Propositions (Stellingen)

UNTANGLING CELLULAR AND MOLECULAR MECHANISMS OF FIBROTIC DISEASE

1. Gli1 expression marks perivascular mesenchymal stem cells (MSCs) across major organ systems (this thesis).
2. Gli1^{+} perivascular MSCs are a major source of fibrosis-driving myofibroblasts in kidney, heart and bone marrow and their genetic ablation ameliorates fibrosis and stabilizes organ function (this thesis).
3. Gli proteins are important drivers of myofibroblast cell-cycle progression and a promising therapeutic target to inhibit myofibroblast expansion and fibrosis (this thesis).
4. Resident pericytes are the major source of myofibroblasts while circulating monocytes show a minor contribution primarily, however, through indirect pro-inflammatory mechanisms (this thesis).
5. Fibrosis is a conserved mechanism across organ systems, which initially aids in tissue repair but during chronic injury becomes a disease by itself destroying organ architecture and leading to organ failure.
6. Switching resident pericytes from a pro-fibrotic towards a pro-angiogenic phenotype might be a novel therapeutic strategy to inhibit fibrosis and promote tissue repair.
7. The tremendous heterogeneity of the pericyte lineage is incompletely understood and of tremendous importance for understanding tissue injury, fibrosis and repair processes.
8. Cross-talk of resident mesenchymal cells and circulating immune cells is a major driver of tissue fibrosis and scar formation.
9. To untangle mechanisms of complex diseases and to develop novel therapeutics large collaborative approaches of academia and industry are needed.
10. The culture of “publish or perish” and the short lifespan of most research grants slow down progression of science.
11. Only those who attempt the absurd can achieve the impossible (Albert Einstein).

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