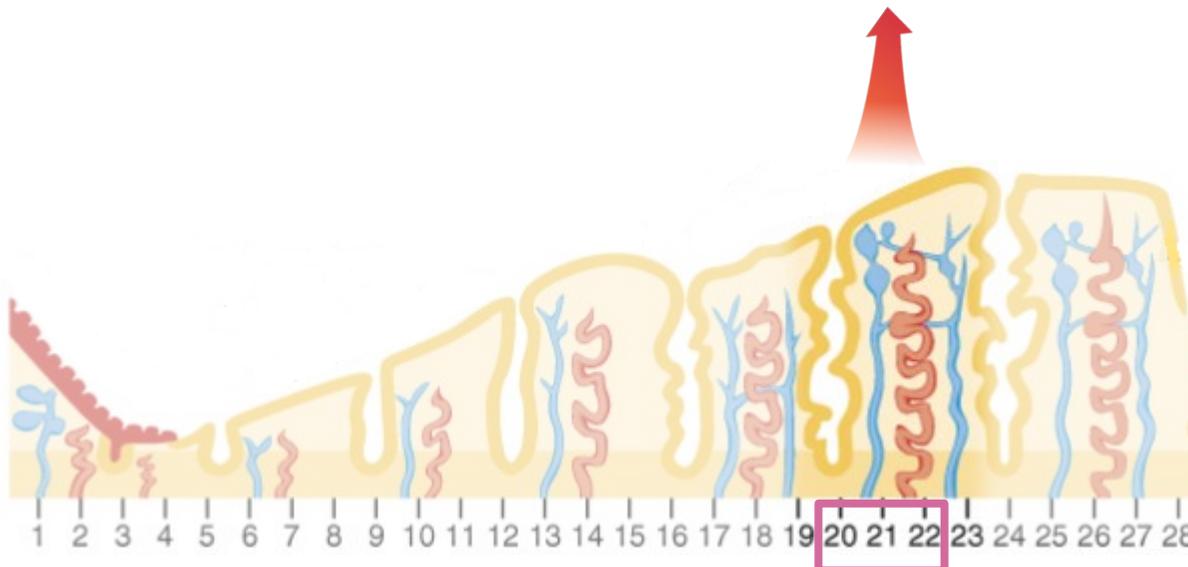
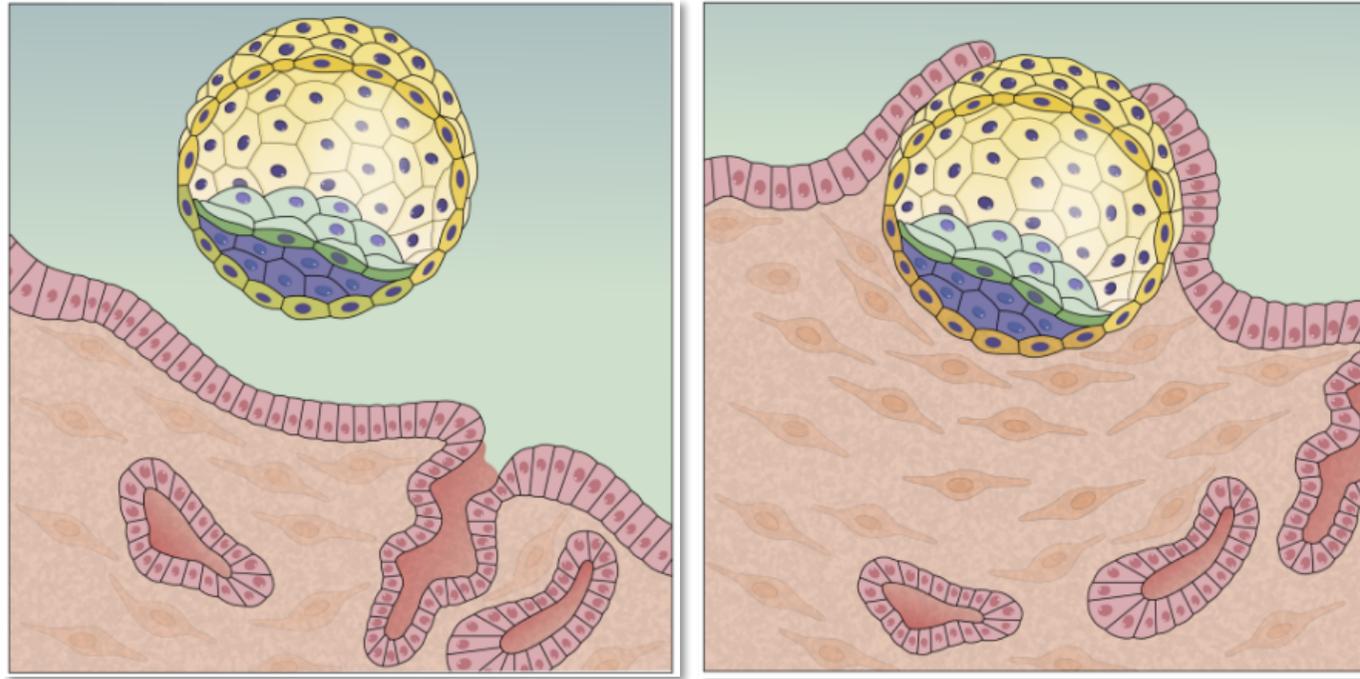


Genomic technologies for assisted reproduction

Kaarel Krjutškov PhD

Where do babies come from?





24-72h window of implantation



Receptive Endometrium – Advanced Diagnostic Yield

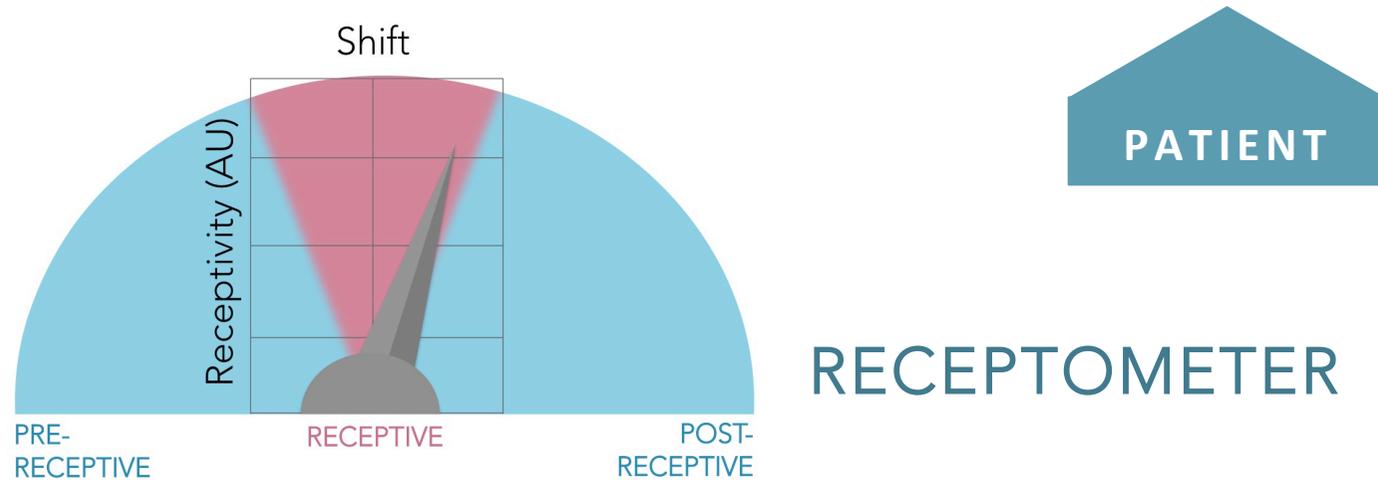


What is the outcome?

1.



2.



Receptive probability	0.782
Pre-receptive probability	0.048
Post-receptive probability	0.170

3.

INTERPRETATION – timing of progesteron treatment and embryo transfer.



ADVANTAGES



GENE SELECTION

Krjutškov et al., Human Reproduction, 2016

Altmäe et al., Scientific Reports, 2017

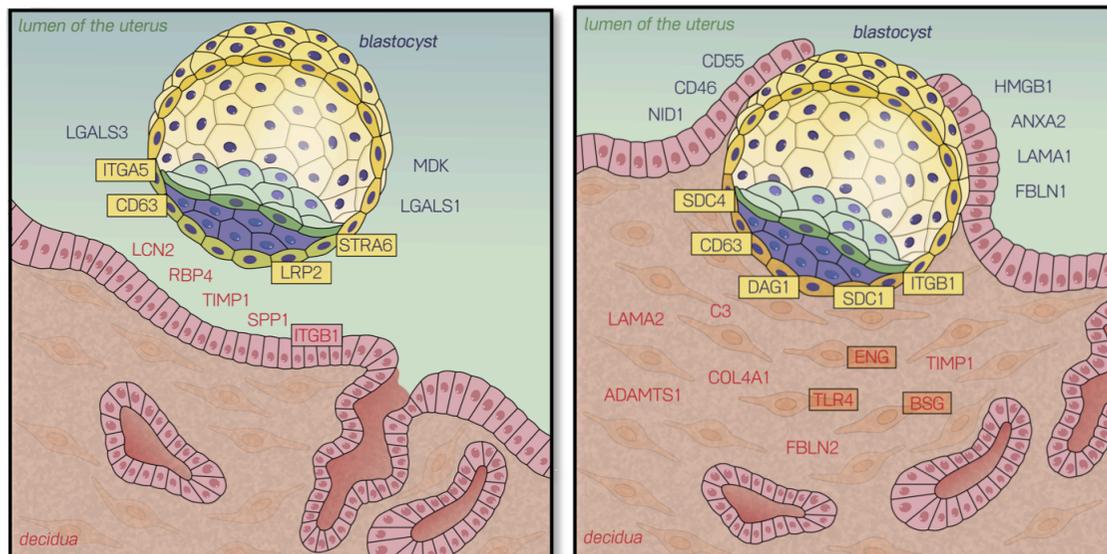
Koel et al., Human Reproduction., under review



Meta-signature of human endometrial receptivity: a meta-analysis and validation study of transcriptomic biomarkers

Altmäe et al., 2017

- ✓ Selection over 9 publications plus original findings
- ✓ 57 significant receptivity genes
- ✓ 39 genes are validated



- ✓ Embryo endometrium molecular interactions

Koel et al., Human Repr., under review



GENE SELECTION

Krjutškov et al., Human Reproduction, 2016

Altmäe et al., Scientific Reports, 2017

Koel et al., Human Reproduction., under review

ADJUSTED ANALYSIS



*Suhorutšenko et al., Human Repr. 2018, **accepted!***

“

As every button makes sense in a cockpit, every gene counts in endometrial receptivity.

Prof Andres Salumets

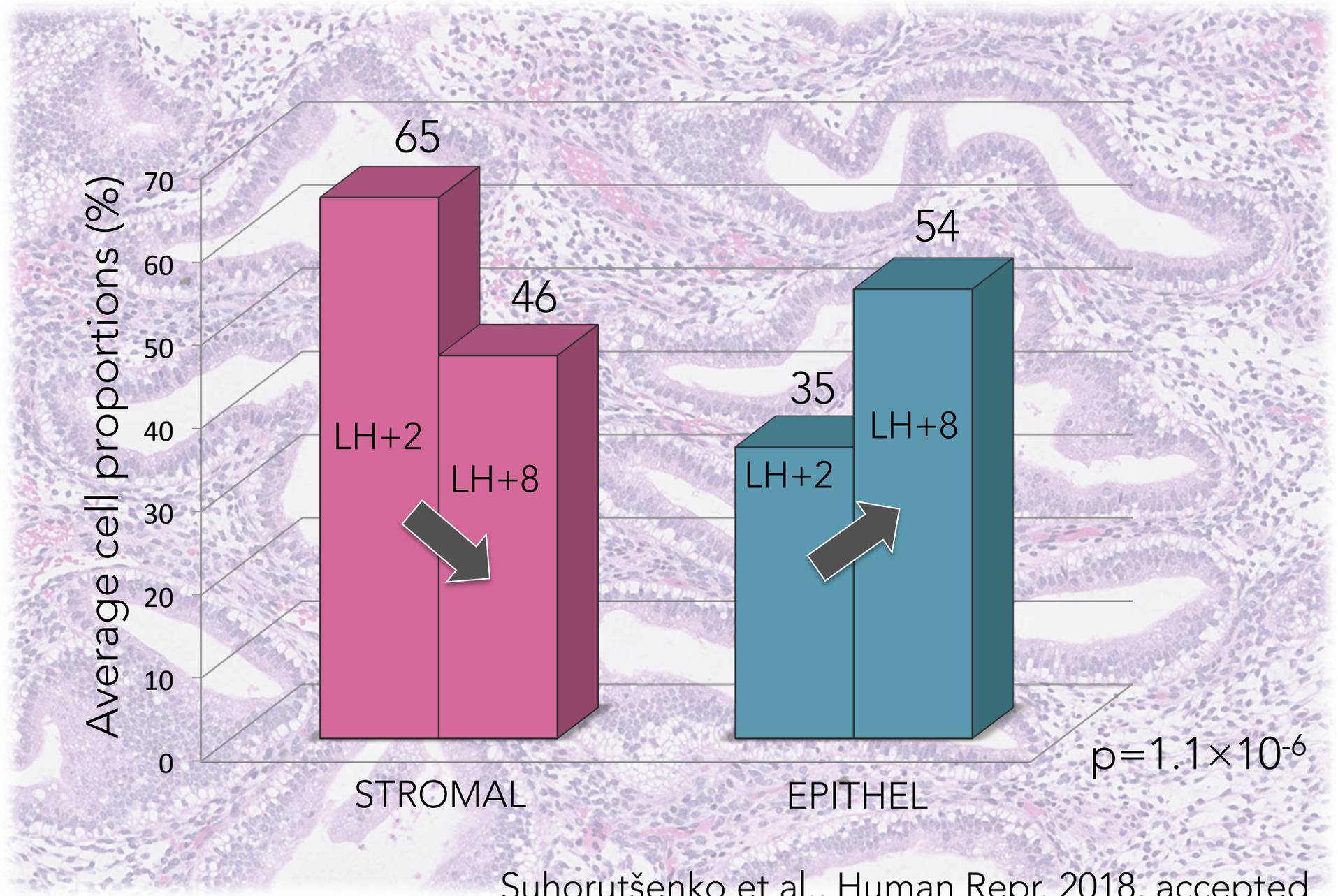
STUDY QUESTION

Does cellular composition of the endometrial biopsy affect the gene expression profile of endometrial whole-tissue samples?

SUMMARY ANSWER

The differences in epithelial and stromal cell proportions in endometrial biopsies modify whole-tissue gene expression profiles, and also affect the results of differential expression analysis.

Transcriptome adjusted for tissue cellular heterogeneity





GENE SELECTION

Krjutškov et al., Human Reproduction, 2016

Altmäe et al., Scientific Reports, 2017

Koel et al., Human Reproduction., under review

ADJUSTED ANALYSIS



Suhorutšenko et al., Human Repr. 2018, accepted!



TECHNOLOGY

TAC-seq method. Patent application PCT/EP2017/083613

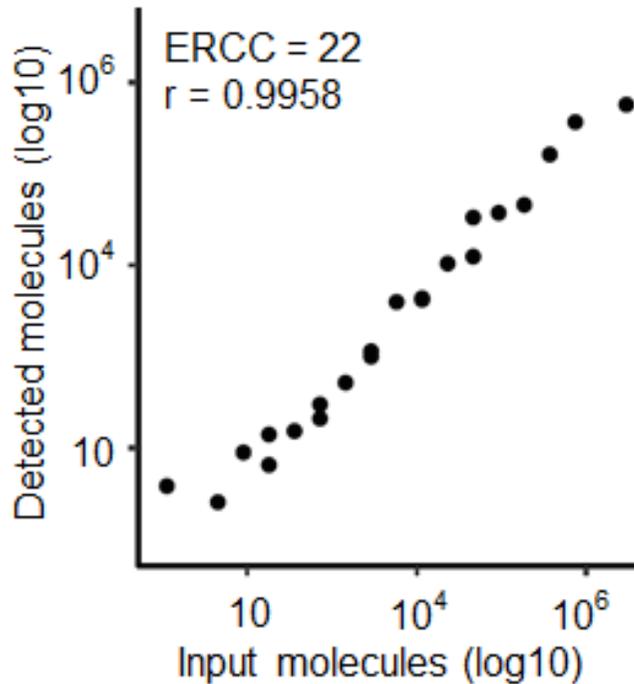
Teder et al., npj Genomic Medicine., under review



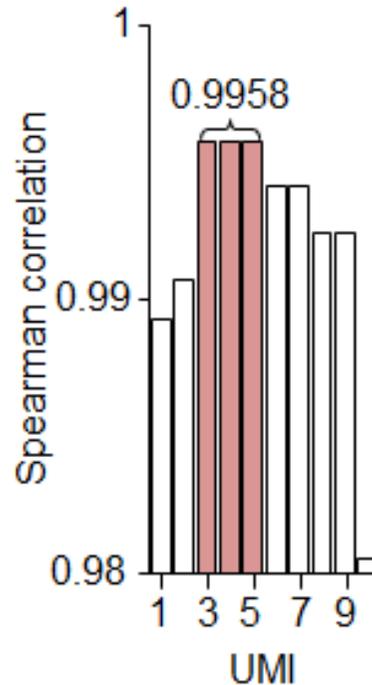
TAC-seq

Targeted Allele Counting by Sequencing

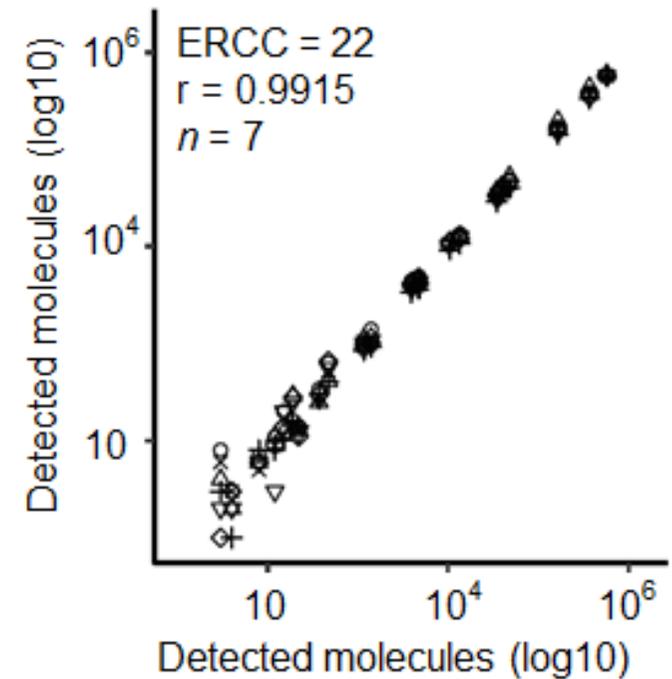
Input = output



UMI makes sense!



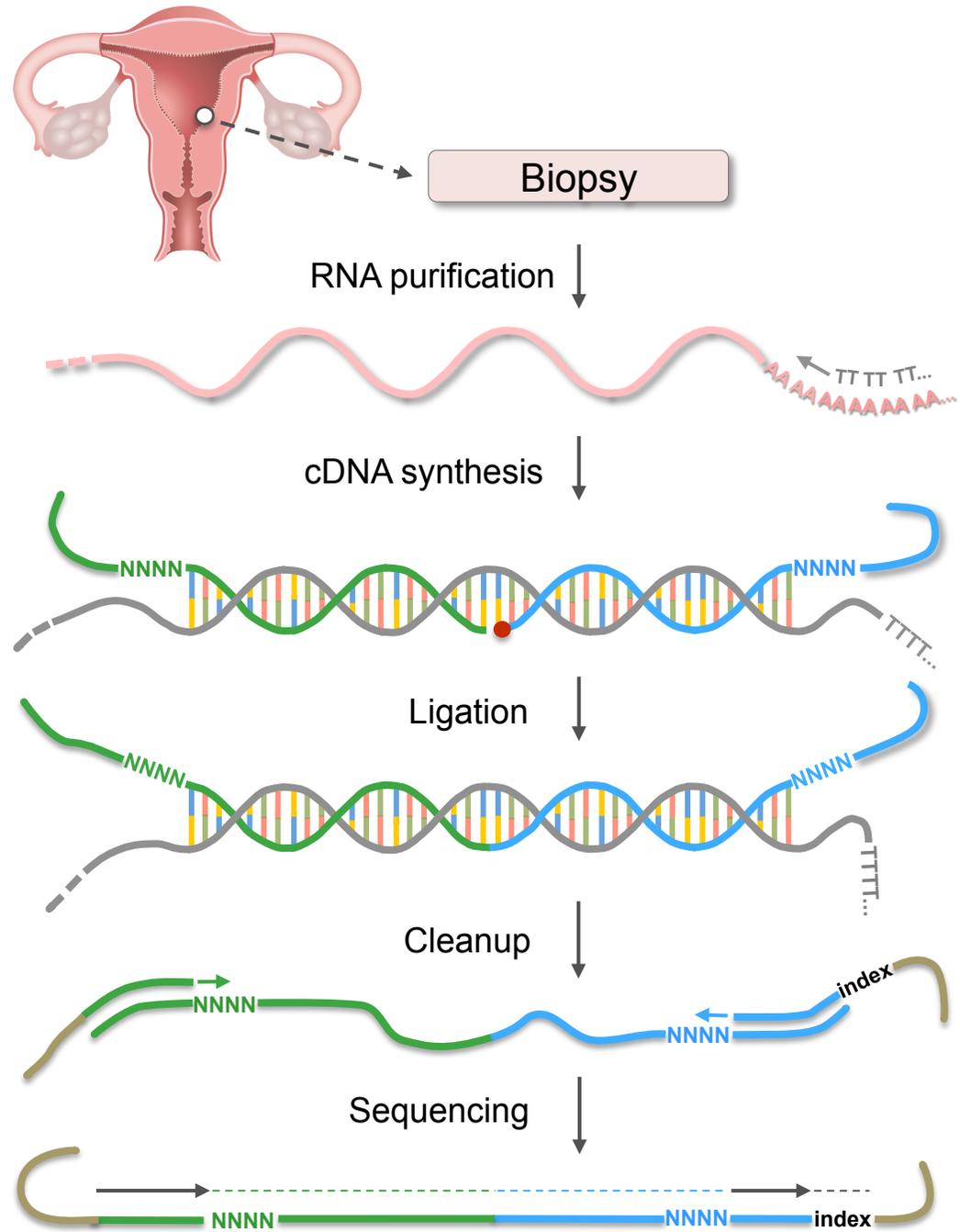
Reproducibility is perfect!



-----NNNNNNNN-----



- ☑ Highly accurate
- ☑ Cost-effective
- ☑ Single-tube assay
- ☑ Multiplex

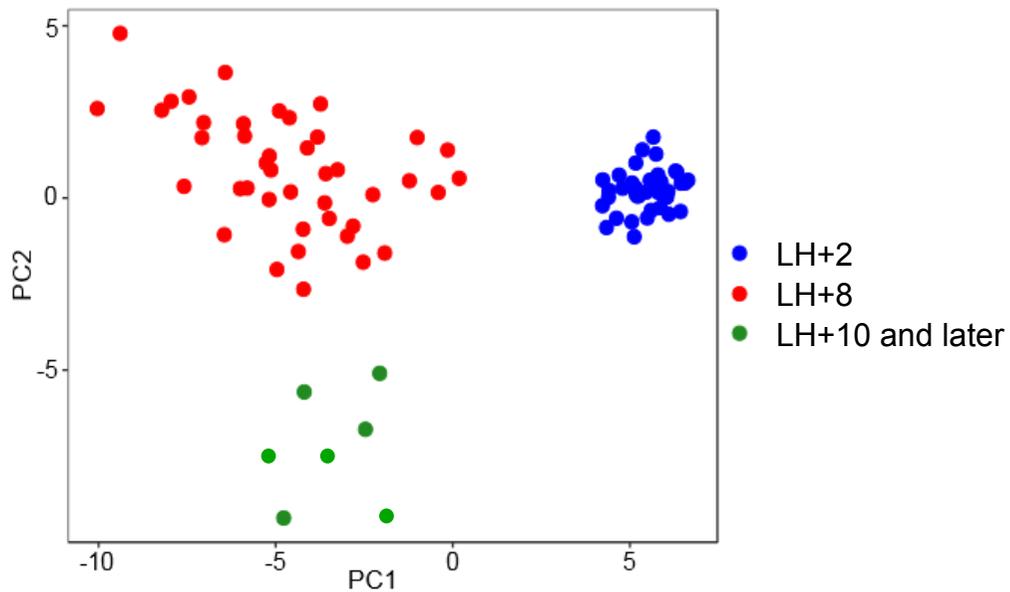


doi.org/10.1101/295253

Teder et al., npj Genomic Medicine., under review

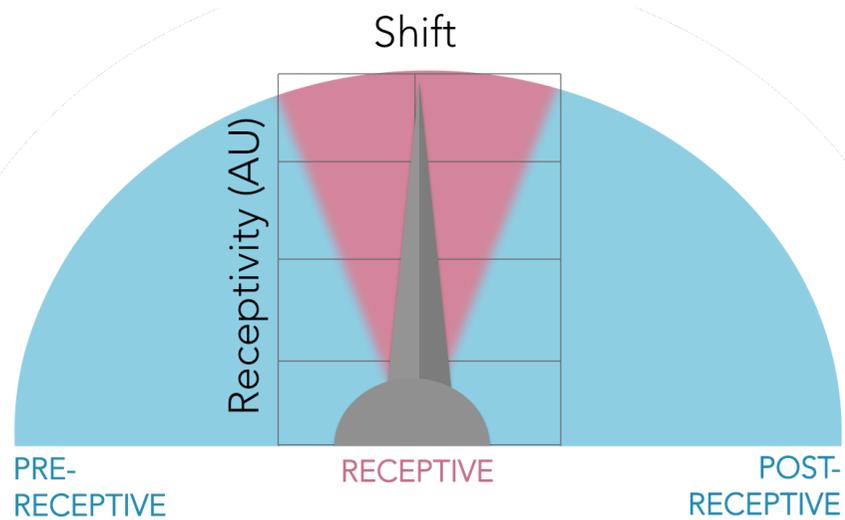
Clinical
interpretation

Scientific plot



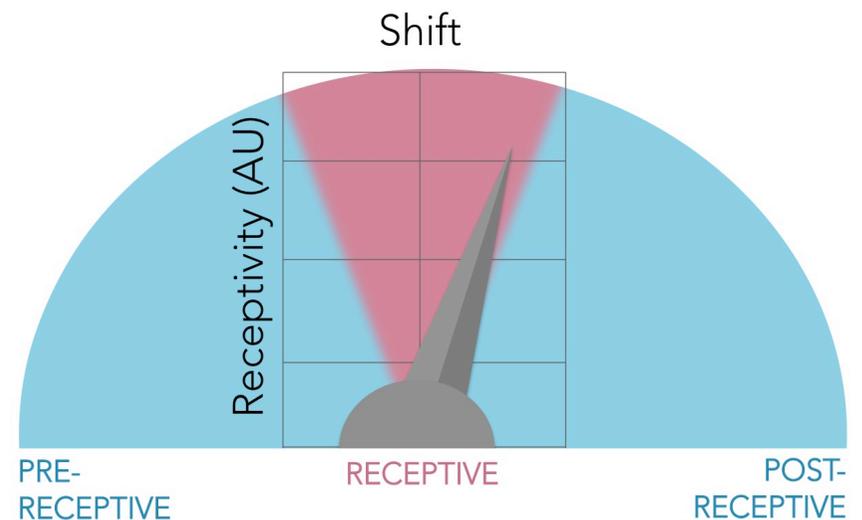
RECEPTOMETER

EXAMPLE 1 – **receptive**



Receptive probability	0.922
Pre-receptive probability	0.047
Post-receptive probability	0.031

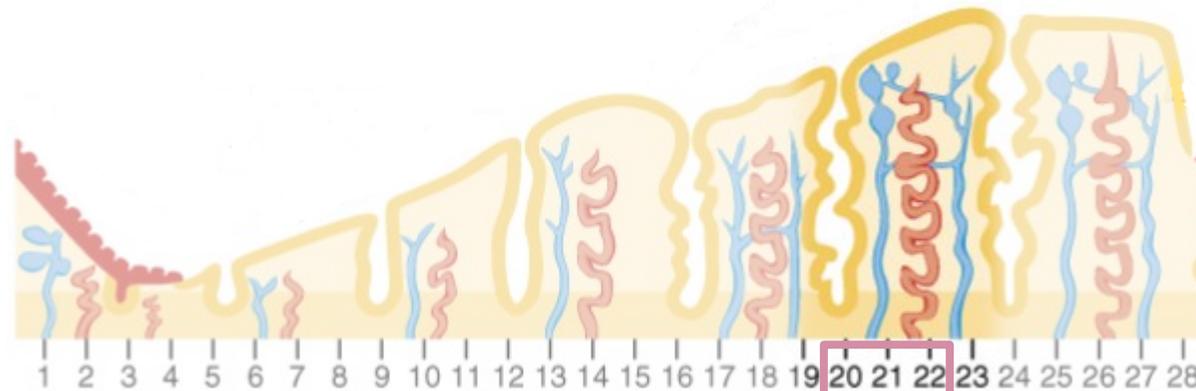
EXAMPLE 2 – **post-receptive**



Receptive probability	0.782
Pre-receptive probability	0.048
Post-receptive probability	0.170

IDEAL CASE

First TEST



LH+7/8
HRT +5/6

Adjusted timing of progesteron
treatment

Second TEST after adjustment is **RECOMMENDED**



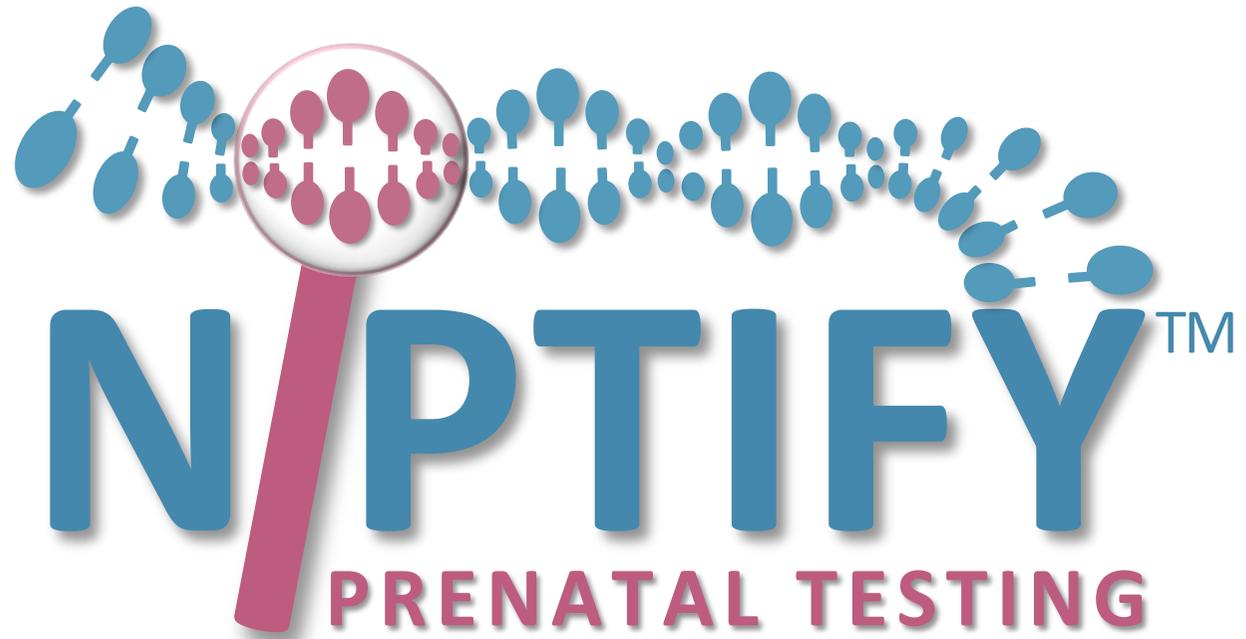
WHO SHOULD USE IT?

Repeated implantation failure

All IVF patients!?



Lets change the topic!

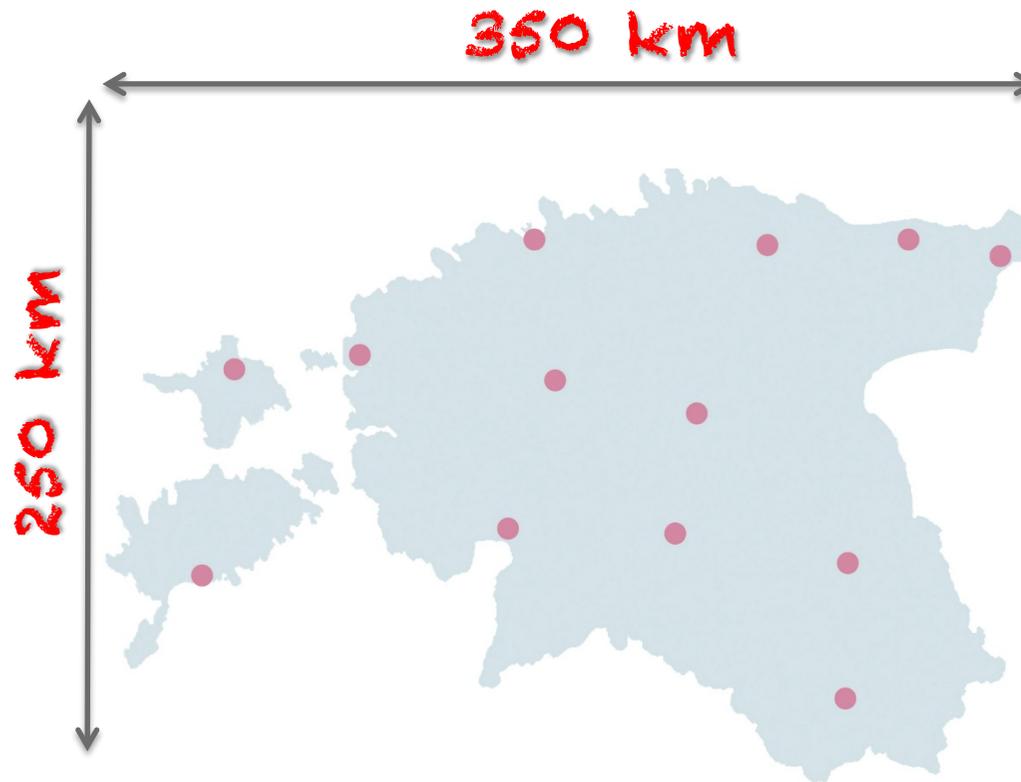


NIPTIFYTM

PRENATAL TESTING



- ☑ Since 10th week after conception
- ☑ Based on DNA-counting technology
- ☑ Chr 13, 18 and 21 aneuploidies





ADVANTAGES



SOFTWARE

Martin Sauk et al., Scientific Reports 2018

SCIENTIFIC REPORTS

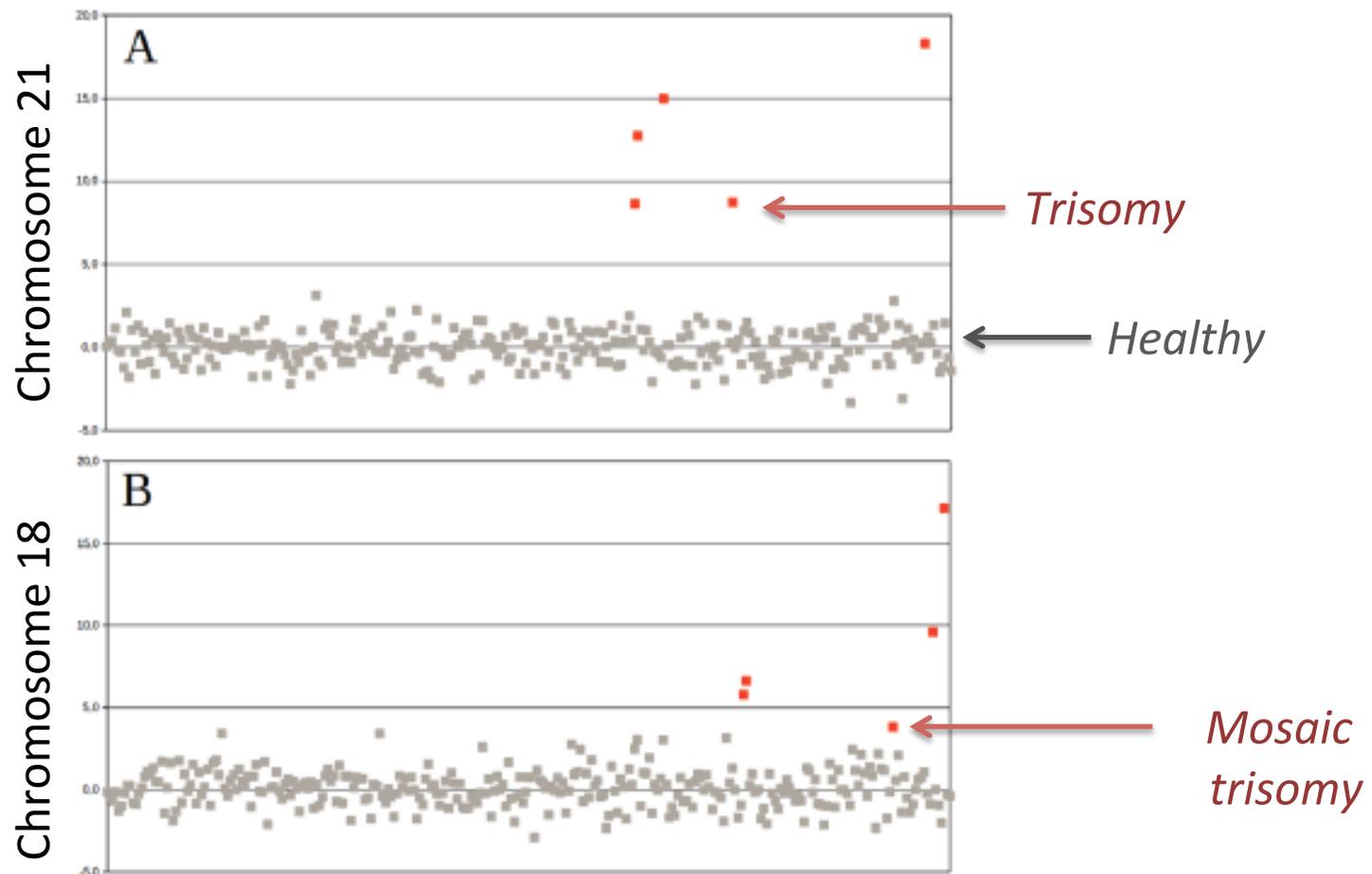
NIPTmer: rapid k-mer-based software package for detection of fetal aneuploidies

Martin Sauk et al., 2018



NIPTmer: rapid k-mer-based software package for detection of fetal aneuploidies

Sauk et al., 2018





ADVANTAGES



SOFTWARE

Martin Sauk et al., Scientific Reports 2018

VALIDATION



*Olga Fjodorova jt., Prenatal Diagnosis,
submission in process...*





NIPT tests	584
Low-risk pregnancies	174
High-risk pregnancies	409
Trisomy 13	4 (100%)
Trisomy 18	15 (100%)*
Trisomy 21	21 (100%)
Sex	YES (100%)
Feal fraction	YES

* *Except one mosaic case*

False positives <1%

NIPTIFY.ee

Only 4 more slides...

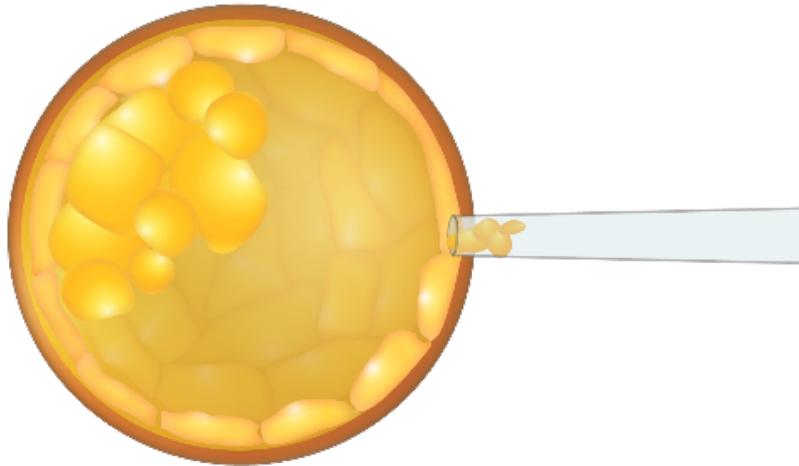


PGS*for***U**TM

EMBRYO CHROMOSOME TESTING



BACKGROUND



**PGS ANALYSES CELLS
FROM TROPHOBLAST**

Ca 5-6 cells

Analysis of all 24 chromosomes

Detects deletions-insertions (from 2-3 Mb)

Detects embryo mosaicism (>20%)

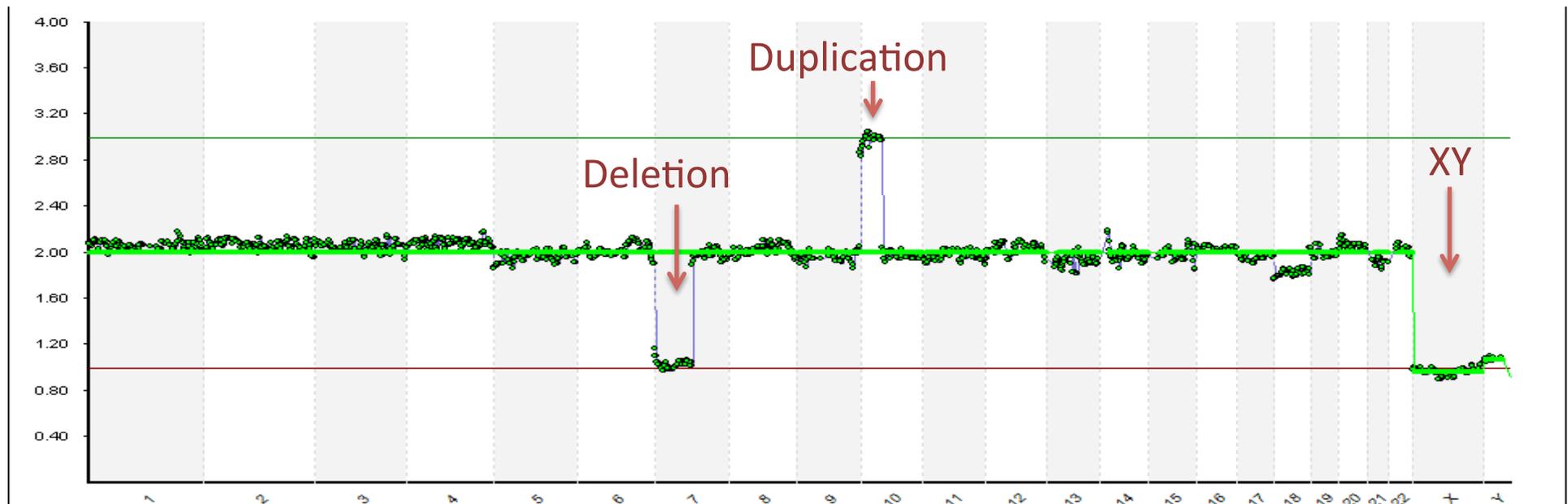


Karyotype of the blastocoel fluid demonstrates low concordance with both trophectoderm and inner cell mass

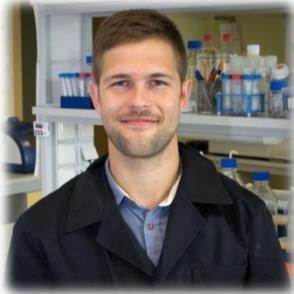
Tšuiko et al., 2018

Fertility and Sterility.

Test-period: 7 patients
2 pregnancies
3 embryos per patient on average



Hindrek Teder



Priit
Paluoja

Merli
Saare



Mariann
Koel

Receipt of success
is simple
—
just choose the best
coworkers!

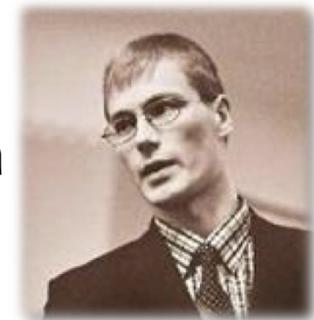


Kadri
Rekker

Juha Kere

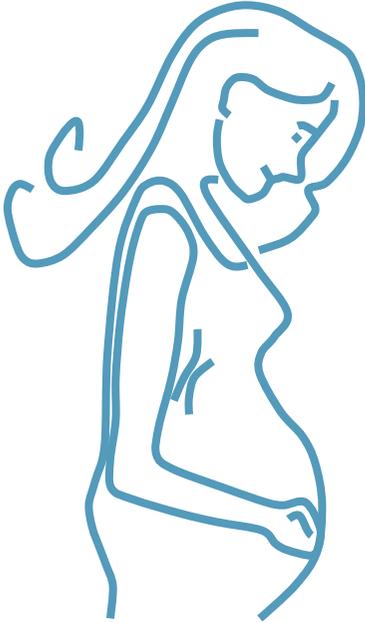


Priit Palta



Andres Salumets

Competence Centre on Health Technologies



European Union
European Regional
Development Fund



Investing
in your future



UNIVERSITY OF HELSINKI



UNIVERSITY OF OULU

