MCW Case Number: C1774

NAMPT Inhibiton for the Selective Elimination of Pluripotent Stem Cells

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Pluripotent stem cells (PSC), which include induced pluripotent stem cells and embryonic stem cells, have the capacity for continued self-renewal and the ability to differentiate into any cell type in the human body. PSC are therefore valuable sources of differentiated somatic cell types for clinical, research, and drug development applications. However, current differentiation protocols are incomplete and variable, yielding "mixtures" of PSC and their differentiated progeny. These mixed cultures pose challenges to data analyses that rely on population averages. Moreover, PSC can form tumors *in vivo* and thus pose significant safety concerns in regenerative medicine. The inventors have developed an *in vitro* method that employs inhibitors of nicotinamide phosphoribosyltransferase (NAMPT) to selectively eliminate undifferentiated pluripotent stem cells from their differentiated progeny. This method should advance the development of clinically-relevant drug discovery platforms and safer stem cell-based therapies.

References: Boheler et al., Stem Cell Reports, 3(1), 2014.; Kropp et al., Stem Cells Translational Medicine, 4(5), 2015.

A) At low concentrations, both NAMPT inhibitors are toxic to human pluripotent stem cells but not to human pluripotent stem cell-derived cardiomyocytes or fibroblasts. **B)** Images of surviving human pluripotent stem cell-derived cardiomyocytes showing that NAMPT inhibition does not affect the structural organization of the cardiomyocytes, where red represents the structural marker cardiac troponin T. **C)** Images of surviving human pluripotent stem cell-derived hepatocyte progenitors showing that NAMPT inhibition does not affect viabilty in endoderm-derived cell types.

Key Advantages:

- Undifferentiated PSC selectively eliminated
- PSC-derived progeny retain viability and function
- Effective independent of cell line and medium
- Effective on sub-confluent and confluent cells
- Applicable to a range of progeny , including cardiomyocytes, neurons, hepatocytes
- Adaptable for use in monolayer, bulk and scaffold/3D cell cultures.
- Inhibitors effective in nanomolar - micromo lar concentrations
- More effective than PluriSIn#1 and glucose deprivation
- Simple and effective alternative to suicide genes and cell sorting techniques

Safe, easy, efficient, inexpensive, and scalable strategy to selectively eliminate unwanted pluripotent cells from engineered tissues and cells

Category:
Method

Stage of Development:
Tested *in vitro*

History:
PCT/US15/12215 filed January 21, 2015.
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