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Structural and energetic determinants of tyrosylprotein sulfotransferase sulfating specificity PRAVEEN NEDUMPULLY-GOVINDAN, Clemson University, Clemson, SC, LIN LI, EMIL G. ALEXOV, MARK A. BLENNER, FENG DING, Clemson University — Tyrosine sulfation is a type of post-translational modification which is catalyzed by the enzyme tyrosylprotein sulfotransferase (TPST). There is no well-defined sequence motif for tyrosine sulfation, and the selection criteria for a sequence undergoing sulfation remain elusive. We estimated the binding affinity of peptides with tyrosines to TPST and attempted to differentiate the sulfated and non-sulfated sequences. We find that sequences which undergo sulfation in general have stronger binding affinity. Even though simple binding affinity score can satisfactorily differentiate the two sets of sequences, we found that the predictions are further improved after including energy costs associated with local unfolding. These include costs for melting secondary structures and solvent exposing the peptide residues. Our results suggest that in addition to binding affinity, the thermodynamic availability of the peptide is important for sulfation specificity. Our method is expected to be useful in predicting potential sulfation sites. Since we use simple physics-based method, we expect it to be transferable to other TPST variants, and also other post-translational modification systems.

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