Start my motor [neurons] again

Screening of prospective ingibitors for mutant SOD1 causing ALS

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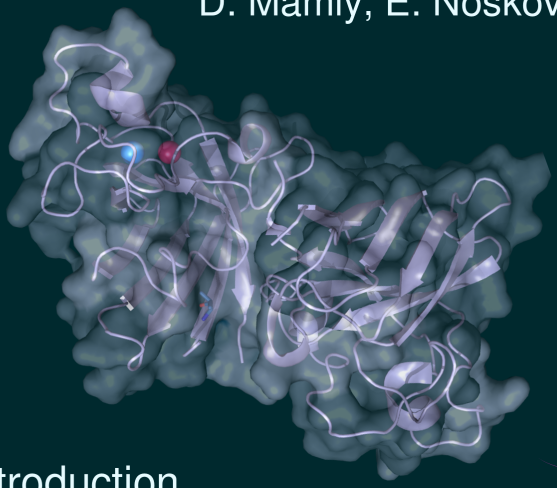
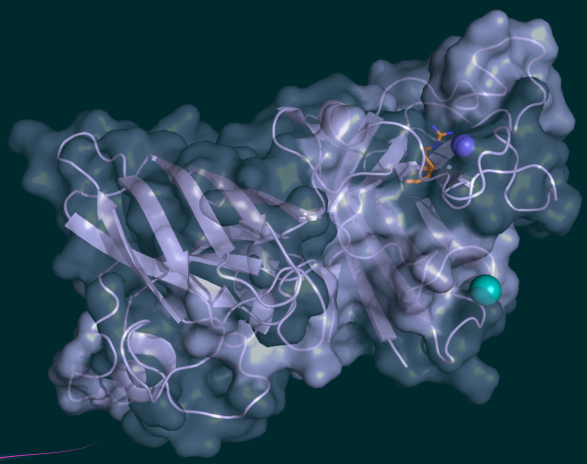
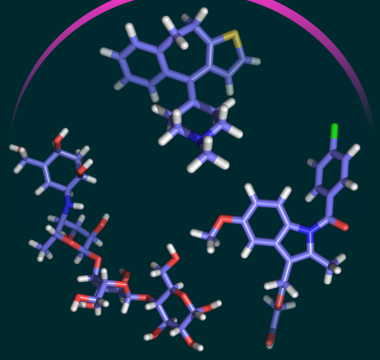




Screening

Introduction

Amyotrophic lateral sclerosis (ALS) is a group of fatal neurodegenerative diseases characterized by loss of motor neurons in the brain and spinal cord. We examined two mutations in superoxide dismutase 1 (SOD1) which lead to the accumulation of mutated proteins and cause various types of cell damage. A4V is the most common ALS-causing mutation in the US, so as H46R in Japan. Experiments on knockout mice show that toxicity of the neurons that contain mutant SOD1 is derived from an aberrantly acquired toxic function, rather than from the loss of protein function. We therefore screened 40,000 molecules to find the best inhibitor candidates.

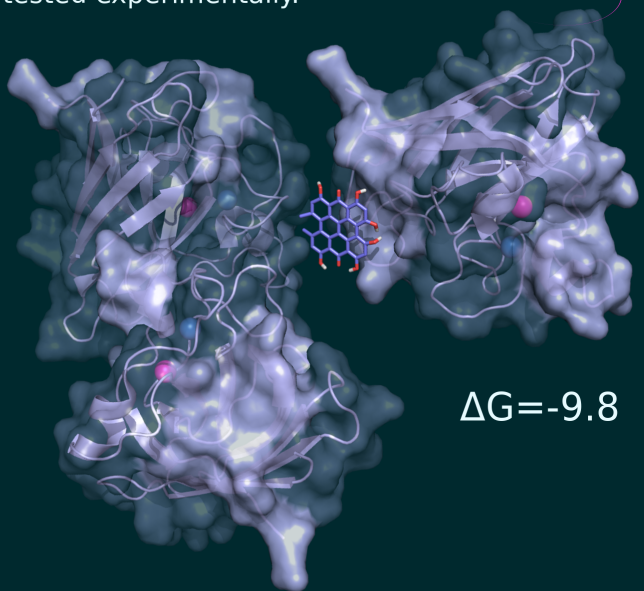


4×10^4

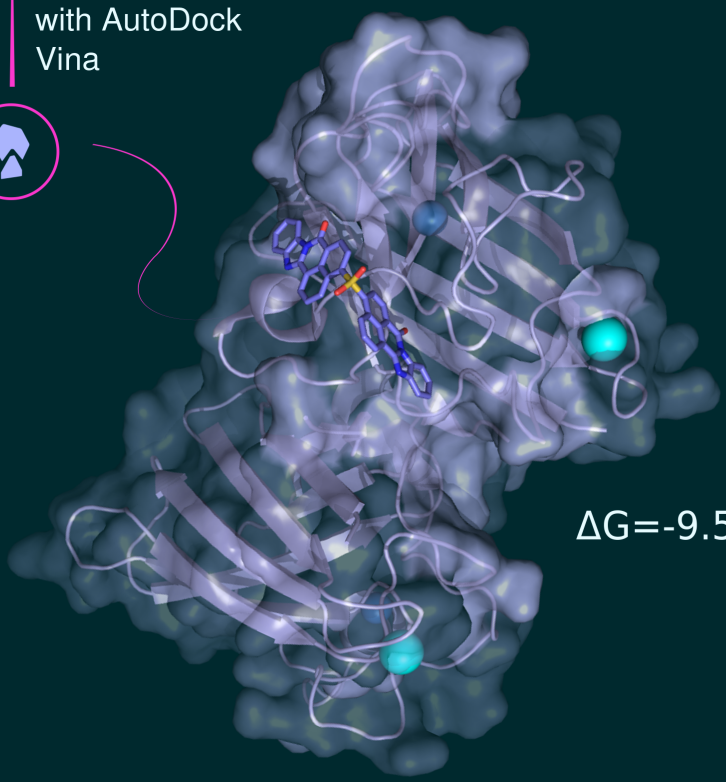
Docking into selected area with AutoDock Vina

Result

Compounds of interest can be obtained for free via the Developmental Therapeutics Program from National Cancer Institute to be tested experimentally.
Potent compounds can be obtained for free via the Developmental Therapeutics Program from National Cancer Institute to be tested experimentally.



ΔG=-9.8



ΔG=-9.5

hhmi SMTB ZIMIN FOUNDATION