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Transfer RNAs as a source of novel small non-coding RNAs with therapeutic implications

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Transfer RNA (tRNA) is traditionally considered to be an adaptor molecule that helps ribosomes to decode messenger RNA (mRNA) and synthesize protein. Recent studies have demonstrated that tRNAs also serve as a major source of small non-coding RNAs that possess distinct and varied functions. These tRNA fragments are heterogeneous in size, nucleotide composition, biogenesis and function. tRNA fragments seem to play multiple roles in cell physiology with relevance to human health and disease. Our research is focused on the investigation of the physiological roles of tRNA fragments and their therapeutic application in cancer biology and neurodegeneration fields. Particular class of tRNA-derived fragment, so called tRNA-derived stress-induced RNAs (tiRNAs), helps cells to adapt stressful conditions. They trigger stress response pathway that is beneficial for cell survival. This tiRNA-mediated stress response is lost in certain neurodegenerative disease causing neuronal death and is amplified in cancers where it provides advantage under hostile tumor environment. Selected tiRNAs and their DNA analogues assemble stable unique G-quadruplex structures that can be delivered to the cells to mimic this stress response and can be used as targets or tools for the treatment of diseases.

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Differential expression of parental alleles of BRCA1 in human preimplantation embryos

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Introduction: The expression of parental genomes is required for completion of embryogenesis. Differential methylation of each parental genome has been observed in mouse and human preimplantation embryos. It is possible that differences in methylation affect the level of gene transcripts from each parental genome in early developing embryos. The aim of this study was to investigate if there is a parent specific pattern of *BRCA1* expression in human embryos and to examine if this affects embryo development when the embryo carries a *BRCA* mutation.

Materials and Methods: Differential parental expression of *ACTB, SNRPN, H19* and *BRCA1* was semi-quantitatively analysed by mini-sequencing in 95 human preimplantation embryos obtained from couples undergoing preimplantation genetic diagnosis (PGD).

Results: *BRCA1* was shown to be differentially expressed favouring the paternal transcript in early developing embryos. Methylation specific PCR showed a variable methylation profile of *BRCA1* promoter region at different stages of embryonic development. Embryos carrying paternally inherited *BRCA* mutations were shown to develop more slowly compared to the embryos with maternally inherited BRCA mutations.

Conclusions: The results of this study suggest that differential gene expression can influence the early development of preimplantation embryos. When the paternal *BRCA1* transcript present in the embryo carries a mutation, the embryo may become more vulnerable to stress due to rapid demethylation of the paternal genome and the gradual demethylation of the maternal genome. Further extrapolation of this data suggests that the risk of transmitting a BRCA mutation may be modulated by the parental origin of the mutation.

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