Pig iPSCs Capable of Generating Chimeric Pigs that Undergo Normal Development and Neural Differentiation In Vitro

Franklin D. West #1,2#, Elizabeth W. Uhl #3#, Jeong Yeh Yang #1,2#, Yangqing Lu #1,2# and Steven L. Stice #1,2#.

#1#Regenerative Bioscience Center, #2#Department of Animal and Dairy Science, #3#Department of Pathology, University of Georgia, Athens, GA 30602

Pigs are a desirable large animal model to study the efficacy and safety of induced pluripotent stem cell (iPSC) therapies for a number of diseases. However, in the mouse numerous tumors were formed in chimeric animals derived from iPSCs resulting in health problems and high mortality rates. This has raised significant questions pertaining to the tumorigenicity of iPSCs and whether data in the mouse will translate to other species and eventually human iPSC therapy. Our lab has for the first time generated chimeric pigs from pig iPSCs (piPSCs) that show iPSC contribution in all 3 germ layers. To begin to address the question of tumorigenicity and potential abnormal development resulting from iPSCs in a non-rodent model, we performed necropsy and histological analysis of collected tissues from chimeric pigs at 2, 7 and 9 months of age. Necropsy results and histological analysis showed that test animals demonstrated normal organ development and lacked tumor formation despite many tissues being comprised of piPSCs as indicated by the presents of the human POU5F1- a human gene utilized in the reprogramming of piPSCs. Ultimately for piPSCs to be beneficial in studying iPSC therapies, piPSCs must be capable of directed differentiation. Utilizing a neural differentiation system, piPSCs neural progenitor-like cells have been derived that express neuronal, astrocytic and oligodendritic markers and are capable of forming axon and dendritic like extensions. piPSCs that do not cause tumors and are capable of neural in vitro differentiation presents a powerful translational model to study the potentially of iPSC therapies.