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YEAR 1 PROGRESS REPORT

Project Title		Energy Metabolism in Renal Fibrosis
Name		Dr Mardiana Lee
Award Received		2017 RACP Jacquot NHMRC Awards for Excellence
Report Date		18 December 2017
Chief Investigator / Supervisor		Professor David Power
Administering Institution		The University of Melbourne
Funding Period	Start Date:	11 January 2017
	Finish Date:	31 October 2018

PROJECT SUMMARY

The development of scarring or fibrosis in the kidney is one of the most important mechanisms that leads to kidney failure. Fibrosis can be due to a number of diseases affecting the kidneys, including diabetes, high blood pressure, and genetic diseases. When the kidneys fail, the individual affected requires dialysis or transplantation, both very difficult, time consuming, expensive and, at times, painful procedures. There is a considerable research effort being mounted world-wide to reduce the occurrence of fibrosis of the kidneys. In this study, we are examining a novel mechanism that has only recently come to prominence. When kidneys are affected by disease, they seem to change their metabolism so that they require less oxygen but generate less energy. The cells that cause fibrosis are able to live in this low energy environment, whereas cells responsible for the normal function of the kidney die. This leads to replacement of normal kidney with scar tissue.

In this study, we aim to confirm that a failure of energy metabolism makes scarring worse after kidney injury. In addition, we will determine whether metabolism of fat or carbohydrates is the most important part of this change.

PROJECT AIMS / OBJECTIVES

The project aims to determine if changes in fat or carbohydrate metabolism modifies the outcome of kidney diseases that cause scarring.

SIGNIFICANCE AND OUTCOMES

So far, this project has found that the ability to maintain fat metabolism is essential for kidney cells to survive injury. A reduced ability to generate energy from fat metabolism lead to increased renal scarring. Metformin is an anti-diabetic medication which has been reported to reduce renal scarring. This study has al;so demonstrated that the anti-fibrotic effect of metformin is dependent on the ability to kidney cells to increase their metabolism of fat. Therapeutic approaches designed to increase fat metabolism in damaged kidney, therefore, may be useful in improving the long term outcome of renal injury.

Next, we are examining the role of glucose metabolism in renal scarring.

PUBLICATIONS / PRESENTATIONS

Lee, M., Mount, P.F., Katerelos, M., Gleich, K., Power, D.A. (2017). Increased Fibrosis in ACC Knockin Mice Following Renal Injury Confirms A Pathogenic Role For Reduced Fatty Acid Oxidation. Nephrology 22 (3): 34. Australian New Zealand Society of Nephrology Annual Scientific Meeting, Darwin, NT, 2nd- 9th Sept 2017

Lee, M., Mount, P. F., Katerelos, M., Gleich, K., Power, D.A. (2017). Inability to Increase Fatty Acid Oxidation Following Renal Injury Worsens Renal Fibrosis. Journal of the American Society of Nephrology 28: 753.

American Society of Nephrology, Kidney Week, New Orleans, LA, USA, 31st Oct - 5th Nov 2017.

Lee, M., Katerelos, M., Gleich, K., Galic, S., Kemp, B.E., Mount, P.F., Power, D.A. Phosphorylation of Acetyl CoA Carboxylase Reduces Renal Fibrosis and Mediated the anti-fibrotic effect of Metformin. (paper in preparation).