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Mount Sinai duo uncovering the molecular events underlying infertility

June 19, 2012

One in eight Canadian couples seeks medical treatment for infertility, most often requiring the help of assisted reproductive technologies (ART). Current pregnancy rates after ART average around 30 per cent per cycle, a figure that has improved only marginally over the past 20 years.

One of the biggest hurdles affecting the outcome is poor embryo quality. Dr. Andrea Jurisicova, Associate Scientist at the Samuel Lunenfeld Research Institute of Mount Sinai Hospital and an Associate Professor of Obstetrics and Gynaecology at the University of Toronto, seeks to improve understanding of the genetic and biomolecular factors underlying female infertility. She is using microscopic imaging techniques to explore embryo quality with the goal of improving the outcome for couples suffering from infertility.



“Very little is known about molecular deficits that are responsible for poor embryo quality in some infertile couples,” says Dr. Jurisicova. “We are focusing on genes involved in the regulation of cell survival and how they contribute to developmental defects in the embryos of patients with repeated in vitro fertilization (IVF) failure.”

Dr. Jurisicova trained in Slovakia as an embryologist, and has been an Associate Scientist at the Lunenfeld since 2007, after completing her PhD studies in the lab of Dr. Robert Casper, Senior Scientist at the Lunenfeld and Medical Director of the Toronto Centre for Advanced Reproductive Technology (TCART).

“Training in Bob’s lab gave me the opportunity and skills to study the molecular pathways underpinning infertility—to understand what goes awry on a molecular level—and to rescue those defects in animal models,” says Dr. Jurisicova.

Within the next few years, Dr. Jurisicova hopes to identify genes tied to repeat failures of IVF and, ultimately, boost the success rate of embryo development for childless couples.

“Andrea is an extremely talented scientist who has been successful in winning a Canada Research Chair to support her research,” says Dr. Casper. “It has been a privilege for me to work with Andrea over the last 20 years during which time we have collaborated on many projects that have started in the lab and been translated to the clinic shortly after.”

In addition to early embryo development, Dr. Jurisicova is furthering an understanding of the genetic and environmental pathways that may trigger premature ovarian failure. Her earlier work focused on toxins that affect a woman’s fertility and that of her offspring. Dr. Jurisicova’s research showed that when females are exposed to polycyclic aromatic hydrocarbons (found in cigarette smoke, car exhaust, fumes from wood stoves and in charred and smoked foods), the number of eggs in their offspring’s ovaries is reduced by two thirds. These compounds can also trigger early embryo loss (miscarriage) as well as retarded fetal growth.

In collaboration with Dr. Casper, Dr. Jurisicova is also investigating the process of mitochondrial activity in oocytes of older females. By studying the quality of oocytes (in an animal model) in older versus younger mothers, the duo have found that mitochondria, the energy-producing power stations of cells, become less metabolically active with age, putting the offspring at greater risk of developing obesity and metabolic syndrome, and predisposing them to diabetes. However, administration of coenzyme Q10—a vitamin-like substance found in mitochondria—can reverse the effects of mitochondrial changes in oocytes, improve fertility, and perhaps reduce the risk of chromosomal abnormalities.

Drs. Casper and Jurisicova are working to translate these findings to clinical settings and improve the chance of pregnancy in older women, while preventing genetic abnormalities including Down syndrome in infants.



“Supplementing the diet with this natural vitamin appears to enhance mitochondrial activity and boost the quality of oocytes,” says Dr. Casper. “In addition, long-term treatment in mice (the equivalent of several years in women) was found to increase the number of oocytes remaining in the ovaries of old mice, possibly prolonging their reproductive life span.”

With promising results shown in mice, Dr. Casper is leading a study at TCART to assess the effects of CoQ10 administration for two months in 50 women over age 35. This study will be completed at the end of this month, and the results analyzed over the next two months.



In addition to the CoQ10 work, Drs. Casper and Jurisicova are studying the protein BCL-xL, which is involved with the regulation of cell survival and mitochondrial metabolism. With the goal to boost oocyte quality, the team found that microinjection of recombinant BCL-xL into fertilized mouse eggs improved the number and quality of mouse embryos by 50 to 80% compared to controls, decreased levels of harmful reactive oxygen species and increased levels of ATP, suggesting enhanced mitochondrial activity in oocytes. Drs. Casper and Jurisicova are hoping to test this protein injection clinically once an appropriate source of BCL-xL can be produced for human use.

More about collaborations:

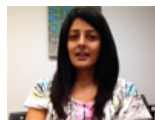
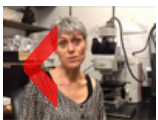
Through research using animal models of disease, Dr. Jurisicova is also investigating abnormalities in the placenta that occur during embryonic development (which may lead to pre-eclampsia and/or miscarriages), as well as intrauterine growth restriction. Her collaborative research with Mount Sinai Hospital physicians including Dr. Ellen Greenblatt (Head of the Division of Reproductive Sciences and the Clinical Director of the Centre for Fertility and Reproductive Health and IVF Unit in the Department of Obstetrics and Gynaecology) is helping to improve the health of women and increase their chances of conception and full-term healthy birth.

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