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Oral Presentations

O-39

A novel biallelic missense variant in cyclin B3 is associated with failure of oocyte meiosis II and recurrent fetus triploidy

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Background: Recurrent pregnancy loss (RPL) is an important infertility-related complication affecting up to 5% of clinical gestations. The both parental and embryonal factors are associated with RPL. Triploidy is one of the common chromosomal abnormalities affecting pregnancy and accounts for an important portion of first-trimester abortions. Triploidy has been reported in some cases of RPL but its underlying molecular mechanism remains unknown.

Objective: The aim of this study was to determine the genetic causes of RPL associated with fetus triploidy in an Iranian family.

Materials and Methods: We examined the status of genomic imprinting, short tandem repeat (STR) markers and performed the whole exome sequencing in a family including two sisters with RPL history. Additionally, we assessed oocyte maturation in vivo and in vitro and effect of the candidate protein variant in silico.

Results: Triploidy of maternal origin was confirmed in the aborted fetuses by STR markers genotyping. All the maternally inherited pericentromeric STR alleles were homozygous in the fetuses and oocytes maturation was deficient. A new deleterious missense variant (c.T4050A, p.V1251D) of the cyclin B3 gene (*CCNB3*) was identified by whole exome sequencing. The homozygous mutation affecting a residue conserved in placental mammals and located in a region that can interact with the cyclin-dependent kinases co-segregated in homozygosity with RPL.

Conclusion: Here, we report a family in which a novel damaging variant in cyclin B3 is associated with the failure of meiosis II in oocyte and recurrent fetus triploidy, implicating a rationale for *CCNB3* testing in RPL patients.

Key words: *Recurrent pregnancy loss, Triploidy, Whole exome sequencing, CCNB3.*

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