Stephen Rayport, GLS1 as a Novel Therapeutic Target for the Pharmacotherapy of Schizophrenia

With a 2009 RISE award, Stephen Rayport and colleagues Scott Small, Joanne Macdonald, Donald Landry, and Hadassah Tamir sought to test glutaminase (encoded by gene GLS1) inhibition for the pharmacotherapy of schizophrenia. Based on the finding that mice heterozygous for GLS1 evince a schizophrenia-resilience profile, the principal aim of the project was to conduct a high-throughput screen for glutaminase inhibitors. When the screen proved unsuccessful (as the two drug candidates identified were not confirmed in subsequent assays), further effort was devoted to testing a genetic pharmacotherapy strategy to induce a reduction in glutaminase expression. This demonstrated that glutaminase inhibition induced in adulthood attenuated amphetamine-induced hyper locomotion, a key dimension of the schizophrenia-resilience phenotype, providing further impetus for developing glutaminase inhibitors for the pharmacotherapy of schizophrenia.