NON -TECHNICAL ABSTRACT:

INDUCED PLURIPOTENT STEM CELLS, OR IPSCS, ARE AT THE VERY FRONTIER OF CURRENT STEM CELL RESEARCH. UNLIKE TRADITIONAL HUMAN EMBRYONIC STEM CELLS (HESCS), WHICH ARE ESTABLISHED FROM THE INNER CELL MASS OF EMBRYOS AT 5-6 DAYS OLD, IPSCS ARE INDUCED FROM MATURE CELLS, SUCH AS SKIN CELLS OR FAT CELLS, THROUGH IN VITRO GENETIC REPROGRAMMING. THESE CELLS SHOW IDENTICAL CHARACTERISTICS AS HESCS BOTH IN VITRO AND IN VIVO AND THEREFORE POSSESS THE SAME POTENTIAL IN TRANSLATION THERAPIES AND DRUG DEVELOPMENT AS HESCS. IN ADDITION, THEY AVOID ETHICAL ISSUES ASSOCIATED WITH THE USE OF HESCS AND ALSO PROVIDE A UNIQUIE ADVANTAGE IN MAKING PATIENT-SPECIFIC PLURIPOTENT STEM CELLS. HOWEVER, IPSCS ARE STILL GENERATED AND SUBSEQUENTLY CULTURED IN THE PRESENCE OF MOUSE EMBRYONIC FIBROBLASTS (MEFS), A FEEDER LAYER USED IN THE TRADITIONAL CULTURE METHOD, WHICH IS ALSO THE MOST FREQUENTLY USED, FOR HESCS. THE ANIMAL FEEDER CELLS PRESENTS A HURDLE TOWARDS CLINICAL AND PHARMACIEUTICAL APPLICATIONS OF THESE IPSCS. DURING THE LAST COUPLE OF MONTHS TWO GROUPS REPORTED CULTURING IPSCS UNDER XENO-FREE CONDITIONS THAT ARE VOID OF ALL ANIMAL COMPONENTS INCLUDING MEFS BY REPLACING MEFS WITH IRRIDIATED HUMAN SKIN FIBROBLASTS. OUR LAB HAS BEEN SUCCESSFULLY CULTURING HESCS ON MEFS. IN ADDITION, WE HAVE ALSO SUCCESSFULLY CULTURED THEM BY USING HUMAN MESENCHYMAL STEM CELLS (HMSCS) AS ALTERNATIVE FEEDER CELLS. HMSCS ARE A TYPE OF ADULT STEM CELLS THAT NORMALLY EXIST IN A NUMBER OF TISSUES INCLUDING BONE MARROW, ADIPOSE TISSUE, PERIPHERAL BLOOD AND UMBILICAL CORD BLOOD. THEY CAN BE EASILY ISOLATED AND EXPANDED IN VITRO AND PRESENTS A WONDERFUL ALTERNATIVE POTENTIAL AUTOLOGOUS FEEDER CELL SOURCE FOR SUPPORTING PATIENT-SPECIFIC IPSCS. THIS PROPOSAL IS AIMED TO INVESTIGATE THE FEASIBILITY OF CULTURING HUMAN IPSCS ON HMSCS, WHICH HAS NOT BEEN REPORTED BY ANY OTHER GROUPS. HMSCS HAVE SEVERAL ADVANTAGES TECHNICALLY OVER OTHER HUMAN CELL TYPES AS FEEDER LAYER, AS DESCRIBED IN MORE DETAILS IN THE PRJECT DESCRIPTION. IF SUCCESSFUL, THIS WILL POTENTIALLY HELP ADVANCE THE USE OF HUMAN IPSCS IN BASIC RESEARCH, DRUG DEVELOPMENT AS WELL AS APPLICATIONS IN REGENERATIVE MEDICINE.