IN BRIEF

Last Exit to Differentiation: Histone Variants as Signposts

After decades as wallflowers, histones have come into the limelight in recent years. Long overlooked as mainly structural proteins, the myriad posttranslational modifications of histones are now recognized as important epigenetic marks, and the existence of variant forms of histones H1, H2A, H2B, and H3 point to an intriguing complexity of histone composition within chromatin. Indeed, data increasingly indicate that changes in histone composition are associated with cell cycle progression (reviewed in Desvoyes et al., 2014). Now, Otero et al. (2016) report distinct patterns of histone composition in cells with different proliferative potential, suggesting that a change in histone dynamics marks the last cell cycle in a developmental program.

Otero and coworkers visualized the dynamics of the canonical histone H3.1 and the variant H3.3 by expressing tagged versions of each from their own promoters. When the authors examined highly dividing embryo cells, they found that most cells contained a strong signal for the cell cycle-regulated H3.1 in addition to the constitutively expressed H3.3. Interestingly, the H3.1/H3.3 ratio was high in cells destined to form the quiescent center early in development but then decreased at the stage when these cells acquire their quiescent center fate, i.e., became less mitotically active.

To further explore this possible relationship between cell division potential and H3.1 content, Otero et al. examined the histone dynamics in the root, in which the spatial organization is highly regulated (reviewed in Petricka et al., 2012). The root apical meristem (RAM) includes a proliferative domain where cells arise before they are displaced in the shootward direction through a transition domain where cells stop dividing in preparation for elongation and differentiation. The authors assessed H3.1/H3.3 ratios along with mitotic activity in the RAM. As expected, they found more mitoses in the rootward half of the RAM (the proliferation domain). Strikingly, however, they observed two different patterns of labeling in double-labeled plants (H3.1-GFP/H3.3-mRFP). Toward the bottom of the RAM, mitotic events had both signals, but the shootward part of the proliferation domain had mitotic figures largely devoid of H3.3 (see figure). As H3.1 is incorporated only during S-phase (i.e., during DNA replication), predominant labeling with H3.3 could reflect an eviction of H3.1 in G2 before mitosis and, given its spatial location in the RAM, could represent a marker of a final cell cycle during the exit from proliferation. Indeed, the decrease in H3.1 seemed to precisely colocalize with the decrease in proliferation potential of cells within the RAM, in terms of spatial positioning and expression of genes related to cell cycle regulators.

Consistent with the idea of a specialized G2 phase during the final cell cycle—possibly with H3.1 eviction from chromatin—the authors found that G2 took much longer in cells about to exit the proliferation domain. In addition, a decrease in H3.1 signal occurred in the last endocycle before terminal differentiation of root cells, as well as in the last cell division during stomatal, lateral root, and hypocotyl development, suggesting that cycles of H3.1 incorporation and eviction could be general features of organogenesis. In sum, Otero et al. have provided compelling evidence that histone H3.1 dynamics are associated with cell division potential, such that declines in proliferative potential (i.e., during a final cell cycle) are associated with large-scale removal of H3.1 from the chromatin.

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