Mechanisms Underlying the Diverse Functions of STAT3 in Embryonic Stem Cell Fate Regulation

Grant Award Details

Mechanisms Underlying the Diverse Functions of STAT3 in Embryonic Stem Cell Fate Regulation

Grant Type: New Faculty II

Grant Number: RN2-00938

Project Objective: The goal of this award is to interrogate the mechanisms underlying STAT3 function in mESC, which are known to require the activity of the LIF/STAT3 pathway, and to determine the role this pathway plays in hESC, if any.

Investigator:

Name:	Qilong Ying
Institution:	University of Southern California
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $2,261,174

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Reporting Period: Year 5

View Report

Reporting Period: NCE (Year 6)

View Report

Grant Application Details

Application Title: Mechanisms Underlying the Diverse Functions of STAT3 in Embryonic Stem Cell Fate Regulation

Public Abstract: Embryonic stem cells (ESCs) are derived from very early stage embryos. ESCs can be maintained in culture indefinitely while retain the ability to make any type of cell in the body. These properties make ESCs a very powerful tool to address basic biology questions. ESCs also offer an important renewable resource for future cell replacement therapies for many diseases such as Parkinson's disease, spinal cord injury, etc. However, before the full potential of ESCs can be exploited in the clinic, we need to understand more about their biological properties so that we can control their fate towards either self-renewal or differentiation into a specific cell type required for cell replacement therapy. STAT3 is a major player in controlling the fates of a variety of cell types including ESCs. Recently we demonstrated that STAT3 has diverse and distinct roles in regulating cell fate in both mouse and human ESCs. In mouse ESCs, STAT3 is involved in cell adhesion, cell growth/survival and maintenance of self-renewal. Interestingly, STAT3 seems to have opposite roles in human ESCs. It induces growth arrest and differentiation of human ESCs. Why does the same factor play such diverse and contradictory roles between these very similar cells? The answer may lie on how STAT3 is in action. STAT3 is present in every type of cell. It contains six distinct functional regions. STAT3 can directly induce the expression of many genes. STAT3 can also cooperate with other proteins to regulate gene expression. We recently derived STAT3-/- ES cells in which the STAT3 gene was removed. These cells will provide us a powerful tool to dissect STAT3 function. We will first determine the role of each of its six functional regions. Then we will try to understand why they function differently. Is it because they induce different sets of genes, or because they cooperate with different partners? Understanding how STAT3 works is important for us to control the fate of ESCs, and for their eventual clinical application.

Statement of Benefit to California: Human embryonic stem cells (hESCs) can reproduce themselves in a culture dish. They can also give rise to every cell type in the body. In the future, hESCs may hold the key to replacing cells lost in many devastating diseases such as Parkinson's disease, spinal cord injury, etc. Before hESCs can be used clinically, however, we must learn more about how to control their fate. STAT3 is a key player in regulating ES cell fate. STAT3 is also involved in the pathogenesis of diverse human cancers. In this proposed research, we will use a unique tool developed by us to understand STAT3's function. Our work will lead to a better understanding how hESC fate is regulated, which will be an important step towards achieving the therapeutic potential of hESCs. We also expect that our research will have a great implication in developing effective cancer therapies against novel STAT3 targets identified in this study.