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EDITORIAL

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Dr. Jan Nolta, Editor of STEM CELLS, is the Director of the Stem Cell Program at UC Davis School of Medicine and directs the new Institute for Regenerative Cures. The UC Davis stem cell program has over 150 faculty members collaborating to work toward stem cell-related cures for a spectrum of diseases and injuries. Her group focuses on "bench to the bedside" research, and she has been involved in numerous clinical trials of gene and cell therapy. She is the scientific director of the new Good Manufacturing Practice clean room facility at UC Davis, where stem cells of different types are being isolated or expanded for clinical trials.

New Advances in Understanding Stem Cell Fate and Function

Dr. JAN A. NOLTA

As we welcome in the new year, let us stop for a moment to reflect how far we have come in our understanding of the vast array of mechanisms that drive the processes of stem cell homeostasis, division, differentiation, migration and engraftment, and induction of somatic cells to pluripotency. Over the course of the past 32 years of STEM CELLS publication, the field has seen amazing growth and development of unprecedented numbers of new tools and technologies to help biologists identify and understand the cells with which we are all so fascinated. In the initial years of the journal, many reports focused on hematopoietic stem cells, and that focus has now broadened to include embryonic, induced pluripotent, mesenchymal (MSCs), and cancer stem cells, as well as tissue-specific progenitors. In this editorial, I highlight my favorite advances in the field that STEM CELLS published in 2014, while we welcome in 2015. The range of tools and methods that our authors and others have developed allow more detailed exploration of stem cell fate than ever before.

A large number of new advances in reprogramming to create induced pluripotent stem cells from a variety of cell types using efficient methods were reviewed in STEM CELLS last year [1, 2]. In addition, altering the extracellular matrix to allow direct in situ reprogramming was reported [3]. A very timely review by Armstrong et al. [4] discussed the evidence for epigenetic influence over tissue-specific stem cell aging. Without the incredible advances in genomics and examination of the epigenome, the important relevance to homeostatic control diminishing tissue/organ integrity and function could not have been realized.

Conway and Schaffer [5] reported de novo neurogenesis in the brains of adult rodents stimulated by delivery of proteins normally found within adult neurogenic niches. This finding might have potential to replace neurons lost in neurodegenerative disease or injury, as an alternative to cell implantation. The importance of membrane biophysics to define progenitor cells of differing fate potential in the neural lineage was also reported [6]. An interesting manuscript uncovered some of the molecular mechanisms behind running/exercise increasing adult neurogenesis [7]. The link between increased physical activity and improvement in symptoms had been reported in clinical studies and case reports [8] but the new molecular studies and transgenic mouse models in the manuscript by Farioli-Vecchioli et al. [7] further explained the phenomenon and brought it into molecular terms for our readers.

The exciting field of cell-to-cell communication was explored in elegant reports in STEM CELLS during 2014 and included transfer of molecules not normally found outside the cell by nanotubules, microparticles, and exosomes, among others. My own research team had previously reported that sufficient quantities of siRNA produced by engineered MSCs could be passed to target cells of the neuronal lineage, to cause a 50% reduction in levels of the mutant Huntingtin protein, the cause of the devastating neurodegenerative disorder Huntington's disease [9]. At the time that we published these findings—just 2 years ago—it was not known whether the siRNA was being passed from cell-to-cell through exosomes or tunneling nanotubules.

Advancements during the past year have introduced to the readers of STEM CELLS exciting details about this type of cell-to-cell communication, and exosomes are fast becoming biomarkers of disease progression and cancer recurrence. Reports published in 2014 show that cell-to-cell communication by microvesicles and exosomes produced by MSCs can be transferred to damaged tissues to help repair lung injury [10]. Xie et al. [11], in the Marban laboratory, showed that cell-to-cell contact plays a role in mediating the therapeutic benefits of cardiosphere-derived cells beyond the known paracrine effects. Xin et al. [12], in the Chopp laboratory, demonstrated that MSCs secreted exosomes that transferred miR-133b to neurons to promote neurite remodeling and functional recovery after stroke. Figeac et al. [13] demonstrated that nanotubular crosstalk with distressed cardiomyocytes stimulated the paracrine repair function of MSCs, and Naphade et al. [14] showed lysosomal cross-

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correction through tunneling nanotubules to combat cystinosis. The field of direct cell-to-cell communication is an exciting one, and we are proud to have contributed these excellent publications to the knowledge base of our readers.

In addition to new detailed reports of advances in understanding the molecular mechanisms that control cell fate, we have had important concise reviews on stem and progenitor cells in lung biology [15] and lung repair [16], eye [17], bone [18, 19], hematopoiesis/blood formation [20], muscle [21], heart [22], intestine [23], liver [24], and brain [25], as well as cancer stem cells [26]. Our 2014 regular manuscripts have reported inspiring new developments in the field of spinal cord repair/regeneration [27, 28], intervertebral disc repair [29], hair follicle growth [30–32] spermatogenesis [33, 34], corneal development and repair from limbal stem cells [35–37], salivary gland [38], cartilage development [39], ALS [40, 41], and knee repair [42], among others. Some of these manuscripts and other reports are highlighted in our online virtual issues "Stem Cells in Regenerative Medicine" and "Leukemia, Breast, and Ovarian Cancer Stem Cells."

With the tools and technologies that we as the stem cell community have available to us today, I cannot wait to see what new and exciting knowledge 2015 will bring us. I look forward to reading the cutting edge manuscripts that will be submitted to STEM CELLS this year! Happy New Year to all of our readers.

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