

The MYND domain of the ETO2 protein is a novel target for drugs aimed at treating sickle cell disease and related blood disorders. This study explored the application of automated quantitative structure-analysis relationship (QSAR) modeling, a machine learning application of *in-silico* drug discovery, to this target protein system using Schrödinger's AutoQSAR software. The protein target in this study currently has no known drug-like binders, allowing the assessment of conducting every stage of lead discovery *in-silico*. A training set was generated using a preliminary docking study, from which QSAR models were built and verified across varying data splitting ratios. The most favorable of these models was subject to further testing to assess overfitting and ligand-inclusion/exclusion dependency, and a test set of QSAR predictions was evaluated for accuracy. The use of AutoQSAR modeling for this system was found to be unsuccessful, likely associated with the lack of verified drug-like binders in the training set.