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Peter G. Pentchev Fellowship Update 04.01.18

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 have designed a high-throughput screen for small molecules that block CHIP's ability to target NPC1 for destruction. We have found several lead compounds that have demonstrated an ability to inhibit CHIP, and in cell based assays using I1061T patient-derived cells treated with a small molecule CHIP inhibitor we were able to significantly improve steady-state levels of NPC1 protein.