CUMULUS CELL GENE EXPRESSION IS ASSOCIATED WITH THE DEVELOPMENT OF A TRANSFERABLE BLASTOCYST IN ICSI PATIENTS STIMULATED WITH r-hFSH OR r-hFSH:r-hLH

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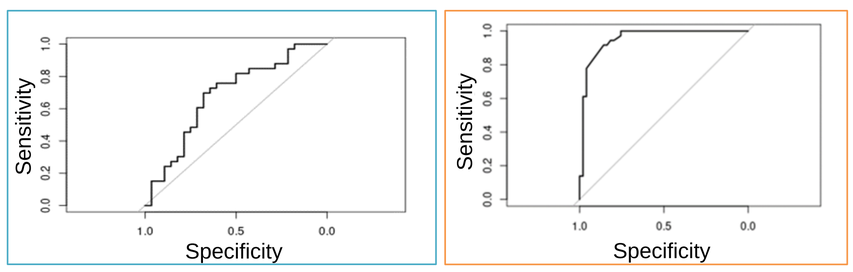
INTRODUCTION

Knowing Biomarkers RNA expression in CC of individual oocytes of ICSI patients can help to increase the efficiency of the first embryo transfer by increasing the live birth rate (LBR).

For patients stimulated with HP-hMG, CC mRNA expression-based models have been developed in retrospective studies (eg: Wathlet et al 2012-'13). These were prospectively validated in an interventional study. When CC analysis was applied, the fresh transfer LBR was significantly increased to 50% compared to 27% in controls without the CC analysis (Van Vaerenbergh et al '21).

For r-hFSH and r-hFSH:r-hLH stimulated patients similar live birth prediction models were only recently developed. LB prediction models comprised GOT1, HAS2, SASH1 and PTGS2 expression for r-hFSH patients (AUC 0.7284; 70% accuracy) and GOT1 and HAS2 expression for r-hFSH:r-hLH patients (AUC 0,9529; accuracy 88%).

Fig 1: Live birth predictive model building, the ROC Curve for both stimulation groups: **r-hFSH** and **r-hFSH:r-hLH**



Using a similar strategy CC based prediction models for blastocyst formation were developed for these patients. These are here reported for the first time.

OBJECTIVE

Can algorithms based on cumulus cell (CC) gene expression predict whether an oocyte will develop into a transferable blastocyst ?

MATERIALS & METHODS

In a cohort study 113 patients scheduled for ICSI and fresh Day 5 SET were stimulated with r-hFSH (n=47) or r-hFSH:r-hLH (n=66). All had all their available oocytes individually denuded and CC collected. From 1.135 CC samples RNA was extracted and mRNA expression of 11 preselected oocyte quality biomarkers (CAMK1D, EFNB2, SASH1, GOT1, SLC6A9, HAS2, PTGS2, HSPH1, VCAN, GSTA4, STC2) and 2 endogenous controls (UBC, B2M) was analyzed with qPCR. Stepwise linear regression was performed for relating the gene expression data to blastocyst formation capacity using R.

RESULTS

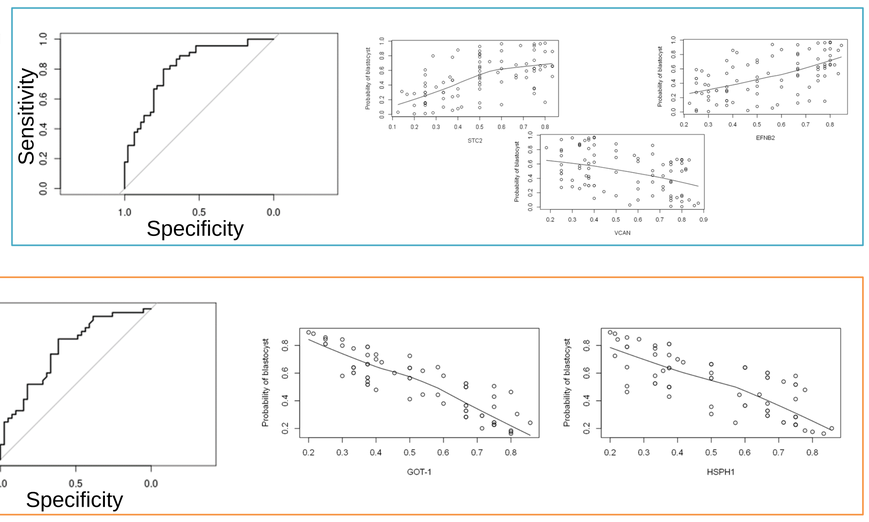
A mathematical model which is predictive for blastocyst formation was built using the mRNA expression of 11 biomarkers in a selected balanced sample set.

Samples were CC of: i) oocytes developing into good or top-quality blastocysts (n=46 r-hFSH, n=40 r-hFSH:r-hLH)

ii) oocytes fertilizing and forming at least a two-cell embryo but failing to develop a good quality blastocyst from the same patient (n=46 r-hFSH, n=40 r-hFSH:r-hLH).

For both stimulation protocols strong prediction models were identified. For r-hFSH patients the prediction model comprised STC2, VCAN and EFNB2 with a ROC AUC=0,813 and predictive accuracy of 77%. For r-hFSH:r-hLH patients the prediction model comprised GOT1 and HSPH1 expression (ROC AUC=0,7308 and predictive accuracy=66%).

Fig 2: Blastocyst formation predictive model building results for both stimulation groups: **r-hFSH** and **r-hFSH:r-hLH**



CONCLUSION

Easy CC gene expression-based algorithms can predict blastocyst development, which is informative for patients and doctors.

POTENTIAL IMPACT

Identifying the oocytes' competence to develop to a blastocyst is especially useful for patients scheduled for oocyte banking or oocyte donation. Also, when the patient or the clinic wants to limit the generation of supernumerary embryos it can prevent ethical, practical or financial burden (Adriaenssens et al. '24).

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