UNIVERSITY OF TARTU
Institute of Computer Science
Computer Science Curriculum

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Predicting endometrial receptivity with targeted second generation sequencing

Master's Thesis (30 ECTS)

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Abstract:

In assisted reproductive medicine, optimal estimation of the time window for embryo implantation (WOI) is considered paramount for increased chance of pregnancy. This estimate is given based on the characteristics of the uterus inner layer, endometrium, and occurs around days 19–21 of the menstrual cycle. During then, the endometrium is considered as "receptive". In one out of three patients, this general estimation is not accurate enough. A personalized approach for determining WOI has shown to be an effective solution in cases of infertility and recurrent implantation failures. While there are some of genomic diagnostic tools developed for evaluating the receptivity through transcriptomic profiling of the endometrium, none of them are currently based on accurate and targeted second generation sequencing.

In this study, a semi-supervised non-iterative approach for predicting the endometrial receptivity was developed. The transcriptomic signature of 68 biomarker candidate genes was captured with targeted allele counting sequencing (TAC-seq) protocol. To develop a suitable computational model, a reference set of 68 sequenced endometrial tissue samples of pre-receptive, receptive and post-receptive origin were used. Based on these samples, the dynamics and grouping of the endometrial transcriptomic timeline was modeled. Finally, a user-friendly web application was developed for interfacing with the model. This application is now used for clinical receptivity diagnostic assay.

Keywords:

Endometrial receptivity, personalized embryo transfer, assisted reproductive technology, window of implantation, targeted second generation sequencing, TAC-seq

CERCS: B110 Bioinformatics, medical informatics, biomathematics, biometrics

Endomeetriumi retseptiivsuse hindamine suunatud sekveneerimese meetodiga

Lühikokkuvõte:

Viljatusravis on esmatähtis hinnata optimaalset embrüo siirdamise ajastust, et suurendada rasestumise tõenäosust. Rasestumiseks sobiva ajastuse hinnang põhineb endomeetriumi kui emaka limaskesta küpsemise füsioloogial. Endomeetrium on embrüo pesastumiseks valmis tavaliselt 19.-21. menstruaaltsükli päeval. Sellel ajal peetakse endomeetriumi "retseptiivseks". Igal kolmandal naisel on endomeetriumi küpsemise aeg keskmisega võrreldes erinev. Personaalmeditsiini lähenemine optimaalse embrüo pesastumise aja hindamiseks on osutunud tõhusaks lahenduseks viljatusravis, et aidata patsiente, kellel on varasemalt olnud korduvad ebaõnnestunud embrüo siirdamised. Kuigi endomeetriumi retseptiivsuse hindamiseks läbi transkriptoomi uuringu on varasemalt välja töötatud genoomseid diagnostilisi vahendeid, ei põhine ükski neist täpsel ja suunatud teise põlvkonna sekveneerimise tehnoloogial.

Selles uuringus töötati välja pooljuhendatud, erinditundlik, mitte-iteratiivne lahendus endomeetriumi retseptiivsuse hindamiseks. Endomeetriumi retseptiivsuse 68 biomarker geeni avaldumise muster tuvastati suunatud teise põlvkonna sekveneerimise tehnoloogiaga, TAC-seq meetodiga. Mudeli väljatöötamiseks kasutati 68 varasemalt analüüsitud endomeetriumi koeproovi, mis kuulusid eelretseptiivsesse, retseptiivsesse ja post-retseptiivsesse gruppi vastavalt varasemale kliinilisele dateerimisel. Nende proovide põhjal modelleeriti endomeetriumi transkriptoomiline ajaskaala. Samuti arendati selles uuringus välja veebirakendus väljatöötatud arvutusliku mudeliga töötamiseks. Viimane on kasutuses kliinilises endomeetriumi retseptiivsuse testimises.

Võtmesõnad:

Endomeetriumi retseptiivsus, personaliseeritud embrüosiire, kunstlik viljastamine, implantatsiooniaken, suunatud teise põlvkonna sekveneerimine, TAC-seq

CERCS: B110 Bioinformaatika, meditsiiniinformaatika, biomatemaatika, biomeetrika

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