CDKL5 Program of Excellence
2025 Pilot Grant Program

Project Title: "Regulation of CDKL5 Function by Type I Interferons"

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CDKL5 is essential for brain health. Mutations in the CDKL5 gene that stop it from working properly cause a severe brain disorder in children called CDKL5 deficiency disorder (CDD). People with CDD struggle with talking, walking, and frequent seizures that don't respond well to treatment. A cure remains elusive partly because scientists still don't fully understand how CDKL5 is controlled inside cells. Our research looks at how CDKL5 helps the body fight viral infections including infections of the brain. We found that immune responses influence CDKL5 levels and activity in cells. When CDKL5 is missing, brain cells are more likely to die from viral infections. Interestingly, virus-infected cells produce more CDKL5 and increase its activity. We believe this happens due to type I interferons, which are special proteins that cells release when they detect a virus. These interferons trigger a chain reaction that turns on immunerelated genes to fight infection. By analyzing large gene databases, we discovered that type I interferons significantly boost CDKL5 levels in many cell types. Another similar protein, CDKL1, also increased, suggesting other CDKL family proteins might be affected too. This is significant because, until now, very little is known about how CDKL5 is controlled. We aim to identify which type I interferons increase CDKL5 and other CDKL levels and how they affect CDKL5's location inside cells. Our evidence suggests interferons not only raise CDKL5 levels but also activate it. We are now additionally investigating how type I interferons regulate CDKL5's activity in cells.