Chapter 2
Regulatory Mechanism of Neural Progenitor Cells Revealed by Optical Manipulation of Gene Expressions

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The basic-helix-loop-helix (bHLH) transcription factors Hes1, Ascl1/Mash1 and Olig2 facilitate the fate determination of astrocytes, neurons and oligodendrocytes, respectively (Imayoshi and Kageyama 2014). However, these bHLH transcription factors are co-expressed in multipotent self-renewing neural progenitor cells even before cell fate choice (Imayoshi et al. 2013). This finding indicates that these fate determination factors are differentially expressed between self-renewing and differentiating neural progenitor cells with unique expression dynamics. Live imaging analysis with fluorescent and bioluminescent proteins is a powerful strategy for monitoring expression dynamics. Our imaging results indicate that bHLH transcription factors are expressed in an oscillatory manner by neural progenitor cells, and that one of them becomes dominant in fate choice. We propose that the multipotent state of neural progenitor cells correlates with the oscillatory expression of several

Electronic Supplementary Material The online version of this chapter (https://doi.org/10.1007/978-981-13-7908-6_2) contains supplementary material, which is available to authorized users.

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Y. Toyama et al. (eds.), *Make Life Visible*,
https://doi.org/10.1007/978-981-13-7908-6_2

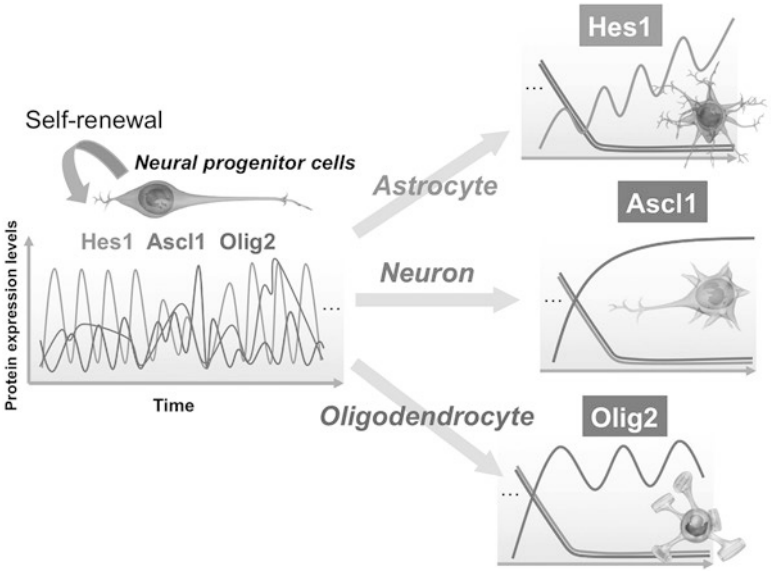

Fig. 2.1 Expression dynamics of bHLH factors in multipotency and cell fate determination. (This figure was modified from Figure 5 of Imayoshi and Kageyama 2014)

bHLH transcription factors, whereas the differentiated state correlates with the sustained expression of a single bHLH transcription factor.

To address the cousal relationships between the expression dynamics (oscillatory versus sustained) and functional outcomes (cell proliferation versus fate differentiation), the optogenetic approach has been employed to control the expression patterns of bHLH transcription factors (Imayoshi et al. 2013). We applied a novel optogenetic method (photo-activatable Gal4/UAS system) to manipulate the expression patterns of bHLH transcription factors using blue light illumination, showing that oscillatory expression activates the cell proliferation of neural progenitor cells, whereas sustained expression induces cell fate determination (Fig. 2.1).

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