 7 3139 6880.

















