The focus of this talk is on connecting functional loci to complex behaviors and intermediate phenotypes as they relate to addictions. The gold standard of gene discovery is not just replication of findings in general but starting out with genome-wide scans and then replicating identified functional loci in subsequent studies. Addictions are moderately to highly heritable. Part of this inheritance are intermediate phenotypes such as frontal-cortical functioning, behavioral inhibition, drug metabolism, drug tolerance reward, stress response, and craving. Research findings show that anxiety and life stress contribute to the initiation and maintenance of drug additions. On the other hand, serotonin transporter alleles are associated with anxiety and stress responses.

Research has shown that the genome-wide locus for an alcoholism/anxiety disorders genes is associated with a low voltage alpha-EEG trait. In particular, serotonin transporter alleles have been found to be associated with stress and cingulate-amygdala interactions. However, COMT and serotonin transporter alleles have additive effects on the interaction between stress and amygdala. It has been shown that pain responses are modulated by emotional factors and opioid receptor binding. More specifically, Met/Met individuals have lower opioid system activation in ventral pallidium and amygdala compared to Met/Val and Val/Val individuals rendering those individuals susceptible to pain and drug abuse. In addition, GCH1 pain and stress gene has been found to be relevant to addictions. Thus, a number of functional loci have been identified that affect intermediate phenotypes and lead to addictions.