# Analysis of Candidate Neural Crest Cells Derived from Human ES Cells

## Grant Award Details

Analysis of Candidate Neural Crest Cells Derived from Human ES Cells

**Grant Type:** SEED Grant

**Grant Number:** RS1-00466

**Investigator:**

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| **Name:** | Alexey Terskikh |
| **Institution:** | Sanford Burnham Prebys Medical Discovery Institute |
| **Type:** | PI |

**Human Stem Cell Use:** Embryonic Stem Cell

**Award Value:** $703,684

**Status:** Closed

## Grant Application Details

**Application Title:** Analysis of Candidate Neural Crest Cells Derived from Human ES Cells

**Public Abstract:** Little is known about human Neurla Crest (NC) cells, a transient population of cells briefly present during very early human development; the reason why these cells are extremely difficult to obtain and study. In the model organism NC cells generate an amazing array of tissues, including peripheral and enteric nervous systems, cranial bones and cartilage, some cardiac muscle and virtually all pigmented cells in the body. Abnormalities in NC cells involved in numerous human pathologies including various skeletal syndromes (e.g. Apert syndrome), diseases of nervous system (e.g. Hirschsprung's disease) and pigment disorders (e.g. Waardenburg syndrome).The lack of fundamental knowledge about human NC impedes technological advancements. Human NC cells have never been isolated and characterized on cellular and molecular levels. The goal of this proposal is to fill this gap in our knowledge. The PI laboratory has recently developed an efficient procedure for the rapid differentiation of human ES cells into uniform neural precursors (hES-NPCs), which was hitherto unachievable. In culture, hES-NPCs become functional neurons and oligodendrocytes. Intriguingly, our preliminary data show that many markers associated with NC cells are upregulated in hES-NPCs or during their derivation process. For instance, genes previously implicated in NC specification and maintenance were clearly detected. Moreover, a subset of hES-NPCs stained positive for cell surface antigen transiently associated with migrating NC cells in chick. Our hypothesis is that human NC cells are present in hES-NPCs, established in our laboratory. To prove (or disprove) this hypothesis we will rigorously examine the molecular and cellular fates of candidate NC cells from hES-NPCs cultures both in vitro and in vivo. To pursue Aim1 we will use in situ hybridization, immunostaining, prospective isolation of candidate NC cells by FACS and in vitro differentiation analysis to determine the vitro fates of candidate human NC cells. However, the in vitro differentiation conditions for all potential human NC cell fates are unknown. In Aim2 we will determine the in vivo fates of candidate human NC cells by transplanting genetically labeled hES-NPCs and their subpopulations into the early chick embryo and following their fates during chick development. To assure the expertise and skills in the NC field (new for this PI) we have established collaboration with {REDACTED} the world's-leading expert in the NC filed. Our analysis will unequivocally determine the in vitro and in vivo fates of hES cell-derived cells with the neural crest cell markers present in our cultures. If our hypothesis is correct, hES cell-derived neural precursors will be a rich source for neural crest cells, thus allowing for the first time the extensive characterization of these rare human cells and the development of strategies of NC cell-based protocols in clinics.

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| **Statement of Benefit to California:** | Abnormalities in neural crest (NC) cells involved in numerous human pathologies including various skeletal syndromes (e.g. Apert syndrome), diseases of nervous system (e.g. Hirschsprung's disease) and pigment disorders (e.g. Waardenburg syndrome).The lack of fundamental knowledge about human NC impedes technological advancements. Human NC cells have never been isolated and characterized on cellular and molecular levels. The goal of this proposal is to fill this gap in our knowledge.<br><br>The PI laboratory has recently developed an efficient procedure for the rapid differentiation of human ES cells into uniform neural precursors (hES-NPCs), which was hitherto unachievable. Intriguingly, our preliminary data show that many markers associated with NC cells are upregulated in hES-NPCs or during their derivation process. Our hypothesis is that human NC cells are present in hES-NPCs, established in our laboratory.<br><br>Our analysis will unequivocally determine the in vitro and in vivo fates of hES cell-derived cells with the neural crest cell markers present in our cultures. We will specifically assay the subsets of cells using specific NC-associated markers to enrich for candidate NC lineages. If our hypothesis is correct, hES cell-derived neural precursors will be a rich source for NC cells, and subsequently for an array of human NC derivatives such as bones, cartilage, muscles, peripheral and enteric neurons and melanocytes. Fundamentally, this will allow for the first time the extensive characterization of rare human NC cells and in the future will help the development of strategies of NC cell-based protocols in drug discoveries and clinics.<br><br>An effective, straightforward, and understandable way to describe the benefits to the citizens of the State of California that will flow from the stem cell research we propose to conduct is to couch it in the familiar business concept of "Return on Investment". The novel therapies and reconstructions that will be developed and accomplished as a result of our research program and the many related programs that will follow will provide direct benefits to the health of California citizens. In addition, this program and its many complementary programs will generate potentially very large, tangible monetary benefits to the citizens of California. These financial benefits will derive directly from two sources. The first source will be the sale and licensing of the intellectual property rights that will accrue to the state and its citizens from this and the many other stem cell research programs that will be financed by the CIRM. The second source will be the many different kinds of tax revenues that will be generated from the increased bio-science and bio-manufacturing businesses that will be attracted to California by the success of the CIRM. |