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Live birth derived from oocyte nuclear transfer for mitochondrial disease

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Mutations in mitochondrial DNA (mtDNA) are maternally inherited and can cause fatal or debilitating mitochondrial disorders. The severity of clinical symptoms is often associated with the level of mtDNA mutation load in heteroplasmy. Current clinical options to prevent transmission of mtDNA mutations to offspring are limited. Experimental nuclear transfer in metaphase II oocytes, also called mitochondrial replacement therapy, has been shown to be a novel technology in preventing mtDNA transmission from oocytes to pre-implantation embryos or pluripotent stem cells. Here, we report a female carrier of Leigh syndrome (24.5% of mtDNA 8993T>G mutation load), with a long history of multiple pregnancy losses and deaths of offspring due to this disease, underwent *in vitro* fertilization following reconstitution of her oocytes by spindle nuclear transfer into the cytoplasm of enucleated donor oocytes. A male euploid blastocyst was obtained from the reconstituted oocytes, which had only a 5.7% mtDNA mutation load. Transfer of the embryo resulted in a pregnancy with delivery of a boy with low mtDNA mutation load in all his tested tissues. The boy is currently healthy at seven months of age although long-term follow-up of the child's longitudinal development remains crucial.

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Brain excitation/inhibition balance and genetic factor in paranoid schizophrenia: An ERP, fMRI and gene RELN study

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We elaborated the hypothesis of pathogenesis of paranoid schizophrenia with positive symptoms (pseudohallucinations etc.). The obtained data have revealed that the positive syndrome in paranoid schizophrenia corresponds to the disturbances of balance of brain excitation/inhibition processes and expression of protein reelin, are caused by infringement of gene's RELN methylation, resulting to dysfunction of neural networks. In the first part of our experimental work, we studied different ERP components to visually present emotionally negative and neutral stimuli. The most surprising results appeared to be simultaneous increase (decrease) of both ERP components parameters–latencies and amplitudes only in patients. The results found in our schizophrenic patients, we called "paradox effect" evidently pointing to the disturbance of the balance between the processes of excitement and inhibition. The fMRI study was aimed to detect brain areas where connectivity is disturbed. We think this can be temporal and frontal (prefrontal) areas as is known that in schizophrenic patients the function of planum temporale, sensory input for auditory stimuli is damaged and frontal areas are greatly deficient. The third part of our work was the study of the gene RELN responsible for microstructural brain anomalies during ontogenesis contributing to the development of schizophrenia. Reelin (protein of gene RELN) contributes to expression of GABA and release of glutamate on NMDA-receptors; its deficit provokes the disturbance of excitation/inhibition balance and could be used as biological marker. Thus, our complex study was done to obtain biological markers paranoid syndrome in schizophrenia.

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