Ovarian follicular fluid reflects the clinical condition and oocyte cumulus homeostasis

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A thesis submitted to the University of Adelaide

for the degree of Master in Medical Science November 2012

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Declaration

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Acknowledgements

I would like firstly to acknowledge Chiang Mai University for the staff development scholarship for my financial support. Acknowledgement also to my supervisors, Professor Robert Norman and Dr. Rebecca Robker who have supported this project.

It is a pleasure to thank the helpful teams of FertilitySA, St Andrews Hospital and Flinders University helping me collecting the samples for this project. This includes, the doctors, nurses, operative staff, embryologists and administrative staff. I also wish to thank all the infertile women participating in this study.

I would like to thank Adelaide Microscopy, Associate Professor David Kennaway and his team, Dr. Linda Wu, Dr. Anne Mcpherson and Mr. David Apps for laboratory assessment. Acknowledgement also go to Mr. Thomas Sullivan for his statistical support.

Special thank for the ovarian biology lab staff for their suggestions in my experiments, presentations and sample transfer. The thanks also go to my PhD candidate friends and the administrative staff of the school of Paediatrics and Reproductive health for their general help and guidance in Medical school.

It is the pleasure to thank the IT service, Dr. Sakrapee Paisitkriangkrai and IBP staff for their wonderful IT support and IBP course.

Finally, I would like to thank my family and friends for their support and encouragement.

Abstract

Infertility is a worldwide problem that is often overlooked. Although assisted reproductive technology has been developed over decades, many women still suffer from infertility. More knowledge is needed to understand ovarian homeostasis to optimise fertility treatment. This study aimed to explore the relationship of lipids and glucose levels in blood and follicular fluid, and compare these substrates among women with normal or abnormal metabolic condition. It also sought to measure lipid content within human oocytes as well as the expression of endoplasmic reticulum stress marker genes in cumulus cells, and their relationship with metabolic substances, obesity and IVF outcome.

The blood, follicular fluid, cumulus cells and unfertilised oocytes from 88 women, who underwent IVF in FertilitySA from February 2011 to August 2011, were collected and analysed for glucose, lipids and endoplasmic reticulum stress markers.

Follicular glucose, insulin, high density lipoprotein cholesterol (HDL-C) and majority of polyunsaturated fatty acid (PUFA) and monounsaturated fatty acid (MUFA) levels correlated with the serum levels (r= 0.16-0.23). Insulin was associated with the BMI, waist circumference, metabolic syndrome and many fatty acids, but not follicular glucose. However, the immaturity rate of the retrieved oocytes correlated with the follicular glucose and total fatty

acids (r = 0.19-0.26, p <0.04). Variability of the unfertilised oocyte morphology correlated with follicular glucose, and the immaturity rate also differed among the metabolic syndrome group.

An increase of follicular 18:3 n-3 (alpha-linolenic) and decrease of 20:3 n-3 (eicosatrienoic acid; ETA) existed in women with a waist circumference of more than 80 cm. The follicular 20:5 n-3 (eicosapentaenoic acid; EPA) percentage correlated with fertilisation and cleavage rate (r = -0.32, p = 0.003 and r = -0.35, p = 0.001). The follicular low density lipoprotein cholesterol (LDL-C) and HDL-C related to follicular fatty acids. Higher levels of serum LDL-C (2.31 ± 0.65 and 1.98 ± 0.61mmol/L, p 0.02) and follicular fatty acid (0.26 ± 0.09 and 0.22 ± 0.05 mmol/L, p = 0.03) were found in non-pregnant women.

There was a wide variability of ER stress expression in cumulus cells among women in this study. There was no obvious correlation between ER stress markers and other measurements. The unfertilised oocyte BODIPY fluorescence intensity had high variability among women and individuals. However, the unfertilised oocyte lipid content correlated with the serum LDL-C level.

Substances with a good follicular-serum relationship may be transported directly from blood to the follicle. The discorrelation might be affected by intrafollicular metabolism. Insulin may be involved in follicular lipid metabolism because it correlated with many follicular fatty acids and cholesterols. The equilibrium between follicular fatty acids involving insulin modulation may affect oocyte quality.

Overall, this study found there were correlations between serum and follicular lipids, follicular insulin and cholesterol with follicular fatty acids and the importance of serum LDL-C and follicular omega-3 fatty acids. Serum insulin and LDL-C screening might be another tool for predicting the follicular lipid dysequilibrium and poor IVF outcome. The unfertilised oocyte may be a useful tool for a study on oocyte quality. A larger study is needed to recruit more women of different ages and BMI for a stronger correlation between follicular insulin, glucose and lipid metabolism, and ER stress markers.

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