Understanding sources of regenerative capacity in animals

Dr Alejandro Sánchez Alvarado
Investigator, Stowers Institute for Medical Research
Investigator, Howard Hughes Medical Institute

Abstract

The study of natural and induced stem cells has ushered an age of re-examination of what it means to be a stem or a differentiated cell. Past and recent discoveries in plants and animals, as well as novel experimental manipulations are beginning to erode many of these established concepts, and are forcing a re-evaluation of the experimental systems and paradigms presently being used to explore these and other biological processes. Proliferating cells known as neoblasts include pluripotent stem cells (PSCs) that sustain tissue homeostasis and regeneration of lost body parts in planarians. However, the lack of markers to prospectively identify and isolate these adult PSCs has significantly hampered their characterization. We used single-cell RNA sequencing (scRNA-seq) and single cell transplantation to address this long-standing issue. Large-scale scRNA-seq of sorted neoblasts unveiled a novel subtype of neoblast (Nb2) characterized by high levels of PIWI-1 mRNA and protein, and marked by a conserved cell-surface protein coding gene, tetraspavin 1 (tspan-1). tspan-1-positive cells survived sub-lethal irradiation, underwent clonal expansion to repopulate whole animals, and when purified with an anti-TSPAN-1 antibody, rescued the viability of lethally irradiated animals after single-cell transplantation. The first prospective isolation of an adult PSC bridges a conceptual dichotomy between functionally and molecularly defined neoblasts, shedding light on mechanisms governing in vivo pluripotency and a source of regeneration in animals.

Bio

Alejandro Sánchez Alvarado, PhD, joined the Stowers Institute for Medical Research in 2011. Sánchez Alvarado received a BS in molecular biology and chemistry from Vanderbilt University in Nashville, TN, and a PhD in pharmacology and cell biophysics from the University of Cincinnati College of Medicine in Cincinnati, OH. He performed postdoctoral and independent research at the Carnegie Institution of Washington, Department of Embryology in Baltimore, MD. In 2002, he joined the faculty of the University of Utah School of Medicine in Salt Lake City where he held the H.A. & Edna Benning Presidential Endowed Chair. In 2005, he was named a Howard Hughes Medical Institute Investigator. Sánchez Alvarado is a member of the National Academy of Science, the American Academy of Arts and Sciences, and the Latin American Academy of Sciences, a Kavli Fellow of the National Academy of Sciences USA, a Fellow of the Marine Biological Laboratory in Woods Hole, MA, and a recipient of a National Institutes of Health MERIT award and the EE Just Medal for Scientific Achievement. He has served on numerous scientific advisory committees and boards including the National Advisory Council of the National Institute of General Medical Sciences, National Institutes of Health, and presently serves on the Board of Directors of American Century Investments.