


Figure 1. **Distinct cell cycle activity in fetal, adult, and old HSCs.** HSC cell cycle activity and cellular output is highly dynamic throughout the lifetime of an organism. During fetal life (left column), HSCs display a high level of cell cycle activity, as their primary role at this stage is the genesis of the nascent blood system. During adult life (center column), HSCs reside in the BM and enter a predominantly quiescent ( $G_0$ ) state, generating a balanced myeloid, erythroid, and lymphoid output to maintain blood homeostasis. As individuals age (right column), HSCs appear to remain predominantly quiescent, but their function begins to degrade (dotted outlines), resulting in the loss of erythroid and lymphoid output and bias toward the myeloid lineage. AGM: aorta-gonad-mesonephros; ND: not determined. See text for detailed discussion and references.



	<b>Fetal HSC</b>	<b>Adult HSC</b>	<b>Aged HSC</b>
Location	AGM Placenta Fetal Liver	Bone Marrow	Bone Marrow
Percent cycling	~100% per 24h	Active HSCs: 5.3-11.1% per 24h Dormant HSCs: 0.8-1.8% per 24h	~5% per 52h
Percent quiescent	0.02%	90-95%	~95%
Frequency of cell cycle entry	~1 per 24h	Active HSCs: ~1 per 36 days Dormant HSCs: ~1 per 145+ days	ND
Cell cycle transit time	14h (~10.5h in $G_1$ )	14h (~10.5h in $G_1$ )	ND
Output	Primarily erythroid & myeloid lineages	Balanced production of all blood lineages	Loss of lymphoid and erythroid potential
Physiological context of HSC activity	Blood development	Homeostatic blood production	Immunosenescence, anemia and myeloid leukemia