
Retinoic Acid-FGF Antagonism during Motor Neuron Differentiation of Human ES Cells

Grant Award Details

Retinoic Acid-FGF Antagonism during Motor Neuron Differentiation of Human ES Cells

Grant Type: SEED Grant

Grant Number: RS1-00193

Investigator:

Name: Gregg Duester
Institution: Sanford Burnham Prebys Medical Discovery Institute
Type: PI

Human Stem Cell Use: Embryonic Stem Cell

Award Value: \$695,229

Status: Closed

Progress Reports

Reporting Period: Year 2

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Grant Application Details

Application Title: Retinoic Acid-FGF Antagonism during Motor Neuron Differentiation of Human ES Cells

Public Abstract:

Retinoic acid is a metabolic derivative of vitamin A that has recently been shown to stimulate differentiation of human embryonic stem cells into motor neurons. However, almost nothing is known about how retinoic acid may perform this function. The recent discovery that retinoic acid antagonizes the action of fibroblast growth factor suggests a possible mechanism for retinoic acid function during motor neuron differentiation. We plan to use our knowledge of retinoic acid-fibroblast growth factor interaction to understand how retinoic acid stimulates human embryonic stem cells to go down the motor neuron lineage. Such knowledge will allow us to devise rational strategies for optimal use of retinoic with other reagents to reliably differentiate human embryonic stem cells into motor neurons. Our studies will contribute to the development of cell-replacement therapies for motor neuron loss in patients with amyotrophic lateral sclerosis or spinal cord injury. We plan to study the effect of retinoic acid on differentiation of human embryonic stem cell lines that are ineligible for federal funding. Because all of the human embryonic stem cell lines approved for federal funding were generated using methods that involved mixing human cells with mouse feeder cells, they are poorly suited for clinical use and are likely to have undergone modifications with unpredictable consequences. Given the scarcity of federally-approved human embryonic stem cell lines, and recognizing that cells passaged for long periods of time in culture tend to become genetically unstable, it is necessary to have the means of characterizing new human embryonic stem cell lines. The studies proposed here on human embryonic stem cell lines that are ineligible for federal funding will provide new insight into how retinoic acid and fibroblast growth factor can best be used to generate motor neurons for therapeutic purposes.

Statement of Benefit to California:

The studies we perform should benefit the state of California in several ways:(1) We hope to increase the ability to generate motor neurons that can be used in cell-replacement therapies for motor neuron loss in patients with amyotrophic lateral sclerosis or spinal cord injury. This will directly benefit patients in California and elsewhere.(2) The human embryonic stem cell research we perform may bring new biotechnology jobs to California, thus increasing the state's visibility as a leader in stem cell technology.(3) New therapeutic methods developed using our discoveries could bring revenues to California due to the ability of the state to obtain licensing fees on technology generated using CIRM funds.

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