On my most recent birthday, a card from my student read “Nancy: Dreamer, Scientist and Mentor”. It meant that the hard work and sleepless nights had been worth it. I had been overwhelmed five months earlier with conflicts amongst my mentees that constantly interrupted my research, largely because I had little experience leading research teams. Each of them had tremendous potential and passion for science, yet we struggled. For example, two of my students, were struggling to work together because they perceived body language differently based on their cultural backgrounds. To improve our communication, I implemented weekly meetings and established an open and democratic culture. I learned to identify our values and strengths, and aligned them to our scientific goals. We turned the team into a productive and happy scientific family. Moreover, it was wonderful to experience how our diverse backgrounds strengthened our science. As my student wrote in the card, my life has been a journey of becoming a dreamer, a scientist and most recently a mentor.

The Dreamer: I value creativity in science as much as I value rigor. I find inspiration for experiments in the most uncommon places, from people watching to my own dreams. Coming from a family of musicians, music drove me to neuroscience. As a child, I wondered how music triggered emotions and why some sounds were noise but others melodies. Nowadays, as a scientist, my curiosity continues. I dream of creating a ‘neuro-biodome’, a place where experiments have no beginning nor an end by integrating neurotechnology to monitor neural activity and behavior 24/7. In addition, I use creativity to solve problems in my actual research. For example, I study social dominance and the established assays to study it lack the trial structure we need for statistical power and manipulations. Inspired by pushing boundaries, I designed a social dominance assay that has both trial structure and ethological validity.

The Scientist: Growing up, I never met a scientist and I did not know what a PhD was, so I started college with no clear path to satisfy my curiosity for the brain. Once I joined a neuroscience research lab I found intellectual satisfaction. As an undergrad, I completed a research project, from beginning to end, which resulted in two peer-reviewed publications. At Columbia University, where I pursued my PhD, I prioritized learning electrophysiology and novel techniques to manipulate neuronal activity to study the circuits underlying behaviors. I also published several papers and collaborated with other groups. I took quantitative classes to improve my scientific rigor, and presented my work and international conferences. Now, I am using electrophysiology and optogenetics to investigate how the brain controls social behaviors. My goal is to become a professor who conducts research that goes beyond existing paradigms and impacts society beyond the bench. For 7 years, I taught neuroscience and organized science fairs for underprivileged students. Recently, I started a project that increases visibility of women neuroscientists by creating online profiles that highlight their scientific contributions.

The Mentor: I had mentors who taught me that science *can* transform lives and society. Certainly, science transformed my life and created opportunities for me. I now aim to pay it forward by mentoring others. I am still learning how to best teach, mentor and instill scientific purpose in my trainees. My journey of mentoring and leading younger scientists has only begun, but my commitment is deep and drives me to become a better scientist every day. During graduate school, I also became aware of the hurdles I would continue to face as a women and minority in a STEM field, which drives me to work even harder and be a better role model. As a Ford Fellow, I will continue doing creative and impactful science, increasing diversity in academia, and creating opportunities for the next generation of neuroscientists.

As a neuroscientist, I seek to elucidate how the brain executes behaviors that come naturally to us, such as avoiding danger, seeking pleasure or social attention. My scientific training has prepared me to investigate the neurobiological basis of innate behaviors in animal models.

I started college with a strong interest in understanding the neural basis of emotion. In Dr. Gregory Quirk's Lab, I learned the basics of using behavioral paradigms to study emotion in rats. Specifically, I used fear conditioning paradigms, wherein a tone is associated with a shock, and neuropharmacology to further our understanding of how the amygdala, the medial prefrontal cortex (mPFC) and the mediodorsal thalamus contribute to fear learning and expression. This work resulted in two peer-reviewed articles, one of which has over 500 citations. Besides learning the fundamentals of behavioral neuroscience, I also learned that not all emotions all learned. This realization drove me to study the neural basis of avoidance behavior, an innate behavior that comes naturally to all animals.

For my doctoral thesis, I joined the laboratory of Dr. Joshua Gordon at Columbia University. There, I learned to assay mouse behavior and functional connectivity using electophysiology. Specifically, I studied how the ventral hippocampal input to the mPFC (vHPC-mPFC) encodes anxiety-like behavior in mice. I performed simultaneous electrophysiological recordings in the vHPC and the mPFC, and used optogenetics to manipulate activity in this pathway during behavior. Optogenetics is a technique that allows controlling neuronal activity by expressing genetically modified proteins that are light sensitive and thus render the neuron light sensitive. My work demonstrated that optogenetically inhibiting the vHPC-mPFC circuit disrupted both avoidance behavior and the prefrontal cortex neural representations of aversion. Moreover, it reduced theta (4-12 Hz) synchrony between vHPC and mPFC, in a

pathway-, frequency- and task-specific manner. These results revealed a specific role for the vHPC-mPFC projection in anxiety-related behavior and its neural representation. This was published in 2016 in a high impact journal. Next, I investigated whether optogenetic stimulation of the vHPC-mPFC at a theta frequency, 8 Hz, was sufficient to increase avoidance behavior. I optogenetically activated vHPC terminals in the mPFC using in an oscillatory light stimulus, to mimic the synchronous oscillations observed during anxiety in this pathway. Oscillatory terminal activation at 8 Hz was sufficient to increase avoidance behavior. Electrophysiological experiments demonstrated that our 8 Hz terminal activation enhanced vHPC-mPFC neurotransmission more than other frequencies and stimuli patterns. Finally, 8 Hz oscillatory stimulation of vHPC terminals entrained neural activity in the entire vHPC-mPFC network during exposure to an anxiogenic environment. In collaboration with my postdoctoral advisor, Dr. Kay Tye, we have expanded this study and submitted it for publication. These findings, combined with my prior results collectively demonstrate bidirectional effects of optically manipulating the vHPC-mPFC circuit, and point to a privileged role for theta-frequency activity in sustaining information transfer within this circuit.

During graduate school, I collaborated with several groups. Together with Dr. Christoph Kellendonk's group, we used *in vivo* electrophysiology and optogenetics to study how mPFC parvalbumin interneurons contribute to anxiety-like behavior and working memory deficits seen in adult mice with prenatal immune activation. This work was published in 2016. Furthermore, in collaboration with Dr. Joshua Huang we targeted and characterized the poorly studied chandelier cells. In 2017, we published that these cells have precise microcircuitry in the mPFC by innervating preferentially pyramidal cells that project to the amygdala. Second,

there has been a long debate on whether chandelier cells are in fact inhibit or excite pyramidal cells, and I provided the first *in vivo* evidence that they are inhibitory *in vivo*.

In September 2016, I started my postdoctoral training in the laboratory of Dr. Kay Tye at the Massachusetts Institute of Technology. Our lab is now moving to the Salk Institute in March 2019 where I will continue investigating how the brain encodes social hierarchies under the mentorship of Dr. Kay Tye. My goal is to elucidate how the prefrontal cortex modulates social rank via downstream hypothalamic nuclei. My previous work studying the mPFC in the context of emotions, avoidance behavior, cognition, and its microcircuitry gives me an excellent scientific framework. Furthermore, my expertise in electrophysiology, optogenetics and mouse behavior provide me the tools I need to succeed in this project.

PUBLICATIONS:

1. Padilla-Coreano N., Canetta S., Garcia-Garcia A., Warren R., Teboul E., Blackman D., Morton M, Tye M. K., Kellendonk C., and Gordon J.A. (2018) Hippocampal-prefrontal theta transmission regulates anxiety-like behavior. *Neuron* (pending revisions).

2. C.M. Vander Weele, C.A. Siciliano, G.A. Matthews, P Nambury, E.M. Izadmehr, I.C. Espinel, E.H. Nieh, E.H.S. Schut, **N. Padilla-Coreano,** A. Burgos-Robles, C. Chang, E. Kimchi, A. Beyeler, R. Wichmann, C.P. Wildes, K.M. Tye. (2018) Dopamine enhances signap-to-noise ratio in cortical-brainstem encoding of aversive stimuli. *Nature*.

3. Jiangteng Lu*, Jason Tucciarone*, **Nancy Padilla-Coreano**, Miao He, Joshua A. Gordon, Z. Josh Huang. (2017) Selective inhibitory control of pyramidal neuron ensembles and cortical subnetworks by chandelier cells. *Nature Neuroscience*.

4. **Padilla-Coreano N**., Bolkan S., Pierce G., Blackman D., Spellman T. and Gordon J.A. (2016) Direct hippocampal-prefrontal input is required for anxiety-related neural activity and behavior. *Neuron*, 89, 857-866.

5. Canetta S., Bolkan S., **Padilla-Coreano N.**, Song L., Sahn R., Harrison N., Gordon J.A., Brown A. and Kellendonk C. (2016) Prenatal Maternal Immune Activation Leads to Selective Functional Deficits in Adult PV Interneurons. *Molecular Psychiatry*, 1-13

6. Padilla-Coreano N., Do Monte F.H. and Quirk G.J. (2012) A time-dependent role of midline thalamic nuclei in the retrieval of fear memory. *Neuropharmacology*, 62(1):457-63.

7. Sierra-Mercado D., **Padilla-Coreano N.** and Quirk G.J. (2011) Dissociable roles of prelimbic, Infralimbic, ventral hippocampal, and basolateral amygdala areas in fear expression and extinction memory. *Neuropsychopharmacology,* 36(2):529-38.

Anxiety is an adaptive state of increased apprehension that helps animals and humans avoid potential danger. However, inappropriate expression of anxiety can lead to psychiatric disorders. To improve anxiety disorder treatments, we must understand the neural circuits that support normal anxiety. Studies in rodents demonstrate that anxiety-like behavior involves the ventral hippocampus (vHPC) and medial prefrontal cortex (mPFC). However, these studies used problematic techniques, lesions and pharmacology, and they do not address the role of the connectivity between vHPC and mPFC. In order to examine the role of the direct vHPC-mPFC projection, I used multi-site neural recordings and optogenetic tools, which allow for precise, fast and reversible control of neural activity. Optogenetic inhibition of the vHPC axons in the mPFC disrupted avoidance behavior, demonstrating that the connectivity between vHPC-mPFC is necessary for avoidance behavior. In addition, inhibition of vHPC-mPFC disrupted single-cell neural activity patterns that indicate context aversion, and reduced theta (4-12 Hz) synchrony in a pathway and frequency specific manner. To understand the frequency specificity of the role of vHPC-mPFC in anxiety, we next stimulated optogenetically vHPC-mPFC at a theta frequency (8 Hz) during anxiety behaviors. Specifically, we stimulated vHPC terminals in mPFC using an oscillatory vs pulsatile light at different frequencies during an anxiety assay. Terminal stimulation at 8 Hz, but not 20 Hz, increased avoidance behavior when delivered in an oscillatory, but not a pulsatile manner. Electrophysiological recordings showed that oscillatory stimulation increased neural transmission of vHPC-mPFC and entrained neural activity throughout the vHPC-mPFC network. Altogether, my thesis work demonstrated that during avoidance behavior, theta-frequencies have a privileged role in facilitating communication in the vHPC-mPFC network and in generating avoidance behavior.

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Review of the neural and biological basis of social status in humans and other animals. Work in this review implicates the prefrontal cortex to social hierarchy.

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This paper demonstrates that social rank, as measured with the tube test, is predictive of the effects of stress in mice.

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This study demonstrates that dominant mice have more excitability in the medial prefrontal cortex than subordinate mice. A manipulation that increases excitability in the mPFC of subordinates increases their rank, thus showing causality of mPFC activity and social rank. Moreover, this study shows that the tube test social rank is correlated to several other assays of social dominance.

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This study uses optogenetics to show that subpopulations of the lateral hypothalamus promotes social interaction. This study was done in our laboratory and demonstrates proof of principal that we can perform optogenetic experiments in mice during social assays.

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This study from our laboratory demonstrates the 'phototagging' technique to identify projector populations using ChR2 expression. It serves as proof of principle that our experiments are feasible.

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This study is the first report to use the tube test to measure dominance behavior in mice.

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This study shows that dominant mice have higher plasma testosterone compared to subordinates and that this is important to gain social rank.