DESCRIPTION FOR THE GENERAL PUBLIC

Somatic cell nuclear transfer (SCNT) is a powerful technique, but still very inefficient despite 20 years passed by from since the cloned mammal was born. The main cause of low efficiency is ascribed to inefficient nuclear reprogramming, which may cause placental abnormalities and early death of conceptuses. The proposed project addresses the limited success of SCNT procedure from the mitochondrial perspective, topics unexplored so far.

Investigations on mitochondria in SCNT are limited to the mtDNA hetero/homoplasmy in cloned offspring, whereas no data is available for an eventual role of mitochondria dysfunction on the developmental failure of clones. Moreover, it is important to point out that activity of mitochondria are strictly control by nuclear signals, thus, we are convinced that incomplete nuclear reprogramming in cloned nucleus might be responsible also for the impaired mitochondrial function in cloned embryos/fetuses.

The major objective of the project is to confirm that one of the cause of abnormalities found in clones is improper mitochondrial function. In particular, will focus on the role of mitofusin 2 (Mfn2) protein (mitochondrial outer membrane protein), which plays a crucial role in embryo development. Mfn2 deficient mice have shown a dramatic disruption in placental development, which cause mid-gestation death in mouse and human model, a phenotype that overlaps placental abnormalities in cloned offspring. The objective will be broken down in tree major Tasks. **Task 1** will try to answer whether **somatic cell nuclear transfer (SCNT) pre-implantation embryos have a poor functioning mitochondria, and that these abnormalities affect cloned embryos development.** In **Task 2** we will verify whether **injection of Mfn2 (mRNA) into enucleated oocytes before nuclear transfer (NT) ameliorate cloned pre-implantation embryos development.** In **Task 3** we will evaluate whether **poor functionality of mitochondria in SCNT effect on cloned offspring health** and whether **normal expression of Mfn2 may improve offspring conditions**.

Our preliminary findings, and the specialized literature indicate that the major cause of abnormalities observed in cloned fetuses are connected to mitochondrial dysfunctions; thus, the injection of mRNA of Mfn2 into enucleated oocytes before nuclear transfer may statistically improve pre- and post- implantation cloned embryo development.

The public perception of SCNT in EU is negative. The negative perception arises by the occurrence of foetal abnormalities in cloned offspring influences decision making people, that ultimately might ban research in this area, crippling SCNT benefits for endangered species multiplication. I believe the project is very timely, and this is the reason why I have chosen this research topic, reasons I hope the evaluators will endorse.