Oocyte Physiology (Study headed by Dr. Rebecca Krisher)

Oocyte energy metabolism

This project involves the investigation of metabolic pathways in the oocyte. Metabolic events occurring in the oocyte are related to the ultimate developmental ability of the resulting embryo after fertilization. The overall metabolism of the oocyte is important, as well as specifically which metabolic substrates it requires and the biochemical pathways it utilizes. At the current time, we are focusing on carbohydrate and fatty acid metabolism. By adding specific energy substrates to culture medium during oocyte maturation, and blocking specific metabolic pathways, we can identify which substrates are critical to oocyte quality. Once we understand these mechanisms, we can manipulate energy substrates, such as fatty acids, glucose and amino acids, in the culture medium to optimally support oocyte quality during the maturation period, resulting in increased blastocyst development following fertilization.

Oocytes from women of advanced maternal age

Unfortunately, advanced maternal age greatly increases the risk of infertility, due to poor oocyte quality. In fact, age is the most important factor effecting success during assisted reproduction, unless donor eggs are used. By understanding the mechanisms responsible for the loss of oocyte competence in older women, we will be in a much better position to provide support both before and after egg collection during assisted reproduction cycles, as well as to select the highest quality eggs recovered. We are using mice as a model to investigate how and why oocytes lose quality as females age, even if they are chromosomally normal. We hypothesize that there are several key mechanisms at work, including damage caused by free oxygen radicals and changes in methylation status of key genes, and our current experiments are evaluating these mechanisms. We are examining follicular fluid obtained from older women, to investigate how the follicular environment in which the oocyte grows changes over time. Investigation of changes in gene expression patterns in the cells surrounding the oocyte with age will also provide insight into mechanisms that are altered. All of this information together will ultimately allow us to develop novel treatment therapies to help support oocyte quality in women who have delayed having children.

Oocyte gene expression

This project focuses on the identification of genes expressed in oocytes that are associated with developmental competence. These molecular markers provide information about what the oocyte requires for successful development after fertilization. With this knowledge, we now have clues as to how we can modify the in vitro environment and develop effective strategies to alter specific oocyte cellular pathways, to produce oocytes of the highest quality. We can also use these gene transcripts as markers, to assess how the changes we make in the oocyte's environment affect its quality. Some of these transcripts encode secreted proteins, and we are investigating if these proteins may also be used as biomarkers to noninvasively assess oocyte quality

after in vitro maturation. This research will ultimately enable the development of assays to test for oocyte developmental competence and strategies to enhance oocyte maturation in vitro, including improved media formulation.

Oocytes and reactive oxygen species

This research project examines how oocytes handle oxidative stress, and how oxidative stress during oocyte maturation influences development after fertilization. Maturation in the in vitro environment can induce high levels of oxidative stress, and the ability of the oocyte to successfully reduce this stress appears to be associated with the overall quality of the oocyte itself, and its ability to successfully develop after fertilization. We are testing different methods to assist the oocyte to combat oxidative stress in vitro, resulting in better quality oocytes and embryos. We are targeting specific genes in the oocyte for manipulation that, from our preliminary data, are critical to oocyte quality and oxygen radical control. Ultimately we hope that this research will help us understand the cellular mechanisms that oocytes use to deal with oxidative stress, and how we can help to support and enhance these processes during the time an oocyte spends in vitro during an assisted reproduction cycle.