PhD Seminar Talk-I

Structure-Guided Computational Identification of Peptides Targeting AURKA and Their Integration into an Ultrasensitive Electrochemical Biosensor

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ABSTRACT

Oral squamous cell carcinoma (OSCC) is a malignant epithelial neoplasm that affects the head and neck region and contributes to around 84–97% of oral cancer. Aurora kinase A is a key regulator of cell cycle progression and mitotic spindle assembly, which plays a critical role in the development and progression of OSCC. Knockdown of AURKA suppresses cell proliferation, migration, and invasion, while inducing apoptosis and reactive oxygen species generation in oral squamous cell carcinoma. This study used *in silico* analysis to screen 116 potential anticancer peptides for AURKA inhibition. ABP-1 peptide exhibited an excellent binding affinity (-1049.8 Kcal/mol) with the AURKA catalytic pocket, stabilized by key interaction residues such as Leu139, Phe144, Val147, Leu210, Trp277, Lys143, Pro214, and Glu260. To enhance the binding affinity of ABP1 peptide, *in silico* mutagenesis was performed wherein a four-point mutation (F5W V6Y V9W M11Y), designated as ABP-2, demonstrated a significantly enhanced binding affinity of -1320.2 Kcal/mol. Molecular dynamics simulations and MM-GBSA analysis confirmed the structural stability of the protein-peptide complexes. Coupled with favorable pharmacokinetics, low toxicity, and high biocompatibility, these findings position ABP-1 and ABP-2 as promising candidates for targeting oral cancer. Building on the *in silico* results, the peptides were immobilized onto a MWCNT-COOH modified electrode via EDC/NHS coupling to develop a sensitive electrochemical biosensor to detect the binding affinity. The MWCNTs facilitate rapid electron transfer and provide a high-density platform for peptide attachment, enhancing the sensor's detection efficiency. Cyclic Voltammetry (CV) and Differential Pulse Voltammetry (DPV) were performed to validate the successful fabrication of the peptide biosensor. The Limits of detection (LOD) of ABP-1 and ABP-2 were found to be 0.010 μg/ml and 0.014 μg/ml, respectively. The Limits of Quantification (LOQ) of ABP-1 and ABP-2 were found to be 0.034 μg/ml and 0.047 μg/ml, respectively. Overall, this integrated *in silico-in vitro* approach establishes a promising strategy for targeting AURKA and provides a foundation for future translational development of peptide-guided electrochemical biosensing platforms.