Propositions accompanying the thesis:

Deconstructing Niche Contributions to Leukemogenesis:

Modeling Shwachman-Diamond Syndrome

1. *Sbds* deficiency in the hematolopoietic lineage induces cellular stress at late stages of myeloid development, resulting in neutropenia.
2. The osteoporotic phenotype in Shwachman-Diamond syndrome reflects impaired osteoblastic differentiation of *Sbds*-deficient mesenchymal progenitor cells.
3. *Sbds*-deficient mesenchymal cells attenuate the genomic integrity of heterotypic cells, namely hematopoietic stem and progenitor cells.
4. Secretion of supraphysiological levels of S100A8/9 in pre-leukemic bone marrow microenvironments induces DNA damage and apoptosis of hematopoietic stem and progenitor cells.
5. Overexpression of S100A8 in mesenchymal cells identifies a subset of low-risk myelodysplastic syndrome patients with poor clinical outcome.
6. Much like in ecology, a shift in the condition of the niche can permit subspecies to thrive, in this case, leukemic cells. (David T. Scadden, *Cell*, 2014)
7. Studying the function of disease-associated genes by *in vivo* genetic deletion approaches is particularly challenging for so-called “housekeeping” genes, whose complete deficiency often results in lethal phenotypes.
8. When investigating mesenchymal cell biology using plastic-adherent cell cultures, one must remember that adhesion signals modulate survival and proliferation programs, thus potentially altering the experimental outcome.
9. The surface marker-based definition of cellular identity is necessarily blurry, as the expression of surface proteins is not fixed but rather influenced by the developmental and functional status of a cell.
10. Together with the required statistical power and the expected standard deviation, the financial resources of a lab often factor in when determining the necessary experimental sample size.
11. If everything seems under control, you are just not going fast enough. (Mario Andretti)

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