Computational Studies of Protein Prenylation

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The protein prenyltransferases represent a family of enzymes that catalyze the attachment of isoprenoid lipid groups to various substrates including the Ras superfamily signal transduction proteins that has been shown to be responsible for 30% of human cancers. Though many structural studies and clinical trials have been done, the mechanism of the prenylation remains unclear, which is very important in order to better understand these important anti-cancer drug design target enzymes. We carried out hybrid quantum mechanical/ molecular mechanical molecular dynamics (QM/MM MD) studies to figure out whether the reaction undergoes a nucleophilic attack or an electrophilic capture mechanism. The role the metal ion(s) played in the mechanism is studied.