Anxiety disorders are the most prevalent mental illness in the US. The overarching scientific purpose of this project is to determine biological mechanisms involved in pathological fear/anxiety. We have previously shown that when the neurotransmitter serotonin is depleted in rodents, there is a significant increase in their fear learning. This behavioral phenomenon occurs with an increase in specific glutamate receptors expression. The objectives of this project are (1) to determine the subtype of serotonin receptor that is involved in pathological fear and (2) to determine the functional significance of increased glutamate receptor expression. To accomplish these aims, we will employ an innovative combination of in vitro and in vivo techniques that couple behavior with cellular and molecular experiments. We will determine the specific serotonin receptor subtype involved by comparing fear behavior in vivo in serotonin depleted and control rats, in the presence of receptor selective agonists and antagonists. We will determine the functional significance of the increased glutamate receptors by performing in vitro electrophysiological recordings in brain slices from serotonin depleted and control rats. Together, this combination of approaches will allow us to make significant advances in understanding the neural underpinnings of complex behavior in a translational model of anxiety disorders.

We expect this project to have a significant positive impact in the following ways: (1) these data will make a significant contribution toward improving the feasibility of forthcoming major external grant applications, (2) this award and future external applications will provide opportunities for Baylor undergraduate students to be involved in meritorious scientific research, (3) we will gain important new information about the neurobiological mechanisms that convert serotonin depletion into increased GluA1 expression and increased fear behavior, which may in turn lead to (4) improved treatments, prevention or recovery from anxiety disorders.