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

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DOI:
[10.33612/diss.118411504](https://doi.org/10.33612/diss.118411504)

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2020

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Peñaranda Fajardo, N. (2020). *The unfolded protein response in glioblastoma stem cells: towards new targets for therapy*. [Thesis fully internal (DIV), University of Groningen]. Rijksuniversiteit Groningen. <https://doi.org/10.33612/diss.118411504>

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Propositions accompanying the dissertation

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

Natalia M. Peñaranda Fajardo

1. In glioblastoma neurospheres, ER stress induced cytotoxicity is mediated by PERK-eIF2 α -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*