

A NOVEL ELECTROCHEMICAL DIAGNOSTIC PLATFORM FOR MALE FERTILITY

ABSTRACT

This white paper introduces JUNO-Checked, an innovative diagnostic platform at the forefront of male fertility assessment. Combining an electrochemical instrument with a biosensor cassette, the JUNO-Checked platform detects binding of human sperms to a biosensor decorated with human JUNO protein. The sperm-binding competitive assay utilizes a proprietary electrochemical method for readout. Finally, the assay performance is demonstrated in an ongoing collaborative clinical study with the Reproduction Medicine Center at Skåne University Hospital, Malmö, and underscores the platform's potential to revolutionize male fertility diagnosis.



BACKGROUND

With a rising concern in male-factor infertility, medical professionals face a glaring gap in male fertility diagnostics. Since the choice of treatment method between Standard IVF (In Vitro Fertilization) and ICSI (Intra-cytoplasmic Sperm Injection) is primarily based on sperm function, JUNO-Checked aims to cater this unmet medical need by helping to assess the binding capacity of sperms, and consequently serve as an important tool for choosing the optimal treatment method.

Recently, the understanding of male fertility has been significantly advanced through the exploration of key reproductive proteins such as JUNO and IZUMO1. JUNO, also known as folate receptor 4, is an egg cell membrane protein essential for fertilization, playing a crucial role in sperm-egg binding. IZUMO1, on the other hand, is located on the sperm membrane and is crucial for sperm-egg fusion. Thus, the interaction between JUNO and IZUMO1 is a fundamental step in the fertilization process.

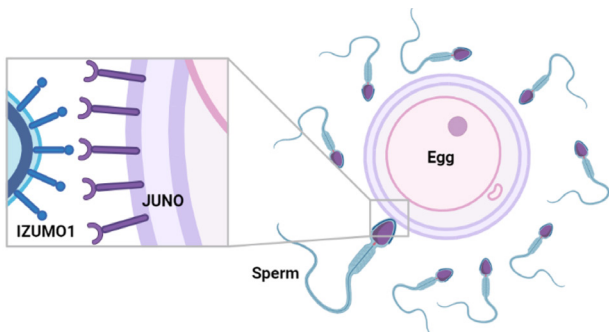


Figure 1: Illustrative representation of sperm-egg cell interaction, mediated by sperm-Zona Pellucida recognition via IZUMO1-JUNO binding.

Recent scientific endeavors have explored the diagnostic potential of JUNO and IZUMO1 in understanding male fertility. The identification and functionalization of these proteins in diagnostic assays offer a new avenue for personalized fertility assessment.

JUNO-CHECKED DESIGN

JUNO-Checked's design integrates an electrochemical instrument and a biosensor cassette (Figure 1). The biosensor, decorated with human recombinant protein JUNO, ensures both specificity and sensitivity.

The competitive assay development employs human recombinant protein IZUMO1 as competitors to the sperms. The proprietary electrochemical readout method ensures precision and accuracy (Figure 2).

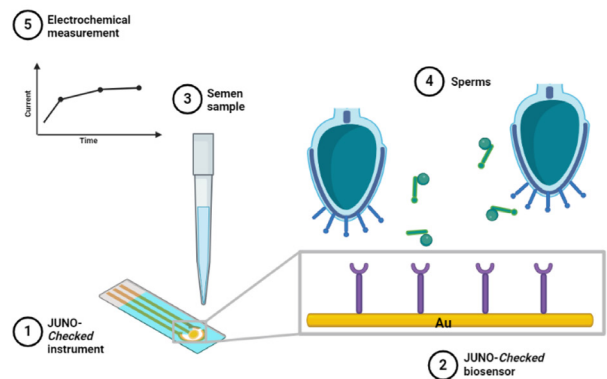


Figure 2: Schematic representation of the JUNO Checked core-technology, comprising of the electrochemical readout and the biosensor containing human recombinant protein JUNO.



JUNOScore IS SPERM-SPECIFIC AND UNIQUE FOR EACH SEMEN SAMPLE

JUNO-Checked has been tested with human sperm samples in a collaborative clinical study, utilizing normospermic samples from patients undergoing andrology examination at Reproduction Medicine Center, Malmö. Leftover clinical semen samples, meeting WHO standards, underwent a simple washing step and the standardized sperm cell concentrations determination. Sample analyzed with JUNO-Checked showed a dose response curve (Figure 3), which unveils unique footprint for each clinical sample, emphasizing the platform's ability to capture heterogeneity of each patient.

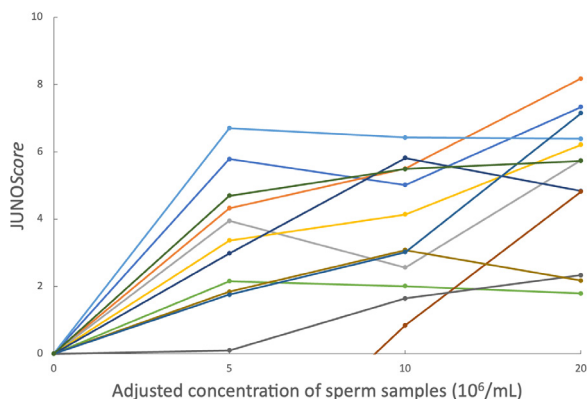


Figure 3: Graphical representation of the dose response of JUNOScore. Concentrations of sperms were adjusted for each clinical sample.

JUNOScore GIVES UNIQUE INFORMATION BEYOND WHO ANALYSIS

Comparing the JUNOScore of the sperm samples with the original ejaculate parameters reveals that JUNOScore does not correlate with the concentration or motility of the original ejaculate as calculated in accordance with the WHO laboratory manual for the examination and processing of human semen.

R-square values consistently remain around 0.05-0.06 (Figure 4). This divergence from traditional semen analysis parameters positions JUNOScore as a novel diagnostic parameter, providing unique information for clinical evaluation.

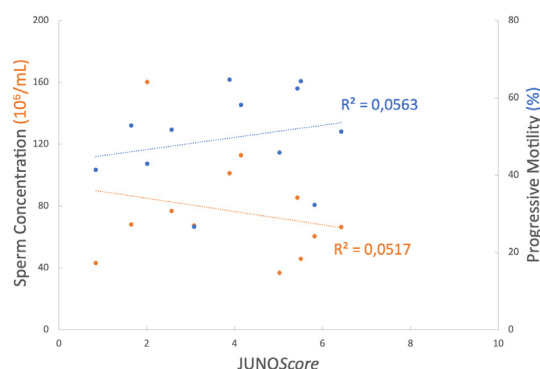


Figure 4: Scatter plot illustrating the lack of correlation between JUNOScore and the concentration and motility of the original ejaculate, with accompanying R^2 values.

CONCLUSION

In conclusion, JUNO-Checked is a paradigm shift in male fertility diagnosis. The platform's design, assay development, and clinical validation collectively demonstrate its potential to offer new insights beyond conventional parameters including sperm motility and concentration in the ejaculate. JUNOScore, derived from the interaction of sperms with gate-keeper oocyte proteins, emerges as a promising diagnostic parameter, providing clinicians with valuable information for personalized patient evaluation. The platform's ease of use, stability, and unique diagnostic contributions position JUNO-Checked as a *solid lead* advancing male fertility diagnostics, and assisting in making the optimal treatment choice between Standard IVF and ICSI.