

STELLINGEN behorende bij het proefschrift

Developmental Origins of the Murine Hematopoietic System

1. The physiological tracing of embryo-generated HSCs to the bone marrow in the mammalian adult remains an interesting challenge (this thesis).
2. Ly-6A strains of mice express Sca-1 on virtually all (99%) marrow repopulating cells, while Ly-6E strains express Sca-1 on only 25% of these cells (Spangrude and Brooks, 1993, *Blood* **82**: 3327-3332).
3. Despite transcription of CreERT in appropriate embryonic and adult hematopoietic tissues, only rare induced recombination/expression events were observed (this thesis).
4. Transcription factor levels determine the balance between proliferation and differentiation (this thesis).
5. The mouse strain and developmental stage of the recipient is one of the most important considerations in *in vivo* HSC transplantation assays (this thesis).
6. In contrast to what has been suggested, the first HSCs appear at day 10 of mouse gestation in the intra-embryonic aorta-gonad-mesonephros region (Müller et al., 1994, *Immunity* **1**: 291-301; Medvinsky and Dzierzak, 1996, *Cell* **86**: 897-906; Yoder et al., 1997, *Immunity* **7**: 335-44; Bertrand et al., 2005, *PNAS* **102**: 134-9).
7. More recent experiments have confirmed and extended the classical lineage tracing of the adult hematopoietic system in chick-quail chimeras and *Xenopus* diploid/triploid chimeras (Dieterlen-Lievre, 1975, *J Embryol Exp Morphol* **33**: 607-19; Turpen et al., 1981, *Dev Biol* **85**: 99-112; Ciau-Uitz et al., 2000, *Cell* **102**: 787-96; Jaffredo et al., 1998, *Development* **125**: 4575-83).
8. The Notch signalling pathways involve membrane-bound ligands and regulate cell fate in a wide variety of systems, including HSCs throughout ontogeny (Varnum-Finney et al., 2000, *Nature Med* **6**: 1278-81; Karanu et al., 2001, *Blood* **97**: 1960-67; Kumano et al., 2003, *Immunity* **18**: 699-711).
9. Hedgehog signalling is at the base of the molecular network driving hematopoietic cell emergence in the embryo (Gering and Patient, 2005, *Dev Cell* **8**: 389-400; Dyer et al., 2001, *Development* **128**: 1717-30).
10. "All methods suffer from some drawbacks either in terms of leaky background, lack of temporal control or, ... " (Jonkers and Berns, 2002, *Nature Rev Cancer* **2**: 251-265).
11. "Science can purify religion from error and superstition. Religion can purify science from idolatry and false absolutes." (Pope John Paul II).