

Mapping differentiation pathways from hematopoietic stem cells using Flk2/Flt3 lineage tracing.

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Public Summary:

This study established the lineage relationship between blood progenitor cells and their more mature progeny.

Scientific Abstract:

Genetic fate-mapping approaches provide a unique opportunity to assess differentiation pathways under physiological conditions. We have recently employed a lineage tracing approach to define hematopoietic differentiation pathways in relation to expression of the tyrosine kinase receptor Flk2. (1) Based on our examination of reporter activity across all stem, progenitor and mature populations in our Flk2-Cre lineage model, we concluded that all mature blood lineages are derived through a Flk2 (+) intermediate, both at steady-state and under stress conditions. Here, we re-examine in depth our initial conclusions and perform additional experiments to test alternative options of lineage specification. Our data unequivocally support the conclusion that onset of Flk2 expression results in loss of self-renewal but preservation of multilineage differentiation potential. We discuss the implications of these data for defining stem cell identity and lineage potential among hematopoietic populations.

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