Expression of a sperm protein involved in Ca^{2+} release is linked to male infertility

Presence of the sperm-specific phospholipase C, zeta 1 (PLCZ1) protein has been associated with free cytosolic Ca^{2+} ($[Ca^{2+}]_i$) oscillations—the signal that activates egg fertilization. The effect of *PLCZ1* absence on male fertility has yet to be determined. Yoon and colleagues, therefore, investigated the ability of sperm from men who repeatedly failed intracytoplasmic sperm injection to induce $[Ca^{2+}]_i$ oscillations, and whether this effect is associated with expression of the PLCZ1 protein.

Data from 17 couples undergoing *in vitro* fertilization with intracytoplasmic sperm injection were analyzed. The researchers injected sperm into mouse eggs to observe whether cytosolic $[Ca^{2+}]_i$ oscillations were induced. Sperm from 14 males induced $[Ca^{2+}]_i$ oscillations; of these couples, 13 conceived within two cycles of intracytoplasmic sperm injection treatment, whereas no pregnancies occurred for the three couples in whom the male sperm failed to induce more than one $[Ca^{2+}]_i$ oscillation. Immunofluorescence and western blot analysis (carried out on all samples) revealed that the sperm from the latter patients lacked the PLCZ1 enzyme usually present in the equatorial and/or postacrosomal region of normal sperm heads. Genomic sequencing did not, however, show conclusive mutations in the gene. Injection of mouse *Plcz1* mRNA induced egg activation in the three cases where sperm had failed to activate the mouse eggs.

The authors conclude that these data indicate a direct role for abnormal *PLCZ1* expression in the inability of sperm to initiate $[Ca^{2+}]_i$ oscillations, resulting in male infertility.

Original article Yoon SY *et al.* (2008) Human sperm devoid of PLC, zeta 1 fail to induce Ca release and are unable to initiate the first step of embryo development. *J Clin Invest* **118:** 3671–3681

Prostate cancer antigen 3 as a prognostic factor for detection of prostate cancer

An American study has shown that, at repeat biopsy, detection of prostate cancer antigen 3 (PCA3), which is highly expressed in over 95% of malignant prostate tissue, is superior to PSA measurements in the detection of prostate cancer. In light of these findings, Haese *et al.* conducted a prospective, multinational, multicenter European study to asses the clinical utility and performance of the PCA3 assay.

Data were assessed from 463 men with 1–2 previous negative prostate biopsies who were scheduled for repeat biopsy, which detected prostate cancer in 128 (28%) men. Increasing PCA3 score corresponded with an increased risk of positive repeat biopsy; mean scores were higher in men with a positive biopsy than in men with a negative biopsy (63.8 vs 35.5). The PCA3 score cut-off of 35 provided optimal specificity (72%) and sensitivity (47%), and had a greater diagnostic accuracy than the percentage of free PSA (cut-off of 25%, specificity 23%).

Increasing PCA3 scores were associated with increasing clinical stage and aggressiveness of prostate cancer, as well as with incidence of high-grade prostate intraepithelial neoplasia, the authors noted. They added that PCA3 score cut-off values could also be used to reduce unnecessary biopsies while keeping the risk of missing cancers low, although further evaluation is needed to confirm this suggestion.

Haese and colleagues conclude that using the PCA3 score together with other diagnostic variables can help to identify patients likely to require a repeat biopsy.

Original article Haese A *et al.* (2008) Clinical utility of the PCA3 urine assay in European men scheduled for repeat biopsy. *Eur Urol* **54:** 1081–1088

Severe maternal hypertension lowers the risk of testicular cancer in the male fetus

The exposure of the fetus to altered levels of pregnancy hormones during gestation is thought to have a role in the initiation of prenatal testicular cancer. Maternal hypertension and preeclampsia reduce the transplacental passage of pregnancy hormones. Pettersson *et al.* have now shown that the risk of testicular cancer is reduced in men who were exposed to severe maternal hypertension and preeclampsia during gestation, but increased in those exposed to the mild forms of these two complications.