Testing pharmacophore-based small molecules for stabilizing GBE-Y329S

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We have designed a peptide which stabilizes the GBE1 Y329S mutant and partially rescues its function in APBD patient-derived cells (Froese *et al* (2015) Hum Mol Genet 24:5667). While the peptide itself is a drug candidate, developing it would require funds sufficient for FDA approval. Therefore, we aimed at testing whether any FDA-approved drugs can serve as structural analogs of the peptide as a GBE1-Y329S stabilizer. Success in this project will lead to a significant reduction in the time and costs of reaching the patient.

We used the 3D binding pattern of the LTKE peptide model to define a pharmacophore. The molecule database was then screened using the pharmacophore. Passing molecules were docked to GBE-Y329S and analyzed by computational chemistry. 28 successful docked molecules are being screened for their effect on GBE activity.