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Whole transcriptome profile of alternative splicing events in decidual cells during uncomplicated pregnancy

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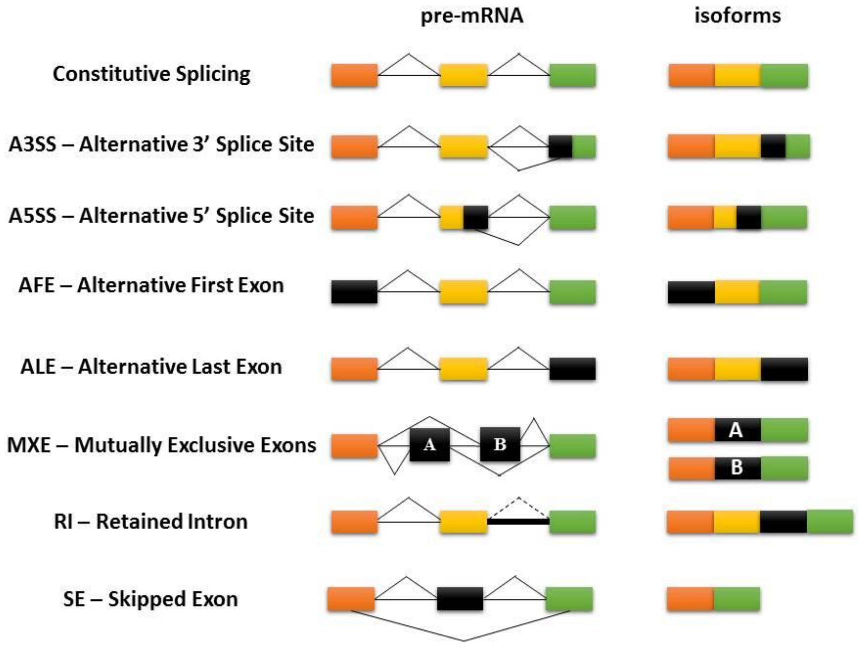
Motivation and Aim

Alternative splicing (AS) is an important mechanism for generating protein diversity and regulating gene expression in eukaryotes. Multiple protein isoforms with distinct functional properties can be important for cell differentiation and tissue-specific functions.



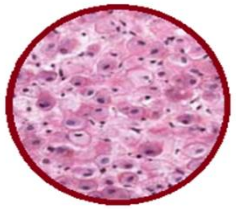
Patterns of alternative splicing

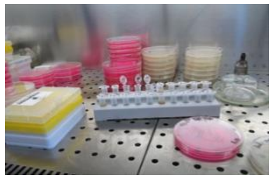
In decidua cells (DC), AS may possibly play a role in several key biological processes that are critical for supporting pregnancy.

Dysregulation of AS can contribute to placental disorders.

Materials and methods

1. Collecting biopsies
2. Laser microdissection
3. Isolation of RNA
4. Genomic libraries
5. RNA-seq
6. Bioinformatics



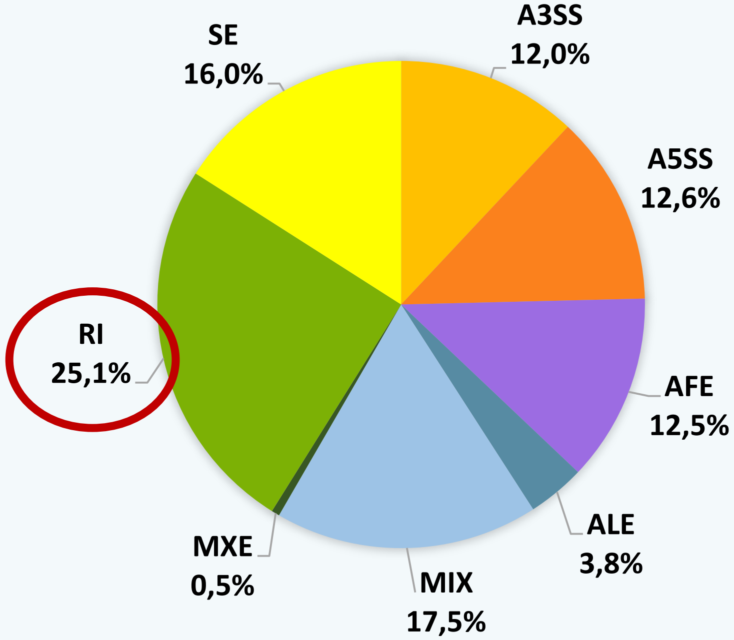


- ✓ RNA of DC was obtained from placental tissue of women with uncomplicated pregnancy.
- ✓ Alignment to the reference genome (hg38) was performed by the "STAR" program.
- ✓ The analysis of AS events was performed in the edgeR by the "SGSeq" package.

Bioconductor
SGSeqBioC2016

Results

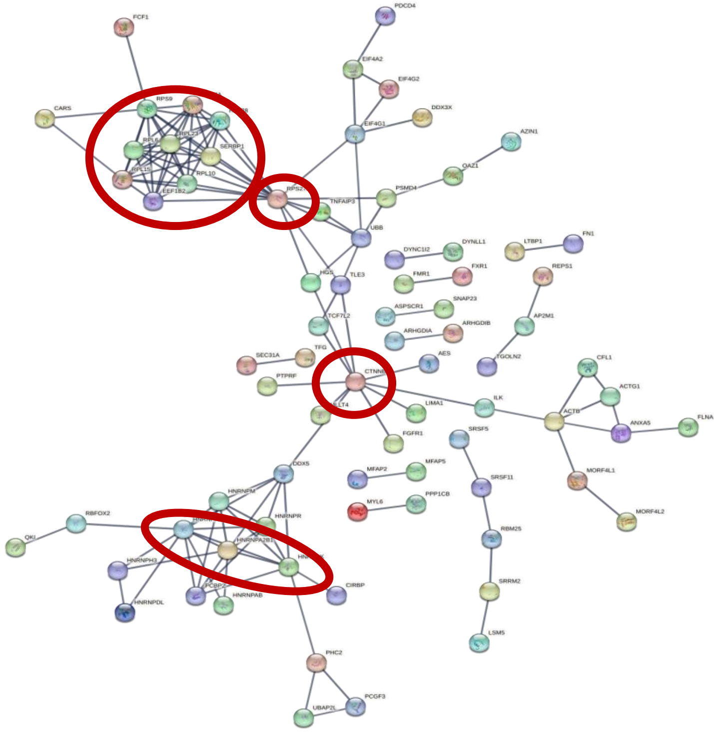
- We identified 151233 AS events annotated in GENCODE v.26 for 19760 genes.
- We selected 1871 AS events for 352 genes according to certain criteria (CPM > 10; the proportion of the event is in the range from 0.05 to 0.95).
- These AS genes are involved in processes related to the canonical Wnt/β-catenin signaling pathway, regulation of mRNA splicing, intercellular communication.
- These AS events were classified into 7 main types.



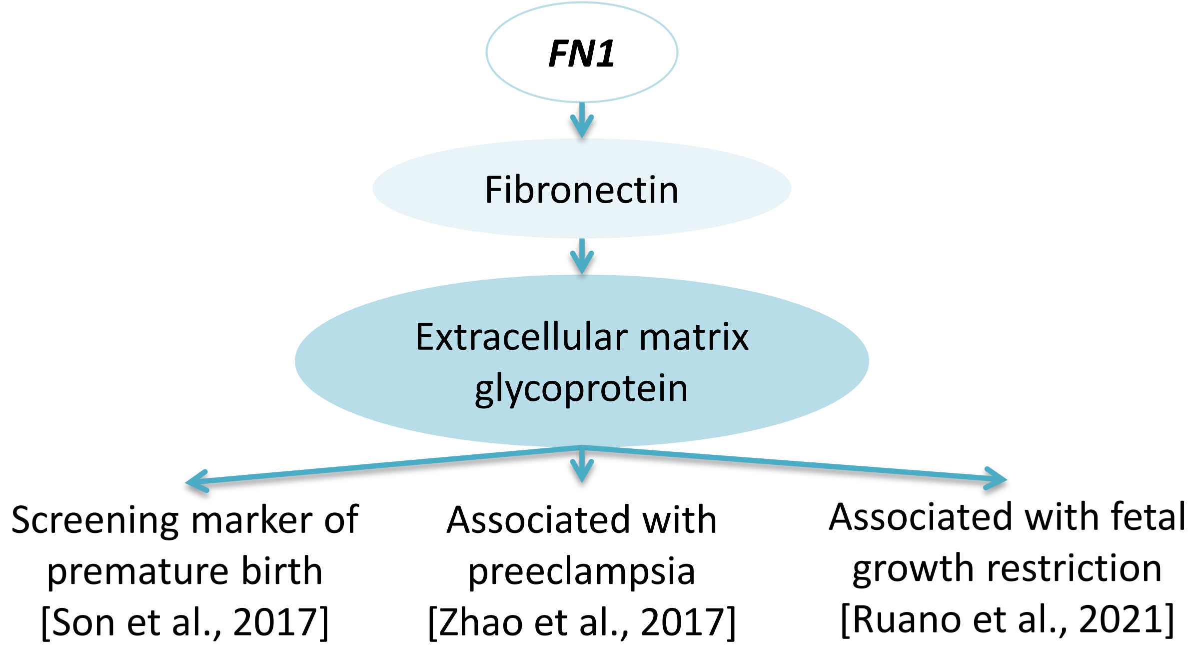
Top 5 genes with the maximum number of AS events

Number of AS events	**Gene**	**Product**
27	***HNRNPH1***	Heterogeneous Nuclear Ribonucleoprotein H1
25	*CAST*	Calpastatin
25	*FGFR1*	Fibroblast Growth Factor Receptor 1
23	*EIF4G1*	Eukaryotic Translation Initiation Factor 4 Gamma 1
18	*FN1*	Fibronectin 1

- 158 genes had 5 or more AS events.
- The network of protein-protein interactions contains 79 products of these genes.
- The central place in the network is occupied by the genes *RPS27A*, *RPS9*, *CTNNB1*, ***HNRNPH1***, *RPL15*, *RPL23*, *RPL38*, *RPL6*, *RPL7A*.



FN1 is the most interesting gene from the top.



FN1

Fibronectin

Extracellular matrix glycoprotein

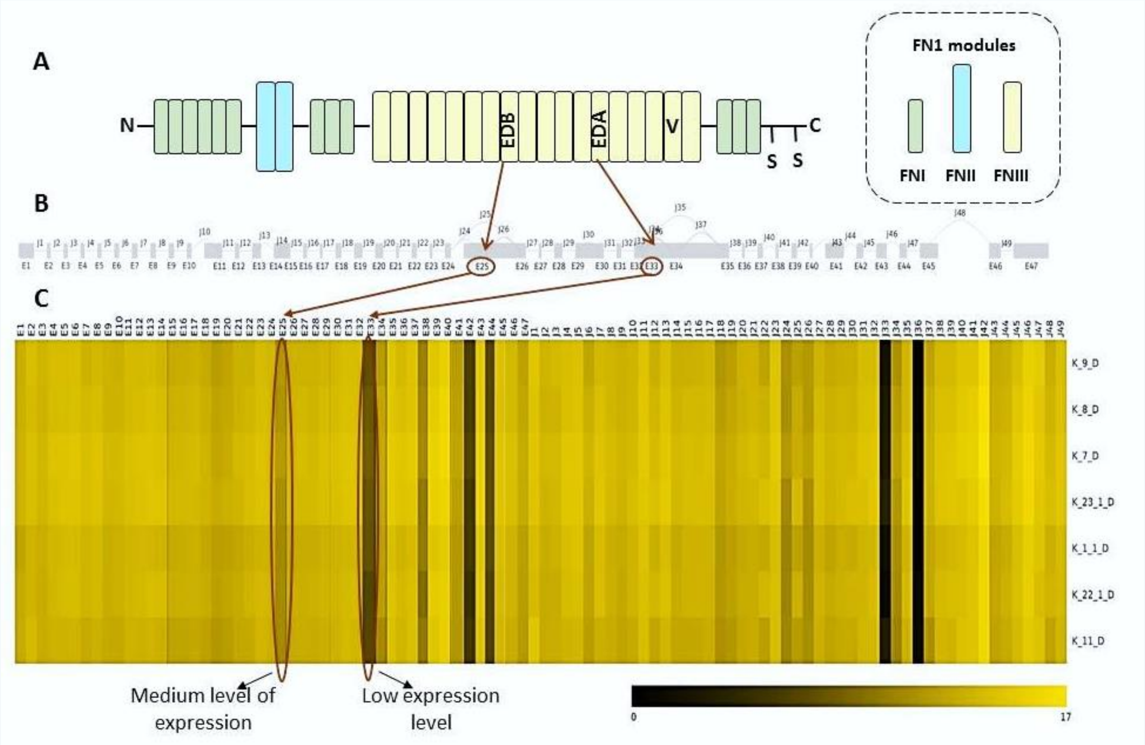
Screening marker of premature birth [Son et al., 2017]

Associated with preeclampsia [Zhao et al., 2017]

Associated with fetal growth restriction [Ruano et al., 2021]

The **EDB** domain of fibronectin supports normal growth of embryonic fibroblasts.

The **EDA** domain of fibronectin can trigger an inflammatory response through activation of TLR4 [Okamura et al, 2001], overexpression of which can lead to preeclampsia.



A – model structure of the fibronectin protein,
B – exons and exon-exon compounds of the *FN1*,
C – expression of exons and exon-exon compounds of the *FN1* in DC, where black is minimum expression level, yellow is the maximum expression level.

The results confirm the importance of AS, which significantly increases transcriptional diversity in DC of placental tissue.
Many genes undergo AS in DC are associated with pregnancy complications.