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Publication status and date:

Published: 17/11/2010

Document Version

Other version

Citation for the published version (APA):

Luis, T. (2010). *Fine-tuning hematopoieses. Microenvironmental factors regulating self-renewal and differentiation of hematopoietic stem cells*. [Doctoral Thesis, Erasmus University Rotterdam]. Erasmus Universiteit Rotterdam (EUR).

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Stellingen behorende bij het proefschrift

Fine-tuning Hematopoiesis

**Microenvironmental factors regulating self-renewal and differentiation
of hematopoietic stem cells**

Rotterdam, 17 November 2010

Tiago Cunha Luis

1. Canonical Wnt signaling is essential for self-renewal of hematopoietic stem cell
(*This thesis*)
2. Canonical Wnt signaling regulates hematopoiesis in a dosage dependent fashion. There is a differential, lineage specific, optimum Wnt dosage in the hematopoietic system that increases from hematopoietic stem cells, myeloid precursors to T lymphoid precursors. (*This thesis*)
3. Hematopoietic stem cells specifically require low levels of canonical Wnt signaling activation. (*This thesis*)
4. Wnt3a non-redundantly regulates fetal liver HSC self-renewal and differentiation. This points specifically to Wnt3a as the Wnt protein of choice to expand HSCs *ex vivo* for transplantation- and stem cell-based therapies. (*This thesis*)
5. Notch signaling has been shown to be active in HSC but has been postulated to play no role in HSC function Furthermore, Notch activation in HSC results in leukemia development (Duncan et al, 2005; Radtke et al, 2010). Why would such a “dangerous” signaling pathway be evolutionarily maintained if it does not play an essential role in the regulation of hematopoietic stem cell function? (*This thesis*)
6. “Methodology is everything and the devil is in the details.” (statement by *Paul Simmons* in: “*Stem cells: the hard copy*” by *Check E, Nature, 2007*)
7. "I have never seen a biological tool as powerful as the stem cells. (...) the use of human embryonic stem cells is an ethical and responsible thing to do with tissue that would have been destroyed in the discards of fertility clinics...So, let's use it instead of discarding it. If you think that that is a holy thing, then value it, treasure

it and keep it. Use it for research and the betterment of lives, don't throw it away."
(*Hans Kierstead in "60 minutes", CBS, by Daniel Schorn, 26 February, 2006*)

8. "Peer review is important to keep the quality of articles and assure that poor or fallacious research does not get published. (...) But, too often, reviews are cursory or negative or even positive without substance. (...) many argue that the anonymity of the blind review process allows a reviewer to freely state what he or she believes about a particular paper without fear of reprisal. (...) *Current Anthropology* has the right idea: open reviews, signed, with bibliographic references." (*K. Kris Hirst, in about.com:archaeology*)

9. It is urgent in Portugal to confer normal working and social benefits to young researchers and technicians. The lack of social recognition has a negative effect for these individuals and for science in Portugal. (*After Antonio Coutinho & Boaventura Sousa Santos in: Newspaper Público, Andrea Cunha Freitas, 25 April 2010*)

10. A constant element of enjoyment must be mingled with our studies, so that we think of learning as a game rather than a form of drudgery, for no activity can be continued for long if it does not to some extent afford pleasure to the participant. (*Desiderius Erasmus, Letter to Christian Northoff, 1497*)

11. "E foste um difícil começo; Afasto o que não conheço; E quem vem de outro sonho feliz de cidade; Aprende depressa a chamar-te de realidade; Porque és o avesso do avesso do avesso do avesso." (*Caetano Veloso, Sampa, 1978*)
(And it was a difficult start; Move away from what I do not know; And who comes from another happy dream of city; Quickly learns to call you reality; Because you are the reversal of the reversal of the reversal of the reversal.)