"In 2017 the acting secretary of the Department of Health and Human Services declared the opioid crisis as a nationwide public health emergency. Recently, it was brought to my attention by Ron Sokol that a flurry of RFAs will be coming out shortly from NIDA and SAMHSA (some have already been issued) regarding pain control and the NIH HEAL initiative (see https://www.nih.gov/research-training/medical-research-initiatives/heal-initiative/funding-announcements-opportunities ). This area of science and medicine requires insight from genetics to cellular and structural biology, pharmacology, epidemiology, clinical trials and implementation reflecting efficacy and effectiveness. We need to be poised as a campus to respond. The article I bring to your attention from the Neurosciences Group in Geneva points to the mesolimbic dopamine system as an important area of emphasis for further study of addictive behavior – enjoy."

https://www.nature.com/articles/s41586-018-0789-4

**Stochastic synaptic plasticity underlying compulsion in a model of addiction**

Vincent Pascoli1, Agnès Hiver1, Ruud Van Zessen1, Michael Loureiro1, Ridouane Achargui1, Masaya Harada1, Jérôme Flakowski1 & Christian Lüscher1,2*

Activation of the mesolimbic dopamine system reinforces goal-directed behaviours. With repetitive stimulation—for example, by chronic drug abuse—the reinforcement may become compulsive and intake continues even in the face of major negative consequences. Here we gave mice the opportunity to optogenetically self-stimulate dopaminergic neurons and observed that only a fraction of mice persevered if they had to endure an electric shock. Compulsive lever pressing was associated with an activity peak in the projection terminals from the orbitofrontal cortex (OFC) to the dorsal striatum. Although brief inhibition of OFC neurons temporarily relieved compulsive reinforcement, we found that transmission from the OFC to the striatum was permanently potentiated in persevering mice. To establish causality, we potentiated these synapses in vivo in mice that stopped optogenetic self-stimulation of dopamine neurons because of punishment; this led to compulsive lever pressing, whereas de potentiation in persevering mice had the converse effect. In summary, synaptic potentiation of transmission from the OFC to the dorsal striatum drives compulsive reinforcement, a defining symptom of addiction.

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**Research Corner**

Dr. Sean Colgan currently holds the Joel Levine-Fred Kern, Jr Endowed Professor of Medicine and Immunology at the University of Colorado. After receiving his Ph.D. in Experimental Pathology at Colorado State University, Dr. Colgan completed a postdoctoral fellowship at Harvard Medical School. He then joined the faculty of Harvard Medical School as one of the founding members of the Center for Experimental Therapeutics. Dr. Colgan was promoted to Professor at Harvard Medical School and in 2006, he was recruited to CU within the GI Division where he founded and currently directs the Mucosal Inflammation Program (MIP), an interdisciplinary research program aimed at identifying molecular targets of disease pathogenesis within the mucosa. He currently holds multiple NIH grants, including an NIH R37 MERIT award. He has published more than 200 papers and trained more than 40 scientists currently on faculty throughout the world.
Research in the Colgan Lab spans all areas of mucosal immunology, with a focus on innate immunity. Their primary interests have evolved toward a basic understanding of the metabolism of mucosal inflammation, particularly related to the inflammatory bowel diseases (IBD). Their interest in immunometabolism stems from work nearly a decade ago that identified a prominent role for the tissue microenvironment in promoting the resolution of inflammation in the colon. This work has lead to the observation that localized oxygen depletion (hypoxia) serves as a pro-resolution signal to the tissue through the activation of transcriptional machinery. Genes induced by these pathways include those that dampen inflammation and promote rapid wound healing. Through the use of molecular and animal models, the Colgan laboratory is translating these findings into human patients. Ongoing studies targeting these pathways hold hope in developing novel therapeutic approaches to the treatment of human IBD and related inflammatory disorders.

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**2019 Boettcher Foundation Webb-Waring Biomedical Research Awards**

**ANNOUNCEMENT**

- The Boettcher Foundation will provide up to five grants of $235,000 each covering up to three years of research activity for promising and talented early-career investigators at CU
- Awardees will carry the prestigious title of “Boettcher Investigator”
- Eligible faculty researchers from all four CU campuses are encouraged to apply

**PURPOSE**
The program is designed to support research that has a direct impact on human health.

- The biomedical research supported pursuant to this grant program will be designed to find ways to prevent disease and improve human health through basic and applied biomedical research
- The intent of the program is to fund meritorious research that has the potential for new discoveries or advances a discovery to the proof of its potential value as an application to improve human health
- This research will help improve the understanding, treatment and prevention of human disease

**ELIGIBILITY**
For purposes of this program, an eligible early-career investigator (ECI):

- Is within four years of appointment to his/her career-track academic position (i.e., whose career-track appointments began no earlier than January 1, 2014);
- Has not previously received a major independent research award;
- Has received a terminal degree or completed his/her medical residency within the 10 years preceding the application (i.e., on or after January 1, 2008); and
- Is either a U.S. Citizen or a Permanent Resident.

For more details, go to: [http://www.cu.edu/bfww/eligibility](http://www.cu.edu/bfww/eligibility)

**PRE-SUBMISSION WEBINAR**
Potential applicants can get more information about the award program, the application and selection process and participate in a Q&A with the chair and vice chair of the 2019 selection panel. The session will cover the purpose of the program, how to apply, the selection criteria and learn more about what the panel is looking for and tips for submitting proposals. To register, click [here](https://www.cu.edu/doc/bfww-applicantinstructions-cu-denver-amc.pdf).

**TIMELINES**
Applications must be submitted to your Grants office for review no later than 5:00 pm, February 8, 2019. Final Applications must be submitted to your Grants office no later than 5:00 pm, February 26, 2019.

- Awards will be announced in May 2019.
- Awards will support work beginning June 1, 2019.

FOR MORE INFORMATION, GO TO: [https://www.cu.edu/doc/bfww-applicantinstructions-cu-denver-amc.pdf](https://www.cu.edu/doc/bfww-applicantinstructions-cu-denver-amc.pdf)

Please do not contact the Boettcher Foundation directly.