Annual Progress Report for Faith's Angels Award, 3-2014 to 3-2015. PI: Ming-Sing Si, MD, University of Michigan, Department of Cardiac Surgery, Mott Children's Hospital.

The past year has seen significant progress and breakthroughs in our laboratory, which was made possible by the Faith's Angel Award. We have evaluated the thymus mesenchymal stem cell (MSC) as a relevant stem cell for use in regenerative medicine therapies for children with heart failure and single ventricle heart disease. These regenerative medicine therapies encompass both tissue engineering and stem cell therapy strategies.

Studies supported in part by the Faith's Angel last year in my laboratory have demonstrated that thymus MSCs, which are isolated from discarded thymus tissue from neonates undergoing cardiac surgery, have an exceptional ability to promote the growth of new blood vessels, a process called angiogenesis. Different stem cell types have been proposed to treat heart disease in adults and children (as well as be used in tissue engineering strategies to build heart tissue). With the support of Faith's Angels Foundation, we have conducted a detailed study to compare the proangiogenic characteristics of thymus MSCs and bone derived MSCs and to understand the molecular mechanisms behind these differences. We found that thymus MSCs are superior to adult bone marrow derived MSCs, the most common type of MSC under investigation. Because of potential effects of age confounding the results of this comparison, we isolated MSCs from both discarded sternal tissue and thymus tissue from the same neonates undergoing cardiac surgery, thus allowing a paired comparison. From this comparison, we again confirmed that thymus MSCs were significantly superior to bone derived MSCs in promoting angiogenesis.

To understand the mechanisms underpinning this important difference, we performed genome wide comparison of paired thymus and bone MSCs using microarray and discovered a number of interesting genes that were differentially expressed between the two stem cell types. One, which we have pursued in great detail, is SLIT3. We then confirmed that the SLIT3 gene was expressed to a greater degree in thymus MSCs at the protein level. We also confirmed that thymus MSCs promoted angiogenesis to a greater degree in mice as compared to bone derived MSCs.

We will be utilizing the above findings as the basis of a NIH grant applications in June and October 2015. We will also submit these finding for publication in a high impact stem cell journal in the fall of 2015; this publication will acknowledge the support of Faith's Angel. A copy of this manuscript will also be sent to Faith's Angel upon acceptance for publication.

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In the coming year, we will use funds from the Faith's Angels Award continue to investigate the ability of thymus MSCs to promote vascularization in vitro for tissue engineering applications. We will also evaluate thymus MSCs in animal models of heart disease to determine their ability to promote cardiovascular regeneration.

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