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# Mitochondrial VDAC1 Porin as a Therapeutic Target in Demyelination Process: Investigation of the Interaction Sites between Hexokinase I and VDAC1

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**Abstract:** Mitochondrial dysfunction has been implicated in many diseases including cancer, cardiovascular and neurodegenerative diseases[1,2]. The voltage-dependant anion channel 1 (VDAC1) is the most abundant protein found in the outer mitochondrial membrane. VDAC1 functions as a gatekeeper and is considered as a multi-functional porin involved in cell survival and cell death[3]. VDAC1 mediates energy production as well as ions and metabolic exchanges between the mitochondria and other cellular compartments, thus modulating mitochondrial permeability. VDAC1 is also involved in the cellular $Ca^{2+}$ homeostasis by its capacity to transport $Ca^{2+}$ in and out of mitochondria[4]. In addition, VDAC1 interacts with multiple proteins implicated in neurodegeneration process[5] as well as with pro-apoptotic and anti-apoptotic regulating proteins, and in particular Hexokinase isoforms I and II, its main ligand. Hexokinase I (HK I) is found in brain tissues and is known as the "guardian of the mitochondria". HK possess a hydrophobic N-terminal structured in $\alpha$-helix that is necessary for the binding of HK to VDAC[6]. The interaction between HK and VDAC1 has attracted much interest, and several studies have proposed different models of binding to VDAC1[7,8]. However, the precise mechanism of binding remains undefined up to now. In order to give some insights to the nature of HK binding to VDAC1, we have developed new peptide analogs of HK I based on Hexokinase I N-terminal sequence. In this study, the *in-vitro* activity of the peptides was studied, the peptide helical content was investigated by circular dichroism and NMR, and peptide proteolytic stability was assessed.

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