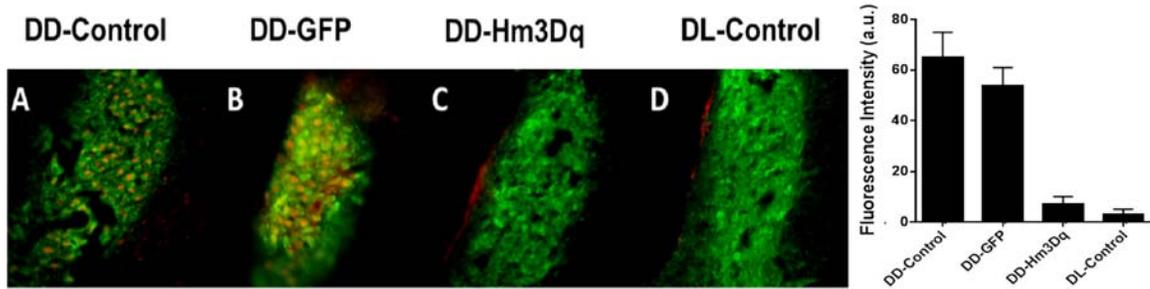
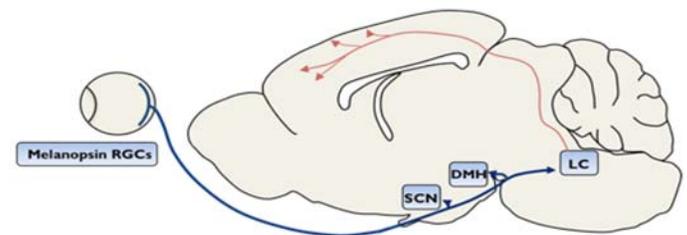


**A Novel Composition & Method for Treating Neuropsychiatric Disorders**



**Gary Aston-Jones, Ph.D.**, Murray and Charlotte Strongwater Endowed Chair in Neuroscience and Brain Health and the Director of the Brain Health Institute, Rutgers Biomedical and Health Sciences, Rutgers University. His research focuses on the modulation of reward behavior, addiction and cognitive functions by ascending brain monoamine and peptide systems, and uses neurophysiology, neuroanatomy and behavioral neuropharmacology in animal studies.

**Title image:** DREADD-mediated activation of retinal cells in constant darkness prevents apoptosis in locus coeruleus



**Above image:** Schematic of the pathway associated with the photic regulation of neuropsychiatric disorders – increased activity of LC neurons during treatment with CNO eyedrops.



**Co-Inventor:** Hannah Bowrey, PhD joined the Aston-Jones lab in 2014. She is an expert in retinal biology and function, as well as locus coeruleus anatomy and behavior.

**Intellectual Property:** PCT application SN: PCT/US2017/49629

**Innovation Summary:** Researchers at the Rutgers Brain Health Institute have developed a retinal-targeted gene therapy treatment for neuropsychiatric disorders including depression. The therapy leverages Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) by transducing retinal ganglion cells with the DNA that codes for these specific receptors. Once modified, these cells can then be activated by drugs administered via eyedrops. When activated, these cells impact the brain’s natural circadian rhythm pathway. Modulations of this pathway by this method have been shown to reduce the symptoms of depression in animal models.

Current neuropsychiatric treatments incorporating DREADDS require invasive brain surgery and systemic delivery of drugs. This proposed technique will only require a single intravitreal injection into each eye. This type of procedure is currently administered millions of times per year for the treatment of diseases such as age-related macular degeneration, and carries far fewer surgical risks than brain surgery. After the injection procedure, patients will be able to activate the new receptors via ligand (commonly clozapine-N-Oxide [CNO]) containing eyedrops.

**Advantages:**

- Does not require an invasive operation through the skull like traditional DREADD treatments for neuropsychiatric disorders
- Successful transfection rates will allow for a single injection per eye for the life of each patient
- Possible treatment for multiple neuropsychiatric disorders
- CNO dosing isolated to the eye prevents systemic exposure and side-effects as compared with current depression drugs

**Market Applications:** Potential treatment for neuropsychiatric disorders such as depression, Schizophrenia and bipolar-disorders. May have efficacy for patient with neuropsychiatric disorders not well controlled by current medications or alternative therapies. May be a supportive or alternative therapy to long-acting injectable (LAI) medications.

**Potential Social and Economic Impact:**

- # of Adult US patients effected by neuropsychiatric disorders:
  - Schizophrenia 2.2 million
  - Bipolar disorder nearly 6 million
  - Major depressive disorder 4.8 million and has a lifetime prevalence of 20-26% for women and 8-12% for men
- US 2015 market sales for major depressive disorder reached \$2.4 billion and is projected to reach \$4.6 billion by 2025
- This treatment could have a profound benefit for those who do not tolerate current pharmaceutical treatments

**Next R&D Steps:**

- Expand animal testing to primate models to verify the potential clinical efficacy for treatment of depression and/or other specific neuropsychiatric disorders
- Engage with an outside partner to identify a regulatory approval pathway and necessary pre-clinical data
- Complete necessary pre-clinical testing for preparation of human clinical trial application