



Special Issue: Recent Advances in Stem Cell Biology in Regeneration and Disease

Brief Review

Recent advances in stem cell biology in regeneration and disease

Atsushi Iwama

Department of Cellular and Molecular Medicine, Graduate School of Medicine, Chiba University, Chiba, Japan

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Correspondence should be addressed to:

Atsushi Iwama, Department of Cellular and Molecular Medicine, Graduate School of Medicine, Chiba University, 1-8-1 Inohana, Chuo-ku, Chiba 260-8670, Phone: +81-43-226-2187, Fax: +81-43-226-2191, E-mail:aiwama@faculty.chiba-u.jp

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Stem cell biology is critical to not only regenerative medicine, but also to diseases such as cancer and aging. This field is expanding rapidly and new topics are emerging ceaselessly. Focused on current advances in stem cell biology, the present special issue picks up 4 recent topics in this field.

Direct reprogramming is a new technology developed from the “induced pluripotent stem (iPS) cell” technology, which reprograms somatic cells into a pluripotent state using defined stem cell-specific factors. It has been demonstrated that various cell types can be induced from somatic cells using lineage specific-reprogramming factors, bypassing the need to go through a stem cell state. Dr. Masaki Ieda at Keio University School of Medicine provides an overview of pioneering and recent studies in cellular reprogramming, and discusses the perspectives and challenges of direct cardiac reprogramming in regenerative therapy¹⁾.

Epigenetics is one of the most promising and expanding fields in the post-genome era. The role of epigenetic gene regulation has been extensively analyzed not only in embryonic stem cells (ESCs), but also in somatic stem cells, par-

ticularly hematopoietic stem cells (HSCs)²⁾. Dr. Shuhei Koide and his colleagues at Graduate School of Medicine, Chiba University review epigenetic regulation of normal hematopoiesis with an emphasis on the role of histone modifiers and DNA-methylation modulators in HSCs and their progeny. Epigenetic regulation plays a key role in cellular memory, the ability of cells to “remember” cell-lineage specific expression patterns induced by transiently expressed factors through subsequent cell divisions. Such epigenetic fine-tuning of transcription maintains hematopoietic homeostasis.

Extensive efforts have been taken to identify and characterize the master regulators essential for the maintenance of stem cells. Understanding of the molecular function of such master regulators has a great impact on both stem cell biology and regenerative medicine. Evi1 is one such regulator of HSCs³⁾. Dr. Keisuke Kataoka and his colleagues at Graduate School of Medicine, University of Tokyo summarize the central role of Evi1 in self-renewal of HSCs and how its expression is beneficial to trace the self-renewal capacity of HSCs, providing a powerful approach for investigating HSC



biology.

Recent progress in stem cell biology and technologies has also successfully identified several types of cancer initiating cells (CICs) in a variety of cancers. CICs are defined as a minor population which possesses a prominent ability to generate new tumors that faithfully reproduce the phenotype of original tumors. Although not all types of cancer conform to the CIC theory, it provides an attractive cellular mechanism to account for the therapeutic resistance and recurrence of the disease. Dr. Toru Kondo at Institute of Genetic Medicine, Hokkaido University, introduces the latest findings on CICs, particularly as they pertain to glioma, which is currently one of the best CIC models⁴⁾.

All of the authors are experts in stem cell biology as it relates to regeneration and disease, and the reviews include the latest information from these important and exciting areas of research. I hope that the readers will find these articles useful and informative.

References

- 1) Ieda M, Fu JD, Delgado-Olguin P, Vedantham V, Hayashi Y, Bruneau BG, Srivastava D: Direct reprogramming of fibroblasts into functional cardiomyocytes by defined factors. *Cell*. 2010; 142: 375-386.
- 2) Sashida G, Iwama A: Epigenetic regulation of hematopoiesis. *Int J Hematol*. 2012; 96: 405-412.
- 3) Kataoka K, Sato T, Yoshimi A, Goyama S, Tsuruta T, Kobayashi H, Shimabe M, Arai S, Nakagawa M, Imai Y, Kumano K, Kumagai K, Kubota N, Kadowaki T, Kurokawa M: Evi1 is essential for hematopoietic stem cell self-renewal, and its expression marks hematopoietic cells with long-term multilineage repopulating activity. *J Exp Med*. 2011; 208: 2403-2416.
- 4) Kondo T: Brain cancer stem-like cells. *Eur J Cancer*. 2006; 42: 1237-1242.