**Computational analysis of UBS109 and murine double minute 2 (MDM2) in pancreatic cancer**

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**Abstract**

**Background/Objectives**: Overexpression of Murine double minute 2 (MDM2) associated with the inhibition of tumor suppressors, enhanced epithelial-mesenchymal transition (EMT), and upregulation of oncoproteins in pancreatic cancer (PC). Curcumin is an extensively studied molecule due to its various anticancer properties. Curcumin is known to upregulate p53, p21, and p27. At the same time, downregulate MDM2, cyclin D1, and cyclin E. UBS109 is a mono-carbonyl analog of curcumin that exhibits comparable anti-tumor and anti-inflammatory characteristics without the restrictions of curcumin. This investigation intends to target MDM2 by curcumin and UBS109 in PC.

**Methods**: Molecular Docking (AutoDock 4.2.) is used to predict the interaction between the drug (curcumin and UBS109) and the protein (MDM2). To confirm the effectiveness of drugs, we performed western blot analysis in PC cell lines AsPC-1, and PANC-1.

**Results**: With the aid of advanced computational approaches, the binding capacity of MDM2 against curcumin and UBS109 was evaluated. Post-MD simulations revealed that UBS109 exhibited higher reactivity and higher kinetic stability than curcumin. Treatment with curcumin or UBS109 caused a low MDM2 protein level in AsPC-1 and PANC-1 cells compared to treatment with DMSO. β-actin is used as a loading control.

**Conclusion:** The collective outcomes of in silico and in vitro analyses revealed that UBS109 can efficiently bind to MDM2 and serve as a probable anti-tumor agent for managing PC. Additional in vivo investigations are vital to solidify our analysis's outcome further and confirm the anti-cancerous effects of the novel curcumin analog, UBS109.