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## Regulation of signal transduction pathways by hypoxia in breast cancer subtypes

Liu, Q.

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# Stellingen

behorende bij het proefschrift

## Regulation of signal transduction pathways by hypoxia in breast cancer subtypes

1. Considering the global impact of HIF on cancer cells and the tumor microenvironment, therapies targeting HIF activity have been used to prevent the interactions of the HIF- $\alpha$  and HIF1- $\beta$  subunits, which may be promising for some groups of patients (Petrova et al. 2018, Oncogenesis).
2. Even though hypoxia was first identified 100 years ago, several clinically applicable techniques for identification were developed, and preclinical and clinical studies identified a variety of approaches for elimination, there is not yet a clear strategy or treatment to target it (Horsman et al. 2021, Clinical oncology).
3. YAP/TAZ transcription factors are prominent for many aspects of cancer biology, which indicates that they are ideal targets for development of anticancer treatments (Zanconato et al. 2016, Current opinion in pharmacology).
4. Inhibitors directly targeting YAP/TAZ are still under development, whereas FDA-approved drugs that indirectly block YAP/TAZ activation or their critical downstream targets have shown promise in the clinic in reducing therapy resistance (Nguyen et al. 2019, Trends in cancer).
5. The Hippo pathway may serve as a signaling integration hub by interpreting both mechanical and biochemical cues (Cai et al. 2019, Frontiers in Cell and Developmental Biology).
6. Even though it was defined in the previous century, hypoxia needs to be further standardized and delimited and this is important as acute and chronic hypoxia differentially impact cell function. (Chapter 2 & 3)
7. Crosstalk between YAP/TAZ-mediated mechanotransduction and biochemical cues in the tumor microenvironment can open a critical door to understanding cancer progression. (Chapter 4)
8. YAP and TAZ have distinct roles in cancer cells and TAZ should not be ignored as a mere partner of YAP. (Chapter 5)
9. YAP/TAZ activity cannot be accurately predicted only based on expression of a set of target genes as we observe when cells are subjected to hypoxia. (Chapter 5 & 6)
10. A PhD is like a Jelly Belly Bean Boozled Spinner Game. You will never know which flavour is waiting for you, but I am sure that every taste is unforgettable.
11. PhD is a staff and experiments are like notes on a staff, where rest(s) and repetitions are needed.
12. 不忘初心，方得始终。初心易得，始终难守。  
It is easy to have an initial intention, but it is hard to persist from the beginning to the end. If you always put the initial intention in your mind, you will gain what you deserve.