論文の内容の要旨

論文題目　The role of H3K27 demethylation in retinal development
(網膜発生における H3K27 脱メチル化の役割)
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The H3K27me3 repressive mark is written by the polycomb repressive complex 2 (PRC2) and erased by the Jumonji C (JmjC) domain-containing proteins Utx and Jmjd3 as such they antagonize the various functional roles of PRC2 including in cellular differentiation. There are many new insights into the roles of Utx and Jmjd3 in development; in the retina, Jmjd3 was found to regulate the differentiation of rod bipolar cells through erasing H3K27me3 from the Bhlhb4 locus, a critical gene. Utx, also a major demethylase of H3K27me3 has some differing effector mechanisms to Jmjd3 in cellular differentiation, however, it's role in the development of the retina has yet to be studied.

In this study, by Utx knockdown in vitro and conditional knockout in vivo followed by immunohistochemical analyses, I demonstrated that Utx is expressed in retinal progenitor cells in development and in cells of the inner nuclear and ganglion cell layers in the mature mouse retina and that it regulates the differentiation of Protein kinase C alpha (PKCα) expressing rod bipolar cells found in the inner nuclear layer. Utx loss did not affect other bipolar cell subtypes unlike Jmjd3 and did not affect retinal progenitor cell proliferation and apoptosis.

Further analyses using Utx/Jmjd3 conditional double knockout mice (DKO) to understanding the interrelationships of Utx and Jmjd3 in retinal development are underway. So far, a research collaborator found that DKO led to greater loss of rod bipolar cells compared to Utx or Jmjd3 single deletion, however, the PKCα loss was incomplete implying possibility of partial redundancy and involvement of a third regulator. In addition, further study of the molecular mechanisms by which Utx regulates rod bipolar cell differentiation is planned. Hopefully this knowledge can in future amount to understanding the possible role of Utx in human retinal diseases such as congenital stationary night blindness caused by lack of rod bipolar cells.