

Preclinical research in critical care — the Australasian perspective

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“Look deep into nature, and then you will understand everything better.”

Albert Einstein

The Australia and New Zealand Intensive Care Society (ANZICS) and the Clinical Trials Group (CTG) have delivered a highly successful model for clinical intensive care research over the past 25 years. They have published many high-impact clinical trials, developed strong international collaborations and have successfully sourced research grants worth millions of dollars. All this has helped clinicians in deciding on the best care for critically ill patients, and has provided an efficient structure on which further large and complex, multicentre clinical trials can be undertaken.

Despite the success of such clinical intensive care research, preclinical research (eg, in-vitro studies, animal studies, biomedical engineering, experimental human models) has remained something of a “poor cousin”. A survey conducted by Laurie and colleagues in 2008 among the Fellows and trainees of the College of Intensive Care Medicine (CICM) revealed strong interest in clinically applicable basic science research, yet few responders review preclinical research in journal clubs, and even fewer report being involved in basic science research.¹

Preclinical research is relatively underrepresented at local scientific forums. At the ANZICS annual scientific meeting over the past 3 years (2012–2014), of 266 submitted abstracts, only 27 (10%) reported preclinical research (animal studies, $n=16$; in-vitro studies, $n=4$; biomechanics studies, $n=7$). Similarly, at the CICM annual scientific meeting over the same period, of 71 abstracts, only 13 (18%) reported preclinical research. This is in striking contrast to other large international meetings, where more than 75% of abstracts report preclinical research (Conference Committee chair, American Thoracic Society, personal communication, 2014). The ANZICS and CICM forums have an embedded opportunity for constructive feedback and encouragement within the Australasian context, and an increased representation may serve the dual goal of heightened interest and a greater recognition of the benefits of preclinical research.

Preclinical research is expensive, requires development of new techniques and is difficult to conduct and master, in part due to lack of protected time and poor access to appropriate facilities.^{2,3} Many preclinical studies have “neg-

ative” results of uncertain clinical relevance, which makes them unpopular to major journals and limits opportunity for further funding. Ultimately, this does not appeal to the upcoming generation of intensive care researchers. Furthermore, our appreciation of basic sciences seems to have diminished as contemporary medical training focuses on problem-based learning and evidence-based medicine.

Nevertheless, preclinical research is an important part of the ongoing development of intensive care medicine. It is essential for testing new devices and pharmaceuticals, conducting proof-of-concept studies and to better understand disease. Appreciating the scientific principles of a proposed therapeutic intervention enhances our ability to conduct and understand subsequent clinical trials. Ultimately, a longer-term investment in basic research pays off, in terms of key discoveries, almost twice as handsomely as other types of research and development combined.⁴ The importance of basic science research has been recognised by major funding agencies and international intensive care organisations. The United States National Institutes of Health, the world’s largest biomedical research agency, spends two-thirds of its research budget on fundamental biomedical research and has embarked on a program to encourage closer collaboration between basic, translational and clinical scientists.⁵ Such institutes have realised that preventing illness through molecular knowledge and interventions is the only viable strategy for maintaining the nation’s health in coming years.⁶ The European Society of Intensive Care Medicine has also recognised the disconnect between clinical and preclinical research and has started a dedicated journal for preclinical research, *Intensive Care Medicine Experimental*.⁷

The Australasian ICU community has the opportunity to build on their strong history of clinical research and move towards also becoming a world leader in preclinical research. This can be done by increasing awareness of preclinical research, incorporating preclinical studies with clinical trials, establishing dedicated funding sources via the CICM, ANZICS and the Intensive Care Foundation, and providing a forum for clinicians and scientists to interact, share experiences, collaborate in future research

projects, and to attract researchers from other parts of the world.

This approach can lead to a program of research which will move between benchtop, animal, healthy volunteer and small Phase II studies before embarking on definitive Phase III studies. This will emphasise the importance of the mechanistic and physiological foundation of any research question and take research from bench to bedside. Recently, a preclinical research session was conducted at the CTG annual Noosa meeting, during which some of the concurrent basic science projects in the areas of renal and lung physiology, sepsis models, critical care nutrition, mechanical assistance of heart and lungs and iron homeostasis in sepsis were discussed. This generated an encouraging amount of interest in this area. Similar meetings are planned for the future. It is now up to all of us to take up and build on this opportunity and foster all domains of intensive care medicine research.

Competing interests

None declared.

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