

Oocytes (eggs) from different mammals contain various amounts and kinds of lipids. The role of those lipids has been not clarified so far. Lipid droplets removal from the fertilized egg doesn't influence development of the embryo until the term of pregnancy. Therefore, *we hypothesized that lipids may serve to the embryo as a source of energy during Embryonic Diapause (ED)*. ED is reversible arrest of the embryo while waiting for uterine receptivity signal for implantation. This natural predisposition of the embryo to wait for the maternal stimulus is possible because embryonic cells are not specialized and therefore are able to arrest and restart cycling. ED was described only in over 100 mammalian species so far. Actually, the occurrence of ED may be much more widespread, as there is no mammalian species in which ED occurrence has been excluded. Studies about ED are limited to those mammals in which this phenomenon is known, such as marsupials or mink. On the other hand, almost 40 years ago, ED was successfully induced in embryos from ferrets, in which this phenomenon does not occur naturally. Few years ago, we demonstrated ED in domestic sheep. We believe that the embryonic diapause (ED) is a natural consequence of delayed uterine receptivity, and therefore may occur in all mammals. It has been said that Mother Nature is 'collecting and hiding useless but harmless traits' because they may come in handy. Therefore, the versatility of ED, which occurs whenever needed, represents an important advantage for species survival. Such versatility does not facilitate the demonstration of the trait. ED duration is variable in mammals and may last from few days in some species (such as domestic mouse) until several months in some carnivores (such as American mink). The quantity of lipids accumulated in oocytes is also species dependent. Based on this, we formulated the HYPOTHESIS that *the quantity of lipids accumulated in the oocyte and in the resulting embryo is proportional to the duration of ED in given species*, so that more lipids are present in the oocyte longer is the ED. The GENERAL OBJECTIVE of this project is to find out if *the quantity and/or quality of lipids in the oocytes is correlated with the duration of ED*. To do this, first we will verify if the duration of the ED is related to the content of lipids stored in murine oocytes and embryos (*specific aim 1*). Second, we will verify if lipid content stored in the oocytes from various naturally diapausing mammals is correlated with previously reported duration of their ED (*specific aim 2*). Third, based on the results of the experiments addressing specific aims 1 and 2, we will estimate the possible duration of ED in 3 domestic mammals, rabbit, sheep and pig (*specific aim 3*) and, by inducing ED in those 3 species for previously calculated period of time, we will evaluate the adequacy of our hypothesis (*specific aim 4-prove of concept*). We propose an original research program, involving well-established experts in developmental biology, reproductive biotechnologies, lipids analysis, cytology, computational biology, bioinformatics and genetics. The selection of key personnel for this project was based on: 1) scientific excellence in particular discipline needed for the project; 2) availability of necessary infrastructures, adequate facilities and conditions for this multitask and multispecies study. First, will use two strains of mice (because ED can be easily induced in mice) to evaluate if the duration of ED is related to the amount of intracytoplasmic lipids in oocytes and embryos from those two strains. Then, we will evaluate the quantity and quality of lipids in oocytes collected from wild mammals in which the duration of ED is known. Based on the results of lipid analyses in oocytes and embryos from two strains of mice and on wild mammals, a statistical model predicting the potential duration of ED in sheep, rabbit, and swine will be proposed. The prognosis will be based on the regression of fat content in embryos and on number of live embryos flushed on particular days in relation to initial fat content and to number of embryos transferred, and further supported by the results relating lipid content in oocytes of wild mammals to the duration of their ED. The last experiment will establish the duration of ED in rabbit, sheep and pig in relation to availability of ooplasmic lipids. To prove the concept that the ED can be induced in rabbit, sheep and pig for the duration as statistically estimated in our model based on the quantity of intracellular lipids in the oocytes and embryos we will keep diapausing embryos for previously calculated period of time in the uterus of recipient females. Then, diapausing embryos will be analyzed and transferred for development to term of pregnancies. **The results of our project will provide crucial information about the fundamental role of intracytoplasmic lipids in the oocytes and preimplantation embryos.** This is a pioneering project because the role for intracytoplasmic lipids is not known. Even basic information on the quantity/quality of lipid droplets in relation to ED in mammals, is lacking. This study will improve our understanding of the causes and mechanisms underlying mammalian embryo development in general. Our hypothesis, if confirmed, will have a great impact on reproductive biology in general, opening up a fertile new investigations into the benefits or otherwise of ED.