Analysis of clone-specific molecular and phenotypic characteristics

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Cell divisions typically result in genetic and often epigenetic differences that are then passed down to the cells progeny. Such clone-specific effects can give rise to distinct phenotypic characteristics of different clones in the context of both healthy tissues and disease. In particular, such heterogeneity can impact stem cells that drive homeostasis and repair of many tissues. To define the extent of-and molecular basis for-heterogeneity, we overlaid functional, transcriptional, and epigenetic attributes of hematopoietic stem cells (HSCs) at a clonal level using endogenous fluorescent tagging[1]. Endogenous HSC had clone-specific functional attributes over time in vivo. The intra-clonal behaviors were highly stereotypic, conserved under the stress of transplantation, inflammation, and genotoxic injury, and associated with distinctive transcriptional, DNA methylation, and chromatin accessibility patterns. Further, HSC function corresponded to epigenetic configuration but not always to transcriptional state. Therefore, hematopoiesis under homeostatic and stress conditions represents the integrated action of highly heterogeneous clones of HSC with epigenetically scripted behaviors.

1. Yu WV et al. (2016) Epigenetic Memory Underlies Cell-Autonomous Heterogeneous Behavior of Hematopoietic Stem Cells, *Cell,* **167(5):**1310-1322.