Research project objectives / Research hypothesis:

By delaying implantation we recently demonstrated that blastocysts of bigger size are characterized by intensive signalling to the mother through exosome release, clearance of damaged particles by autophagy, cessation of cell apoptosis and activation of DNA damage repair (DDR) pathways, which all favours its implantation. Conversely, high apoptosis and impaired DDR characterize embryos from aged and obese mothers and embryos obtained through Assisted Reproduction Technologies (ART). Because those compromised embryos are also smaller in size, it may be speculated that allowing them to growth further will improve their developmental potential. Maternal ageing, obesity and ART are all associated with pregnancy failures, impaired neurodevelopment and metabolic health alterations in offspring. We hypothesise that maximising blastocyst's size prior implantation ensures long term health of offspring.

Research project methodology:

First, we will verify if maximising blastocyst size determines pregnancy success and postnatal health of offspring (specific aim 1, SP1). Because it is not known which size of the blastocyst is optimal in term of developmental potential, we will evaluate first the development of blastocysts at four progressive growth stages (6, 8, 10 day post coitum, dpc) in comparison to normal (4 dpc). To delay the implantation until required time of blastocyst's growth, females will be ovariectomised at 2 dpc and then blastocysts from young fertile mice (Group 1-young), aged (Group 2-aged) and nourished with high fat diet mice (Group 3-HFD), and cultured in vitro (Group 4-ART) will be collected and evaluated. We will then evaluate how the blastocyst's structural and functional features are reflected by its size and provenience (SP2). Finally, part of blastocysts (Groups 2-4) at an optimal growth stage (defined on the basis of previous experiments outcome) will be transferred to prereceptive pseudopregnant recipients for evaluation of full term development and health of offspring (SP 3 - proof of concept).

Pioneering nature of the research project:

This is a pioneering project because the effect of blastocyst size and delayed implantation in short term outcomes – direct improvement of blastocyst functionality, and long term outcomes – offspring health, is not known. The project will provide high level research outcome with high translation validity (from basic embryology to applied science). Our hypothesis, if confirmed, would have great impact on reproductive medicine, opening up new investigations into the benefits of delayed implantation. By increasing blastocyst's size before implantation, this original project aims to prove that such a strategy can be proposed as a therapeutic tool in reproductive medicine in humans as well as in animal breeding programs.