

## Propositions

1. Age-related loss of fitness and loss of renal integrity can be reversed through therapeutic targeting of senescent cells with FOXO4-DRI. (Chapter 2)
2. Targeting senescence features such as SASP factors and FOXO4-p53 binding in cancer cells impairs chemotherapy resistance. (Chapter 5)
3. MiR-30 is an interesting target in aging research, since it controls p53 expression. (Chapter 6)
4. Age-related DNA damage responses can be transferred to neighboring cells through extracellular vesicles, possibly inducing pro-survival cues in neighboring cells. (Chapter 7)
5. Organotypic tissue slices are a valuable tool to study age-related responses and therapeutic interventions within a relevant environment. (Chapter 8)
6. Senescent cells contribute mainly to aging through the senescence associated secretory phenotype (SASP), while their permanent cell cycle arrest contributes mainly to preventing carcinogenesis.
7. A better understanding of the subtypes of senescent cells is required to achieve optimal responses to anti-senescence therapy.
8. Unraveling the mechanism behind tissue rejuvenation after senescent cell clearance is key to minimizing adverse effects.
9. Apoptosis is actively inhibited in a subset of tissues to prevent loss of tissue integrity during aging. Although damaged cells are less inclined to die, this does not necessarily explain the increase in cancer incidence later in life.
10. Cell fates such as senescence and cell preservation cannot be described as one well defined cellular state, since both are dynamic causing heterogeneity.
11. A short term vision is incompatible with aging research.