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Title: "c-kit and SSEA-1 define temporally and spatially distinct retinal progenitor subsets"

Date: Tuesday, June 7

Time: 16:00 -17:00

Place: 7F Conference Room of Building A, CDB

Summary:

Neural retina is an important target organ for regenerative medicine, and isolation and expansion of retinal progenitor cells are critical issues from both scientific and clinical views. However, the characters of the immature retinal cells are not elucidated because of the lack of prospective approach to identify retinal progenitor cells. We screened the expression pattern of cell surface proteins in mouse immature retina by flow cytometer using more than 150 monoclonal antibodies against different membrane proteins. Among them, 25 antibodies recognized sub-populations of immature retina, and we examined the proliferation and differentiation abilities of purified those sub-populations of retina by various in vitro assay systems. Results obtained with SSEA-1 (CD15) and c-kit (CD117) positive populations showed that these molecules marked temporally and spatially distinct retinal progenitor subsets. SSEA-1 positive cells are in the peripheral region of retina of the E17 embryo and then dramatically disappeared along with retinal development. SSEA-1 strong positive cells were Ki-67 antigen positive and had prolonged proliferation activities than that of SSEA-1 negative cells in reaggregation culture. Moreover, differentiation of SSEA-1 cells into late born retinal subtypes took longer period, suggesting that these cells are at more immature stage than SSEA-1 negative cells. Differential expression of Wnt signal-related genes between SSEA-1 positive and negative subpopulations of retinal cells was revealed, and involvement of Wnt signaling pathway for maintenance of SSEA-1 positive cells was suggested. This observation was in accordance with our in vitro results suggesting the role of Wnt as prevention of premature differentiation of retina. c-kit, which was positively regulated by Notch signals, also labeled a subset of progenitor cells, and c-kit/SSEA-1 double positive cells had more immature characters than single positive cells. Although SCF did not induce proliferation, c-kit positive cells proliferated in response to bFGF and EGF stronger than that of c-kit negative cells, suggesting permissive role of SCF for retinal proliferation. Taken together, we showed cell surface molecules as useful tools not only to mark temporally and spatially distinct retinal subpopulations, but also to study the regulation of differentiation of neural retina.

Host: Shin-Ichi Nishikawa < Stem Cell Biology, CDB>

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