Glucose stimuli prompts insulin secretion by human spermatozoa

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Spermatogenesis is sensitive to metabolic alterations, where insulin is considered one of the most important regulators. Even 100 years upon its discovery, not much is known concerning the role of insulin in the testis. It is hypothesized that insulin plays a major role on human spermatozoa capacitation, a phenomenon where spermatozoa suffer morpho-physiological alterations in order to achieve fertilization capacity. However, the molecular mechanisms remain to be elucidated. Herein, we aimed to evaluate the insulin synthesis and secretion capacity of human spermatozoa, by assessing the expression of enzymes responsible for proinsulin cleavage, PC1/3 and PC2. In addition, our goal was to assess whether insulin secretion was responsive to glucose stimuli. For this purpose, human sperm samples from normozoospermic men were used (n=15). A density gradient protocol was performed and two fractions of spermatozoa were then collected according to its motility condition (high vs low motility). Gene expression of insulin, PC1/3 and PC2 mRNA was evaluated by RT-qPCR in both spermatozoa fractions. Protein expression of insulin, PC1/3 and PC2 in spermatozoa was evaluated by immunofluorescence. The fraction of highly motile spermatozoa was incubated in culture medium under capacitating conditions and supplemented with increasing glucose concentrations (in mM: 0, 5.5, 11 and 22). Insulin concentrations in the medium 6 h later were quantified by ELISA. Our results showed that insulin, PC1/3 and PC2 mRNA, as well as the respective proteins, are expressed in human spermatozoa. The mRNA expression was found to be higher in highly motile spermatozoa. Additionally, human spermatozoa released insulin to the medium in a glucose concentration-dependent manner. This study shows that insulin plays a role in human spermatozoa capacitation though the mechanisms mediated by insulin remain unknown, opening an exciting new line of investigation.