



RESEARCH TOPIC MEM13

Valosin-containing protein (VCP): biomarker of radioresistance in glioblastoma (VALOR study)

Curriculum MEM Clinical

Clinical Unit name and address

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Abstract

Glioblastoma (GBM) is the most aggressive glioma. Radiotherapy (RT) is essential, but radioresistance limits its efficiency. Recognition of radioresistant tumors, through specific markers, may enable the identification of more tailored and effective radiation regimens. Valosin-containing protein (VCP), an ATPase involved in DNA damage repair after ionizing radiation, may decrease the cellular radiation sensitivity. Aim of this project is to investigate the VCP role in radioresistance and as prognostic and predictive biomarker in GBM. GBM patients will be treated as clinical practice with surgery followed by RT. VCP expression on tumor samples will be evaluated and correlated with patient's outcome. Tumor samples will be irradiated. Consequent DNA double strand breaks will be analyzed and related with VCP expression. To distinguish if VCP, and not other factors, could be responsible for the decrease of radiation sensitivity, homogeneous GBM cells, with and without VCP expression, will be irradiated and compared.

Main technical approaches

VCP expression analysis on GBM tissue samples after surgery. Fresh tissue samples irradiation and DNA DSB evaluation through the analysis of γ H2AX foci. GBM cells irradiation and evaluation of their survival after RT.

Scientific references

1. Luo H, Song H, Mao R, Gao Q, Feng Z, Wang N, Song S, Jiao R, Ni P, Ge H. Targeting valosin-containing protein enhances the efficacy of radiation therapy in esophageal squamous cell carcinoma. *Cancer Sci.* 2019 Nov;110(11):3464-3475. doi: 10.1111/cas.14184. Epub 2019 Sep 13. PMID: 31454136; PMCID: PMC6825005.
2. Biau J, Chautard E, De Koning L, Court F, Pereira B, Verrelle P, Dutreix M. Predictive biomarkers of resistance to hypofractionated radiotherapy in high grade glioma. *Radiat Oncol.* 2017 Jul 28;12(1):123. doi: 10.1186/s13014-017-0858-0. PMID: 28754127; PMCID: PMC5534104.
3. Jiang N, Shen Y, Fei X, Sheng K, Sun P, Qiu Y, Larner J, Cao L, Kong X, Mi J. Valosin-containing protein regulates the proteasome-mediated degradation of DNA-PKcs in glioma cells. *Cell Death Dis.* 2013 May 30;4(5):e647. doi: 10.1038/cddis.2013.171. PMID: 23722536; PMCID: PMC3674378.
4. Meerang M, Ritz D, Paliwal S, Garajova Z, Bosshard M, Mailand N, Janscak P, Hübscher U, Meyer H, Ramadan K. The ubiquitin-selective segregase VCP/p97 orchestrates the response to DNA double-strand breaks. *Nat Cell Biol.* 2011 Oct 23;13(11):1376-82. doi: 10.1038/ncb2367. PMID: 22020440.

Type of contract

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