Addressing the Cell Purity and Identity Bottleneck Through Generation and Expansion of Clonal Human Embryonic Progenitor Cell Lines

Grant Award Details

Addressing the Cell Purity and Identity Bottleneck Through Generation and Expansion of Clonal Human Embryonic Progenitor Cell Lines

Grant Type: Early Translational I

Grant Number: TR1-01276

Project Objective: Overall objective of the grant is to chracterize monoclonal embryonic progenitor cell lines derived from hESC, determine the fate and determine if they can be re-derived from cultures using predicted cell surface markers

Investigator:

Name:	Michael West
Institution:	BioTime, Inc.
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Cell Line Generation: Embryonic Stem Cell

Award Value: $4,721,706

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Addressing the Cell Purity and Identity Bottleneck Through Generation and Expansion of Clonal Human Embryonic Progenitor Cell Lines

Public Abstract: Human embryonic stem (hES) cells and induced pluripotent (iPS) cells, such as reprogrammed skin cells, offer the potential to revolutionize medicine because they can replicate indefinitely and become virtually any cell in the body. They therefore have the potential to provide a limitless source of cells to replace cells lost to injury (spinal cord, skin wounds, etc.) or degenerative diseases like diabetes, Alzheimer's, Parkinson's, ALS, MS, and heart disease to name a few. Similarly they can be a source of cells that model human disease for improved drug development. As researchers develop new and better ways to make hES and iPS cells they are running into a bottleneck of how to provide enough cells of sufficient purity for clinical applications. Industrial scale production is needed and both hES and iPS cells are difficult and costly to manufacture in large quantities. Moreover, the manufactured cells must pass the scrutiny of the FDA. Purity and identity are essential qualities that are needed for any drug approval and are even more important for cell therapy because unlike a drug which may persist in the body for a matter of hours or days, a cell can persist in the body for a lifetime. Contamination of hES derived cells with the wrong cells could lead to toxicities resulting from normal but inappropriate tissue growth or tumor formation.

We therefore propose to develop a new type of cell, the embryonic progenitor (hEP) cell, from hES and iPS cells that is ideal for cell therapy because of its scalability and purity. The nature of hEP cells lies somewhere in between a hES cell and a fully mature cell like a nerve, heart muscle, or pancreatic cell. Many different specific types of hEP cells can be made for cell replacement of specific kinds of tissues. We have already begun to make over one hundred hEP cell lines. Because they divide using standard cell culture methods hEP cells could be readily grown in industrial scale quantities using standard bioreactors. Indeed, we propose here to optimize and standardize industrial scale up of hEPs lines. Importantly, hEP lines are clonal, meaning that they are derived from a single cell, and therefore have the potential to grow as a pure cell line. We propose here to map the surface markers on hEP lines so that we can identify a molecular signature specific to a given hEP line. The molecular signature will be key to assuring identity and reproducibility in preclinical and clinical studies and will facilitate purification of hEP cells from any hES or iPS line so that they can be easily and cost effectively obtained from cells of various genetic backgrounds. We will use our mapping technology us to identify antibodies and other cell purification reagents. The successful completion of our proposed project will provide well characterized hEP cells that are precursors of therapeutic cells such as nerve, blood vessel, heart muscle, and skin.

Statement of Benefit to California:	Safety is critical to the development of any new drug candidate and is even more essential when considering cellular therapies where cells can persist in the body for years. Thus, the primary benefit of our proposed project of generating well characterized cell lines and markers for their isolation is to provide a means of manufacturing sufficient quantities of cells with the needed purity to provide safer cell therapies. By providing California researchers with a bank of well characterized intermediate precursor cell lines and cell purification reagents we will help overcome the cell purity and identity bottleneck that is currently stalling the successful translation of basic stem cell research to clinical applications. A key beneficial outcome of our project will be to shorten the time it takes to get stem cell therapies from the research laboratory and into the hands of physicians to treat patients suffering from degenerative diseases and injuries. By accelerating the translation of research to drug approval more Californians that are currently in need of treatment will have the opportunity to benefit from stem cell therapies and Californians will see a more rapid return on their investment in the form of reduced health care costs. Another significant benefit of our proposed project is in the application of pluripotent stem cells for modeling diseases. Our work will provide the cost effective means to purify well characterized precursor cells from various sources of embryonic stem cells including reprogrammed skin cells of different genetic backgrounds and disease states. This will reduce the need for animal models and the cost of disease models for drug discovery. Finally, in addition to our cell bank and cell purification kits, we will provide Californians with a database of cell surface antigens that define the various intermediate cell types that occur during embryogenesis by their lineage and cell fate. This resource will provide California researchers with information that will help accelerate the pace of stem cell research. Thus, our proposed project will help bring stem cell therapies to Californians sooner by directly addressing the critical issue of cell safety and at the same time it will provide valuable resources for accelerating stem cell based drug discovery and our knowledge of human development.