Genomic instability during culturing of human embryonic stem cells

Grant Award Details

Genomic instability during culturing of human embryonic stem cells

Grant Type: Basic Biology III
Grant Number: RB3-05020

Project Objective: The goals of this project are to investigate how cell culture conditions influence telomere loss and chromosome instability in hESC, and whether telomere loss in hESC can cause cancer. The PI has conducted studies analogous studies in mESC and human cancer cells and will adapt his approaches towards this effort.

Investigator:

Name: John Murnane
Institution: University of California, San Francisco
Type: PI

Human Stem Cell Use: Embryonic Stem Cell
Award Value: $1,070,919
Status: Closed

Progress Reports

Reporting Period: Year 1
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Reporting Period: Year 2
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Reporting Period: Year 3
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Grant Application Details
Application Title: Genomic instability during culturing of human embryonic stem cells

Public Abstract: Human embryonic stem cells (hESCs) have important potential in the treatment of human disease. Because they can change into a large number of different cell types, they may be useful in restoring a variety of damaged tissues. One potentially harmful side effect of hESC therapy is cancer due to unregulated growth of the hESCs introduced in the body. hESCs have the potential to grow almost indefinitely. Therefore if they should become "transformed" into cancer cells while being cultured in the laboratory, they may cause cancer in the individuals into which they are injected. Transformation of normal cells into cancer cells can occur through changes in their DNA, which contains the information telling cells to grow or not to grow. Because multiple changes must occur for cells to begin the unchecked growth of cancer cells, the likelihood of cancer is low. However, some cellular changes can increase the rate at which subsequent changes occur, which greatly increases the probability that a cell will acquire all of the changes necessary to become a cancer cell. This increased rate of changes in DNA is called genomic instability, which is proposed to be an early step in many cancers. One mechanism by which genomic instability can occur is through the loss of the caps that protect the ends of chromosomes that contain the DNA. Loss of these caps, called telomeres, can make the DNA highly unstable. This proposal will study whether the loss of telomeres is a cause of instability in hESCs during their growth in the laboratory. Information on this process will allow steps to be taken to avoid this potential harmful effect during hESC therapy.

Statement of Benefit to California: Human embryonic stem cells (hESCs) have important potential in the treatment of human disease. Because they can change into a large number of different cell types, they may be useful in restoring a variety of damaged tissues. This study will investigate a potentially harmful side-effect involving genetic changes that may occur during growth of hESCs in the laboratory that could lead to cancer when they are introduced into people. Understanding how culture conditions can influence genetic changes in hESCs will allow scientists to avoid these changes and limit the likelihood of complications resulting from hESC therapy.

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