

tRNA halves: a striking new discovery in preeclampsia

Authors

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Introduction

The placenta releases approximately 3g of syncytiotrophoblast-derived extracellular vesicles (STB-EV) into the maternal circulation each day at term. In preeclampsia, STB-EV release is upregulated and these vesicles have different proteins expressed on their surface. We investigated the RNA content of STB-EV in normal pregnancy and preeclampsia, to see if this also varied by disease state.

Methods

Dual-lobe placental perfusion was used to isolate STB-EV ex vivo from six normal and six preterm preeclampsia placentae. RNA was extracted from STB-EV and whole placental tissue; deep sequencing was performed with bioinformatics analysis. RNA expression was corroborated using a novel qPCR technique involving ligation of RNA adaptors, enabling specific sequence amplification. Biological activity was investigated by treating cultured fibroblasts and measuring protein synthesis using a fluorescent-labelled methionine analogue.

Results

More than 95% of RNA reads in STB-EV are tRNA species; in whole placental tissue this was 10-40% (rRNA predominates). Most tRNA reads are 5'tRNA-halves (cleaved at 30-32 nucleotides); the most abundant is 5'tRNA-half-Gly-GCC. Fibroblasts treated with 5'tRNA-half-Gly-GCC show 12.4% suppression of global protein synthesis compared to scrambled tRNA-controls. Expression of specific tRNA-halves is markedly different in STB-EV from women with preeclampsia compared to normal women.

Conclusion

This is the first study to report tRNA halves in pregnancy. Our data show they are the predominant RNA expressed in STB-EV, and there is enrichment from whole placental tissue suggesting active export. Studies from other biological systems suggest tRNA-halves are potent and precise signalling molecules; we demonstrate tRNA-halves abundant in STB-EV are biologically active.

STB-EV tRNA-half expression is markedly different in women with preeclampsia. tRNA-half release is stimulated by cellular stress; their differential expression in preeclampsia is consistent with known oxidative stress in this disease. tRNA-halves might be useful to predict and diagnose preeclampsia; critically they also point towards the pathogenesis of this complex disease.

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