

Title: New Approaches of IVF-based Gene and Cell Therapy

Mutations in mitochondrial DNA (mtDNA) are associated with severe human diseases and are maternally inherited through oocyte cytoplasm. To prevent transmission of mtDNA mutations from mothers to their children, we are exploring IVF-based gene therapy where mutant mtDNA in patient unfertilized oocyte is replaced with healthy donor mitochondria by metaphase spindle transfer. More recently, we expanded mitochondrial replacement to nuclear transfer of the first polar body (PB1) genomes from metaphase II (MII) oocytes into enucleated donor MII cytoplasm (PBNT). After fertilization with sperm, reconstructed PBNT oocytes underwent *de novo* meiosis II and formed diploid embryos and ES cells. We conclude that, in addition to spindle transfer, PBNT could be used as additional mitochondrial replacement technique. Moreover, PBNT offers a novel source of patient oocytes for treatment of female infertility.