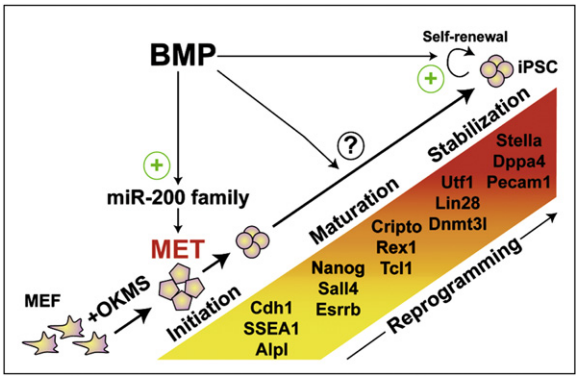
Editors' Notes

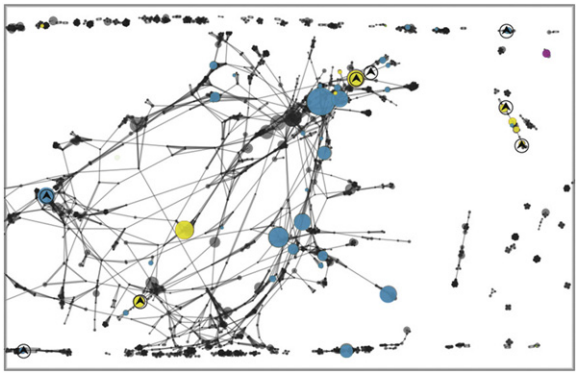
Reprogramming Transitions

What cell type is the "best" to use for the generation of patient-specific iPSCs? As Shinya Yamanaka discusses in his Preview of three independent Brief Reports published in this issue, recent advances that yield human iPSC lines from the peripheral blood of untreated donors may herald a move away from the use of fibroblasts for this purpose. The results presented by the Fukuda, Jaenisch, and Daley laboratories and their respective colleagues demonstrate that human iPSCs derived from T lineage cells serve as an attractive alternative starting material by avoiding the need for relatively invasive biopsies and longer culture periods. Meanwhile, two other independent groups provide new information that helps identify important early steps that take place during the reprogramming process. As discussed by Polo and Hochedlinger, early stages of the conversion of fibroblasts to pluripotent iPSCs appear to entail a mesenchymal-to-epithelial transition (MET). Pei and coauthors demonstrate that the reprogramming factors Sox2 and Oct4 influence components of the MET machinery, whereas Wrana and colleagues provide evidence that miR-205 and -200 family miRNAs participate in BMP-dependent activation of MET at an early phase of the reprogramming process. Extending these findings to other starting cell types will be of great interest as the "behind the scenes" workings of iPSC generation continue to be elucidated. You can listen to the senior authors of both of these studies discuss their findings with Editor Deborah Sweet in this month's Cell Press Podcast.



It Must be Fate

The question of how microRNAs participate in stem cell function is discussed in detail in two Minireviews in this issue. Martinez and Gregory outline the role of miRNAs during the maintenance of pluripotency, as well as during reprogramming from differentiated somatic cells. Ivey and Srivastava look at miRNAs from a different angle and discuss their influence on cell fate and differentiation. The question of how cell fates are regulated is also a major point of the work presented by Dillon and colleagues. The authors show that tissue-specific genes are primed in pluripotent ESCs according to epigenetic modification of enhancers, prior to their stabilization by factors expressed by more mature lineage cells following differentiation. In the case of the neural cells, Zhang and colleagues show that one specific factor, Pax6, is necessary for human neuroectoderm specification from ESCs. The authors suggest that coordinated binding of Pax6a and Pax6b mediate the transition from a pluripotent state to commitment to human neural ectoderm.



Analyzing Growth

The regulation of fate is more than just a question of lineage choice. Sometimes the decision is a matter of when to divide. NSCs in the adult hippocampus are under tight regulation by BMP signals, as Mira and colleagues demonstrate. Analyses of various murine models reveal that the sustained birth of new neurons is dependent on a precise balance of quiescence and proliferation, which can be skewed by altering the BMP signaling cascade. Balancing proliferation is also an essential aspect of hematopoietic stem cell regulation. Sauvageau and coauthors carried out an in vivo RNAi screen and identified several factors that either enhance or restrict HSC function. Using this modern, in vivo functional genetics approach, the authors found that HSC number and function can be elevated by depleting Prox1 levels. Furthermore, gene profiling studies suggest that both Prox1 and Msi2 may function by influencing cell-cycle regulation. The development of analytical tools used to address diverse questions relevant to the stem cell field is an important motivation behind the launch of a new article format in this issue. Synthesis articles offer readers meta-style analyses that combine resources from a range of sources. In this case, Bubela and colleagues utilize bibliometrics in a case study of how research funding policies that aim to promote commercialization may influence the tendency of individuals to coauthor academic publications. Both a showcase for the use of data mining, analytical methods, and for a message delivered about the potential for commercial and academic policies to work at cross-purposes, we hope that this first Synthesis article will open doors for our readers to consider the utility of meta-analysis tools.