The vertebrate telencephalon has the most complex region of the nervous system and is responsible for the highest level of neural function, such as learning, memory, consciousness, emotion and so on. To analyze the complicated function of the telencephalon, one of the important issues is that how the neural cell fate is determined during development. However, the molecular mechanisms of neural cell fate determination have not been fully elucidated. To make clear these molecular mechanisms, we have taken a forward genetics approach in zebrafish. We isolated a novel zebrafish mutant *kuririn* (*krr*) and found that *krr* gene is expressed in the dorsal telencephalon, ventral diencephalon, and olfactory placode. In consequence of the phenotypic analyses of *krr* mutant, we showed that the number of GABAergic neurons is increased instead of the glutamatergic neurons in the telencephalon. Since this phenotype of *krr* mutant is very similar to that of *Neurogenin1* (*Ngn1*); *Neurogenin2* (*Ngn2*) double mutant in mouse, we examined the expression of *ngn1* in *krr* mutant, and found that its expression is reduced in the dorsal telencephalon. It is well known that *ngns* are negatively regulated by the transcription factor Hes1. We next examined the expression of *Hes1*-related gene, *her6* in *krr* mutant, and confirmed that this expression is expanded in the dorsal telencephalon. Together, we propose that Krr regulates *ngn1* through the regulation of *her6* gene in the telencephalon.

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Program/Abstract # 292
Six1 is indispensable for production of functional apical and basal progenitors during olfactory epithelial development
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The olfactory epithelium (OE) is a good model system for studying principles of stem/progenitor cell biology, because of its capacity for continuous neurogenesis throughout life. The development of mouse OE is divided into two stages, early and established neurogenesis. We previously reported that *Six1* is essential for production of pioneer neurons in the early neurogenesis that occurs at embryonic day (E) 10.0. Here, we focused on the role of *Six1* in the established neurogenesis. In the established neurogenesis, which starts at E12.5, sustentacular cells and olfactory receptor neurons (ORNs) are produced from apical and basal progenitors, respectively. We found that *Six1* is expressed in both apical and basal progenitors. In $Six1^{-/-}$, apical proliferating cells were absent and no morphologically identifiable sustentacular cells were observed. Consistently, the expression of *Notch2* and *Jagged1* in the apical layer was absent in $Six1^{-/-}$. On the other hand, basal proliferating cells were observed in $Six1^{-/-}$, but the expression of *Ngn1, NeuroD, Notch1*, and *Jagged2* in the basal layer was absent in $Six1^{-/-}$. The expression of *Mash1*, the determination gene for ORNs, and *Hes* genes was enhanced in $Six1^{-/-}$. As a result, $Six1^{-/-}$ showed lack of mature ORN throughout development and disorganization of OE after E12.5. We conclude that *Six1* regulates production of functional apical and basal progenitors in the established neurogenesis during OE development through regulating various genes such as neuronal basic helix–loop–helix and genes involved in Notch signaling pathway.

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Program/Abstract # 293
Sensory neuron differentiation is regulated by Notch signaling in the trigeminal placode
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Trigeminal sensory neurons develop from the neural crest and neurogenic placodes, and have been studied as a principle model of sensory neuron formation. While the Notch pathway has been extensively characterized in central nervous system development and other developmental processes, it has not been well characterized in sensory neurogenesis. Here we studied the functional role of Notch signaling in the ophthalmic placode, a prime model of sensory neurogenesis. To establish a good spatiotemporal description of Notch pathway genes in the chick trigeminal placode, a stage-specific expression analysis was conducted, showing that expression of most Notch pathway genes and effectors are expressed in the placode, with expression primarily being confined to ectodermal cells. Expression was highest at stages of peak neuronal differentiation. To test the function of Notch signaling in opV placode differentiation, Notch was blocked using DAPT, or signaling was activated by misexpression of the Notch intracellular domain. Notch activation resulted in a significant reduction in sensory neurogenesis. Cells remained in the ectoderm and did not differentiate ectopically. DAPT exposure resulted in a dramatic increase in neurogenesis without increasing proliferation, where many differentiated cells were found in the mesenchyme and, surprisingly, within the ectoderm. This is the first result clearly showing ectopic neurogenesis in the trigeminal placodes after experimental manipulation of a molecular signaling pathway, thus identifying Notch signaling as a primary regulator of the sensory neuron fate in the opV placode.

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Program/Abstract # 294
The polycomb repressive complex PRC2 regulates retinal differentiation in *Xenopus*
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The mechanisms that govern the transition of retinal progenitors from proliferation to differentiation are not fully understood. Recent studies have established that the chromatin remodeling complex PRC2 is a key switch required for dividing cells to execute correct genetic reprogramming as they exit the cell cycle and undergo differentiation in a variety of biological contexts, including in embryonic stem cells and during cortex development. PRC2 represses genes by trimethylating lysine 27 of histone 3 tail (H3K27 me3), a histone mark that is associated with chromatin compaction. Here we report the involvement of PRC2 in regulating the transition from retinal proliferation to differentiation during eye development. We show that the transcripts of the core subunits of PRC2 are coincidently expressed in retinal progenitors and are downregulated upon retinal differentiation. Surprisingly, we found that H3K27me3 levels greatly increase in terminally differentiated cells. Inhibition of Xez, the catalytic subunit of PRC2, using a translation blocking morpholino leads to a marked decrease in H3K27me3 levels in retinal cell types. Blocking Xez causes a reduction in eye size and inhibition of differentiation genes. Importantly, targeted knockdown of Xez in retinal progenitors biases cell fate toward late born cell types, suggesting that retinal differentiation is delayed or inhibited. Our data establishes PRC2 as a major player in retinal neurogenesis and suggests that it may have multiple roles in eye development, including regulation of retinal proliferation and/or differentiation. This work was supported by NIH grant# EY012274 to MLV.

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