Statement of novelty

Valosine-containing Protein (VCP) is a multidomain, ATP-binding protein that is involved in ubiquitin-dependent protein degradation and has a role a role in cancer diseases. The physiologically relevant form of VCP is a homohexamer which is targeted by a set of different small molecules. In this paper the atomic level interactions and the action mechanism of three families of VCP targeting molecules are studied with molecular modeling techniques and results are used to complement the available experimental data. These results shed light on different mechanism of inhibition of the same protein through either a competitive or allosteric mechanism.