DESCRIPTION FOR THE GENERAL PUBLIC (in English)

Since its first use in 1978, Assisted Reproductive Technology (ART) has completely transformed the field of reproductive medicine, giving the possibility of parenthood to a growing number of infertile couples. It is estimated that ART has allowed the birth of > 5 million babies worldwide, thus suggesting that infertility must be regarded as a health and social issue, affecting 10-15% of couples at child-bearing age. Moreover, due to the growing request of medical response to infertility problems, the technical advance of ART has led to the introduction in a clinical settings of new and quite invasive procedures (ie. Blastomere Biopsy, BB, that is the removal of one cell [blastomere] from an early embryo for genetic screening). Notwithstanding the majority of babies conceived by ART are healthy at birth, there is a mounting evidence that ART, particularly, invasive procedures, like BB, may affect long-term health of the resulting individual. During early development embryos are "programmed" to form all tissue/organs of the future individual, through the progressive establishment of epigenetics marks on the genome. This window is very sensitive to external stressors, and even the simple culture *in vitro* might result in epigenetic deregulations. Severe epigenetic alterations result in arrested development, while subtle ones might be responsible for obesity, high blood sugar level, hypertension, altogether described as "Metabolic Syndrome" (MS). This phenomenon has been described in several species and has been termed "embryonic adaptation", or foetal programming for adult diseases (Barker hypothesis). Although there is no evidence of a direct cause-effect link between BB and MS in human owing to its recent introduction in the clinic, animal studies suggest instead a causal one. Therefore, I ***hypothesize that the use of BB may predispose the embryo and resulting individual to Metabolic Syndrome***. To test my hypothesis, I will perform a carefully designed research plan using mouse as animal model. The mouse model is the more appropriate for my work, as experimental research may not be done on human embryos, and because mouse embryology and genomics are the most advanced ones. Offspring will be generated from embryos subjected to Blastomere Biopsy (BB - removal of one cell from 8 cells stage embryo), as well as sham BB (that is removing and repositioning the blastomere), *in vitro* culture (standard procedure common to all ART) and *in vivo* control. Resulting mice will be screened for general health and metabolic function through a battery of molecular and clinical/analytical tests. Next, I will investigate the metabolic pathways deregulation in BB group by transcriptome profiling of two major organs: hypothalamus and liver. In the proposed project, hypothalamus and liver have been selected as target organs because their dysfunction (i.e. impaired integration of feedback signals from periphery, sensing of energy balance for the brain; altered glucose and lipid metabolism for the liver) play a major role in the onset of metabolic syndrome. Other organs will also be collected however, due to budget limitations they will be available for analysis funded by other projects of Polish/EU scientists willing to address other relevant ART-connected pathologies.

The project will provide useful information to researchers, medical practitioners and society. As infertility and metabolic syndrome are two of the main contemporary health issues and their incidence is growing, understanding if invasive ART are responsible of increased predisposition to metabolic syndrome is extremely important for infertile couple and, mainly, for future generations health and well-being. Normally, the safety of ART procedures - potentially affecting the long term disposition of a human life - are only investigated retrospectively, once the babies are born. This project follows an opposite path, and will provide the objective and unquestionable evidence on whether or not BB is responsible for an increases occurrence of metabolic syndrome in BB derived offspring.