Major vault protein

Major vault protein is a protein that in humans is encoded by the MVP gene.

78 copies of the protein assemble into the large compartments called vaults, illustrated and discussed in the article on Vault (organelle).

This gene encodes the major vault protein which is a lung infection resistance-related protein. Vaults are multi-subunit structures that may be involved in nucleo-cytoplasmic transport. This protein mediates drug resistance, perhaps via a transport process. It is widely distributed in normal tissues, and overexpressed in multidrug-resistant cancer cells. The protein overexpression is a potentially useful marker of clinical drug resistance. This gene produces two transcripts by using two alternative exon 2 sequences; however, the open reading frames are the same in both transcripts.

Several central nervous system (CNS) tumors have been reported to exhibit high levels of major vault protein (MVP).

Although further studies are needed to elucidate the mechanisms of endogenous vault function, these advances may enable the development of targeted therapies to prevent cancer cells from acquiring MVP-related drug resistance. In addition, they seem suited for use as nanocapsules for delivering various therapeutic agents and immunogenic proteins, representing a promising prospect for CNS tumor immunotherapy [1)].

A study demonstrated that human astrocytic brain tumours including glioblastoma are generally high in vault levels while MVP expression in normal brain is comparably low. However a direct contribution to the malignant phenotype in general and that of glioblastoma in particular has not been established so far. Thus they address the questions whether MVP itself has a pro-tumorigenic function in glioblastoma. Based on a large tissue collection, Lötsch et al. re-confirm strong MVP expression in gliomas as compared to healthy brain. Further, the impact of MVP on human glioblastoma aggressiveness was analysed by using gene transfection, siRNA knock-down and dominant-negative genetic approaches. The results demonstrate that MVP/vaults significantly support migratory and invasive competence as well as starvation resistance of glioma cells in vitro and in vivo. The enhanced aggressiveness was based on MVP-mediated stabilization of the epidermal growth factor receptor (EGFR)/phosphatidyl-inositol-3-kinase (PI3K) signalling axis. Consequently, MVP overexpression resulted in enhanced growth and brain invasion in human glioblastoma xenograft models. The study demonstrates, for the first time, that vaults have a tumour-promoting potential by stabilizing EGFR/PI3K-mediated migration and survival pathways in human glioblastoma [2)].

Amplification of EGFR and MVP was found in a 63.7% and 56.6% of the GBM, respectively. An inverse correlation between MVP and PTEN dosage values was observed. Besides, an inverse relationship between the survival of the patients treated with chemotherapy and the levels of MVP copies was determined. In conclusion, our study reveals an important role of MVP, together with EGFRvIII and PTEN, in the progression of GBM and proposes it as a novel and interesting target for new treatment approaches [3)].

Upregulation of breast cancer resistance protein (BCRP) and major vault protein (MVP) is associated with MTLE and FCD and these molecules not only may have the potential to predict pathology specific phenotypes but may also have therapeutic potential as adjunct treatment in these pathologies. [4)].

1)
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