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RACP Foundation Research Awards

PROGRESS REPORT

Project / Program Title		Molecular and structural determinants of myocardial dysfunction and prognosis in left and right heart failure
Name		Dr Louis Wang
Award Received		2015 RACP NHMRC CRB Blackburn Scholarship
Report Date		28 March 2017
Chief Investigator / Supervisor		Professor Diane Fatkin
Administering Institution		Victor Chang Cardiac Research Institute
Funding Period	Start Date:	1 January 2015
	Finish Date:	31 December 2017

PROJECT SUMMARY

Investigations in cardiovascular basic science performed during my doctoral work have provided new insights in comparative vertebrate cardiac physiology and the impact of certain heart failure risk factors common in both humans and animal models of cardiac disease. I have successfully pioneered zebrafish echocardiography in Australia, employing reverse-translation of clinical chocardiography to enable the use of high frequency ultrasound for in-vivo assessment of cardiac structure and function.

My key discoveries have, so far, included:

1. providing the first comprehensive report in the scientific literature demonstrating a validated and standardised method of echocardiographic assessment of zebrafish heart structure and function in health and disease;

2. identifying for the first time that zebrafish heart structure and function differ between genders and change with age;

3. showing that, despite significant differences between humans and zebrafish, certain aspects of cardiac physiology between zebrafish and humans are conserved in heart failure.

These insights will be vital for guiding future cardiovascular research questions in this animal model system

PROJECT AIMS / OBJECTIVES

1. Establish a standardised method of echocardiography to allow in-vivo study of cardiac structure and function in the zebrafish animal model system.

2. Model human heart failure and disease mechanisms using zebrafish (in progress)

3. Elucidate similarities between humans and zebrafish, with regards to disease mechanism and diagnosis.

SIGNIFICANCE AND OUTCOMES

The zebrafish is a model of organism of significant interest to cardiovascular researchers as it is able to regenerate damaged heart muscle and can also be genetically modified to simulate how mutations in certain genes can affect heart function in humans. My research has enabled the study of heart functions in living zebrafish. I pioneered the technique of high frequency ultrasound in Australia to allow accurate study of heart structure and function in living zebrafish. I have made several world-first discoveries relating to gender- and age-dependent differences in cardiac structure and function, as well as illustrating, in living fish, similarities and differences between the zebrafish and human cardiovascular system. Our lab has also successfully challenged the existing view of bradycardia being part of the heart failure phenotype in zebrafish (see reference 2 below). These findings will have enormous influence on future research aimed at unlocking the zebrafish's regenerative potential and understanding genetic heart disease.

PUBLICATIONS / PRESENTATIONS

1. Wang LW, Hutter IG, Santiago CF, Kesteven SH, Yu ZY, Feneley MP, Fatkin D. Standardization echocardiographic assessment of cardiac function in normal adult zebrafish and heart disease models. Disease Models & Mechanisms. 2017;10(1):63-76.

2. Wang LW, Huttner IG, Santiago CF, Fatkin D. Bradycardia in zebrafish heart failure: a true physiological response or anesthetic induced red herring? Zebrafish. 2016;13:475-6.

This work in establishing a novel method of assessing heart structure and function in live zebrafish was featured in The Daily Telegraph 16/06/2017 p.11 . http://www.dailvtelegraph.com.au/news/nsw/heart-disease-hope-forvictims-as-tiny-tropical-fish-leads-victor-chang-scientists-to-worldbreakthrough/news-story/b78504ebd1433961be7e22395fa4da2f

Best Oral Presentation, Australian Society of Medical Research NSW Scientific Meeting. "Echocardiography in normal adult zebrafish and cardiac disease models". Proceedings from the 24th Australian Society of Medical Research NSW Annual Scientific Meeting, Sydney 2016: OP1-5, p21 .