Propositions accompanying the dissertation

The unfolded protein response in glioblastoma stem cells: towards new targets for therapy

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1. In glioblastoma neurospheres, ER stress induced cytotoxicity is mediated by PERK-eIF2α-ATF4 activation associated with CHOP accumulation and cell death activation. (*this dissertation*)

2. PERK is an important regulator of glioblastoma stem cells (GSCs) and differentiation. (*this dissertation*)

3. Identified novel PERK signaling involves noncanonical mechanisms regulating stemness in GSCs under both regular and acute ER stress conditions, the latter mediated by down-regulation of SOX2 protein levels. (*this dissertation*)

4. PERK targeted therapy in glioblastoma potentially provides a double-edged sword resulting in either cytoprotective or cell death inducing/ anti GSC activity likely depending on levels and type of ER stress and the cellular UPR status. (*this dissertation*)

5. High ATF4 levels may be predictive for poor prognosis of glioblastoma patients. (*this dissertation*)

6. The small effects of PERK inhibition on gene transcription in regular cultured GSCs suggest the involvement of signals at the protein level to be responsible for stemness regulation. (*this dissertation*)

7. Glioblastoma is characterized by intratumoral heterogeneity and cellular plasticity that provides a hurdle for effective therapy. *(Neftel C et al., Cell. 178:835-849, 2019)*

8. “Those who cannot change their minds cannot change anything.” *George Bernard Shaw*

9. “Ever tried. Ever failed. No matter. Try again. Fail again. Fail better.” *Samuel Beckett*