CDKL5 Program of Excellence
2018 Pilot Grant Program

Project Title: "Development of Targeted Frameshifting Technologies"

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Genome editing technologies have the potential to repair the mutations that cause genetic disease. Although a significant number of genetic diseases arise from the insertion or deletion of a small number of DNA base pairs that result in frameshift mutations within genes, current methods to correct small insertions or deletions are inefficient, are limited to cells that are actively dividing, and typically result in an excess of unwanted stochastic insertions or deletions at the target site that inactivate, rather than repair, the target gene or regulatory sequence. We propose to develop an entirely new class of genome editing technology that will enable the efficient site-specific correction of small insertion or deletion mutations, including mutations that can give rise to CDKL5 Deficiency Disorder (CDD). To do so, we propose to engineer and evolve a targetable molecular machine that site-specifically inserts individual nucleotides into genomic DNA at a target site, enabling the correction of different frameshift mutations that can cause CDD and numerous other genetic diseases.