

Propositions (Stellingen) accompanying the doctoral dissertation

### The Hematopoietic Stem Cell Niche in Leukemia Predisposition

1. Niche-derived S100A8/9 induces genotoxic stress in HSPCs. (This dissertation)
2. S100A8/9 expression, associated with activated p53 and TLR signaling in mesenchymal cells, predicts leukemic evolution and progression-free survival in a cohort of homogeneously treated low-risk MDS patients. (This dissertation)
3. Mesenchymal NF- $\kappa$ B activation is a common finding in LR-MDS patients, leading to transcriptional upregulation of inflammatory programs associated with negative regulation of hematopoiesis and attenuation of HSPC numbers and function. (This dissertation)
4. Neutropenia, in itself, does not contribute to attenuation of the cellular integrity and transformation of HSCs. (This dissertation)
5. Long-term depletion of neutrophils ameliorates features typically associated with aging of the hematopoietic system, such as HSC expansion and loss of long-term repopulating ability. (This dissertation)
6. HSCs have previously been proposed to be maintained in osteoblastic (endosteal) niches, but the available evidence no longer supports this model as osteoblasts are not a necessary source of niche factors known to be required for HSC maintenance. (Adapted from Crane *et al.*, 2017)
7. Single-cell genomics hold the potential to revolutionize the way we characterize complex immune cell assemblies; bulk-methods may mask the intrinsic differences of cells expressing the same surface markers. (Adapted from Giladi and Amit, 2017)
8. If a finding is true, but it's only true with one cell line, and it has to be in a Boston zip code, and the Red Sox won the night before, it may be true, but it's not very robust. Reproducibility is of vital importance and raising major concerns in the contemporary scientific community. (Adapted from William Kaelin)
9. It is the mark of an educated mind to be able to entertain a thought without accepting it, critical thinking and questioning are necessary but not sufficient for enjoying academic research. (Adapted from Aristotle)
10. Pressure makes diamonds, yet not all the 'diamonds' made under pressure are necessarily good. (Adapted from George S. Patton Jr.)
11. 橘生淮南则为橘，生于淮北则为枳，叶徒相似，其实味不同。所以然者何？水土异也。  
– 晏婴 《晏子春秋》  
The fruits of orange plants are sweet when grown in the region south of river Huai, bitter when grown in the region north of river Huai, the plants may look the same, but the fruits taste very different. Why is that? The water and soil in their surroundings cause the differences. (Translated and adapted from Yan Ying, Yanzi chunqiu)

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