Vacquinol

A novel drug, Vacquinol-1 (Vac), a quinolone derivative, displays promising properties by inducing rapid cell death in Glioblastoma (GBM) but not in non-transformed tissues. Features of this type of cell death are compatible with a process termed methuosis. Here we tested Vac on a highly malignant glioma cell line observed by long-term video microscopy. Human dental-pulp stem cells (DPSCs) served as controls. A major finding was that an exogenous ATP concentration of as little as 1 µM counter regulated the Vac-induced cell death. Studies using carvacrol, an inhibitor of transient receptor potential cation channel, subfamily M, member 7 (TRPM7), demonstrated that the ATP-inducible inhibitory effect is likely to be via TRPM7. Exogenous ATP is of relevance in GBM with large necrotic areas. Our results support the use of GBM cultures with different grades of malignancy to address their sensitivity to methuosis. The video-microscopy approach presented here allows decoding of signaling pathways as well as mechanisms of chemotherapeutic resistance by long-term observation. Before implementing Vac as a novel therapeutic drug in GBM, cells from each individual patient need to be assessed for their ATP sensitivity. In summary, the current investigation supports the concept of methuosis, described as non-apoptotic cell death and a promising approach for GBM treatment. Tissue-resident ATP/necrosis may interfere with this cell-death pathway but can be overcome by a natural compound, carvacrol that even penetrates the blood-brain barrier [1)].

1)
Sander P, Mostafa H, Soboh A, Schneider JM, Pala A, Baron AK, Moepps B, Wirtz CR, Georgieff M, Schneider EM. Vacquinol-1 inducible cell death in glioblastoma multiforme is counter regulated by TRPM7 activity induced by exogenous ATP. Oncotarget. 2017 Mar 30. doi: 10.18632/oncotarget.16703. [Epub ahead of print] PubMed PMID: 28410232.