Presynaptic biogenic amine transporters mediate reuptake of released amines from the synapse, thus regulating serotonin, dopamine and norepinephrine neurotransmission. Medications utilized in the treatment of depression, attention deficit-hyperactivity disorder and other psychiatric disorders possess high affinity for amine transporters. In addition, amine transporters are targets for psychostimulants. Altered expression of biogenic amine transporters has long been implicated in several psychiatric and neurodegenerative disorders. Therefore, appropriate regulation and maintenance of biogenic amine transporter activity is critical for normal amine homoeostasis. I will present our efforts to understand (1) how cellular protein kinases and phosphatases regulate serotonin transporter expression, activity, trafficking and degradation, (2) how transporter phosphorylation regulates amine clearance, (3) how transporter phosphorylation is dysregulated in human disease and (4) our translational approach from in vitro, ex vivo to in vivo animal model to understand the role of transporter phosphorylation in aminergic neurotransmission and in human disease. We believe that understanding the molecular mechanisms by which phosphorylation events affect amine transporter activity is essential for understanding the contribution of transporter phosphorylation to the regulation of monoamine neurotransmission and for identifying potential new targets for the treatment of various brain diseases.