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Topic of Research: Identification of Potential Human Cyclin Dependent Kinase 6 Inhibitors: Towards Therapeutic Management of Cancer

Increased CDK6 protein expression and activity are linked with characteristics of cancer. Our study revealed that the secondary structure of CDK6 is disrupted in highly acidic conditions forms aggregation in this pH range. However, CDK6 maintains native-like conformation with no secondary structural disruption at other pH range. Enzyme assay suggests that CDK6 shows optimum pH at 8.0. The change in the structure of CDK6 based on the pH can further help understand the disease condition and cellular homeostasis for protein function under a variable range of pH conditions.

Insilco, kinase inhibition assay and fluorescence quenching studies suggested that EA, QC and vanillin bind to CDK6 with excellent affinity. Furthermore, ITC experiment was performed for the validation the binding data. We obtained significant values of binding parameters. EA, QC and vanillin meaningfully decrease the growth of human cancer cells by decreasing the CDK6 expression. They inhibiting the colony formation and induces the apoptosis in cancer cells.

This study warrants a further detailed therapeutic evaluation of these molecules concerning the CDK6 targeted therapies. Besides, the structure of these molecules may be further chemically modified to develop effective preclinical leads with high selectivity and improved drug-likeness features.