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Fragment molecular orbital method based interaction analysis between cell adhesion factor FimH and mannose derivatives

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FimH plays a critical role in cell-cell adhesion of adherent-invasive *Escherichia coli* (AIEC) and uropathogenic *Escherichia coli* (UPEC) by the interaction with mannose in their host cell. Hence, a number of mannose derivatives are reported for inhibiting the interaction, and they become drug candidates for these infections. To find notable information for structure optimization, we calculated inter-fragment interaction energy (IFIE) of their complexes by fragment molecular orbital (FMO) method and analyzed the strength of the correlation by comparing it with the experimental data. If the correlation is fine in the system, IFIE is a major parameter of the modification to develop more potent inhibitor. In our study, twelve crystal structures of the FimH and mannose derivatives were used for FMO calculation. The complexes for calculation were prepared by MOE (CCG Inc.). One of the crystal water was included in the complexes. ABINIT-MP6.0+ software, MP2 levels, and 6-31 g(d) basis set were used for FMO calculation. Then we considered the correlation between IFIE and the enthalpy change of ligands. From the result of the calculations, correlation between IFIE of twelve complexes and their enthalpy change, ΔH was moderate (R=0.51). However, when we removed three outliers, the coefficient R was improved to 0.90. An excellent correlation between IFIE and the enthalpy changes was observed. The results suggested that IFIE is available for the prediction of ΔH in these systems. This work is a part of construction of the FMO-based drug discovery platform, using HPCI system. Computational resources of the K computer provided by the RIKEN Advanced Institute for Computational Science through the HPCI System Research project were also used in this research.