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The impact of reproductive age on metabolism and gene expression indices of oocyte quality in germinal staged oocytes

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Study question:

How does reproductive age alter oocyte energy metabolism and the molecular mechanism(s) regulating oocyte maturation and subsequent developmental competence or quality?

Summary answer:

Pyruvate and glucose metabolism were significantly (P<0.05) different in prepubertal vs. adult oocytes. Metabolic differences were associated with altered expression patterns of glycolytic pathway genes.

What is known already:

The reproductive ageing process is associated with a deterioration of oocyte quality, which has been confirmed in both natural conception and assisted reproduction treatment. Several studies have linked the non-invasive and invasive measurement of embryo amino acid metabolism to embryo developmental potential and to be predictive of successful treatment. Furthermore, measurement of the embryo and metaphase II oocyte glucose, pyruvate and lactate metabolism have been proposed as determinants of embryo quality. The relevance of energy metabolism to the subsequent developmental competence of immature GV-staged oocytes has yet addressed.

Study design, size, duration:

Prepubertal and adult GV sheep oocytes were used as a model to study the impact of reproductive ageing on metabolic and molecular markers of oocyte quality. Glucose, pyruvate, and lactate metabolism were quantified for 126 prepubertal and 144 adult GV oocytes. Gene expression was evaluated in 6 oocytes/group in relation to the functional assessment of oocyte metabolism using a quantitative real-time PCR array

Participants/materials, setting, methods:

Cumulus enclosed oocytes (CEOs) were harvested from abattoir-derived ovarian tissue from prepubertal and adult animals. CEOs were immediately stripped and the denuded oocytes were individually incubated in microdrops of defined media for 6 hours. Spent culture media were frozen for later carbohydrate metabolism analysis using an established enzyme-linked ultramicrofluorescent assays. For genetic study, individual GV oocytes were snap frozen in RNAGEM buffer before RNA extraction and SMART amplification for analysis by real-time PCR.

Main results and the role of chance:

The data demonstrated that carbohydrate metabolism can be used to evaluate quality of GV-staged oocytes. Both glucose and pyruvate utilization showed significant differences between the 2 age groups studied (P=0.014 and P<0.0001, respectively) while no significant different was found in lactate production between ages (P=0.889). Adult GV oocytes consumed more pyruvate and less glucose when compared to prepubertal GV oocytes. The data confirmed that oocytes utilize pyruvate rather than glucose as a major substrate for energy production. Molecular genetic analysis revealed that there were significant differences (P<0.05) in expression of key genes including those involved in the glycolytic pathway. Increased mRNA expression of SLC2A3, SLC16A1, IGF1R, GSK3B, and PRDX2 was detected in prepubertal GV oocytes when compared to adult oocytes. This data served to both highlight the close link between molecular control mechanisms and the metabolic function of oocytes and shows how these relationships change with reproductive age.

Limitations, reasons for caution:

Denudation of CEOs was necessary to facilitate measurement of glucose, pyruvate and lactate metabolism by individual oocytes as the multiple cells in the cumulus compartment would have a major impact on CEO metabolic assessment. Further, the oocyte denudation procedure per se might have impacted on oocyte metabolism and/or gene expression.

Wider implications of the findings:

Assessment of energy metabolism is a non-invasive method of determining oocyte and embryo quality. Calibration of oocyte energy metabolism against other more invasive molecular genetic indices of oocyte health may be a useful means to fully characterize the developmental competence of oocytes.

Trial registration number:

NA