
Role of Glycans in Human Embryonic Stem Cell Conversion to Neural Precursor Cells

Grant Award Details

Role of Glycans in Human Embryonic Stem Cell Conversion to Neural Precursor Cells

Grant Type: SEED Grant

Grant Number: RS1-00200

Investigator:

Name:	Hudson Freeze
Institution:	Sanford Burnham Prebys Medical Discovery Institute
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Award Value: \$708,000

Status: Closed

Progress Reports

Reporting Period: Year 2

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Reporting Period: NCE

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Grant Application Details

Application Title: Role of Glycans in Human Embryonic Stem Cell Conversion to Neural Precursor Cells

Public Abstract:

Like a thick frosting on a cake, complex sugar chains decorate every surface of every cell. Try to approach a cell, as friend or foe, and the canopy of sugars is the first gate-keeper. Each cell makes and organizes these sugar chains, called glycans, on its surface. They are very complicated molecules, and different cells choose to decorate themselves with different glycans—for reasons best known to the cells themselves. Because glycans have such complicated structures, it is hard to work with them and understand their function. They are much more diverse than DNA and proteins, and so the technology for dissecting their structures and functions has lagged behind the others in the molecular revolution in biology and medicine. Glycans are complicated molecules, hard to work with, difficult to understand, but they are absolutely indispensable to life. Human genetic disorders where just one step in their assembly is missing causes mental retardation, seizures, blindness and poor motor skills. Glycans are used for communication both within and between cells, and this is especially true when cells signal each other about their past and future journeys within the developing body and exactly where they will go and what they will become during development. Embryonic stem cells have a particular set of glycans on their surface and change as the cells develop into different cell types. What directs these changes? Are they all important? Can we manipulate a cell's fate or convince it to behave in a certain way by changing—or maintaining—the sugar coating? The scientific literature shows that changing surface sugar chains can have profound effects. New technology in the field of "Glycobiology" makes it possible to analyze minute amounts of material with great precision and define these structures. Thanks to our collaborators, we can produce substantial amounts of human embryonic stem cells that uniformly transition into neural precursor cells. Our plan is to describe in detail these glycan changes as they occur and then determine which are actually essential for cells to reach that point. How do these glycans allow them to go further on to neurons, oligodendrocytes and astrocytes? We hope to exploit these unique sugar signatures to identify and isolate cells that will have a particular developmental fate. This is only the beginning. It is a catalog of events and a parts list, but we know how the parts are assembled and what machines are needed. Since we are only beginning the stem cell enterprise, it's important to define these elements from the beginning. We hope to use this knowledge to direct and influence stem cells to travel down the paths we prefer, since we already know the path is sugar coated and the coating is essential.

Statement of Benefit to California:

The necessary existence of the CIRM is the largest benefit for the state and demonstrates our commitment to the concept that research and understanding are the keys to a better life for all citizens.

By understanding how the NPC's differentiate and which glycans are important, we may be able to forecast which genes will be likely to cause developmental problems if they contain specific polymorphisms. As individual genome scans for disease susceptibility become more commonplace in the community, we will need to identify those genes. Localized manipulation of the cell surface glycans on injured nerve cells may help stimulate their growth. This has already been seen using injected chondroitinase and sialidase digestions to stimulate robust nerve growth in mechanically injured, debilitated rodents.

This specific project benefits the state economically. Success in recognizing specific cell types during the differentiation enables the development of reagents and assay kits to isolate such cells, scaling up the isolation, and adapting the lectin-binding purification concept to other types of differentiating cells. The demand for more therapeutic use of stem cells will require an industry prepared to identify and fractionate those cells with special surface properties, some of those being defined by lectin binding.