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Peter G. Pentchev Fellowship Update 10.01.18

Lay Summary:

Niemann-Pick disease type C (NPC) is most commonly caused by mutations in NPC1. Frequently, these mutations cause NPC1 protein to be prematurely targeted for degradation and methodologies to increase levels of functional NPC1 would be therapeutic for individuals with NPC. The E3 ligase, C-terminus of HSC70-interacting protein (CHIP) has been implicated in targeting NPC1 for degradation. Here, we utilized our positive hits from a screen of small drug-like compounds to derive a small molecule that inhibits CHIP's ability to target NPC1 for destruction. We demonstrate this small molecule selectively inhibits CHIP, and in cell-based assays using I1061T patient-derived cells treated with our inhibitor we were able to significantly improve steady-state levels of NPC1 protein.