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Snyder-Robinson Syndrome: Rescuing the Disease-Causing Effect of G56S mutant by Small Molecule Binding[1] ZHE ZHANG, Clemson University, VIRGINIE MARTINY, DAVID LAGORCE, Université Paris Diderot, EMIL ALEXOV, Clemson University, MARIA MITEVA, Université Paris Diderot, CLEMSON UNIVERSITY TEAM, UNIVERSITÉ PARIS DIDEROT TEAM — Snyder-Robinson Syndrome (SRS) is an X-linked mental retardation disorder, which is caused by defects in a particular gene coding for the spermine synthase (SMS) protein. Among the missense mutations known to be disease-causing is the G56S, which is positioned at the interface of the SMS homo-dimer. Previous computational and experimental investigations have shown that G56S mutation destabilizes the homo-dimer and thus greatly reduces the SMS enzymatic activity. In this study, we explore the possibility of mitigating the effect of G56S mutation by binding small molecules to suitable pockets around the mutation site. It is done by combined efforts of molecular dynamics simulations and in silico screening. The binding of selected molecules was calculated to fully compensate the effect of the mutation and rescue the wild type dimer affinity.

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