Chandler, Peggy

From:	Maren E. Imhoff [redacted]
Sent:	Wednesday, September 24, 2014 5:00 PM
To:	Debra Black
Cc:	Marc Tessier-Lavigne; Chandler, Peggy
Subject:	Re: CONFIDENTIAL: Greengard/Heintz OCD/Depression Project
Attachments:	Black Gift Agreement re OCD--DRAFT September 2014.doc; Black Payment Schedule re OCD --DRAFT September 2014.doc; Black Proposal and Budget re OCD Sept 2014.docx; mtl.black.memo9.24.pdf

Dear Debra:

I hope you have been enjoying these beautiful fall days. As promised, I am pleased to forward to you the memorandum that Marc has written that you asked for when we last spoke.

We look forward to seeing you at the Board meeting on Wednesday, October 15th. Until then, this comes with best wishes and warm regards,

Marnie

From: Maren E. Imhoff
Sent: Monday, September 8, 2014 5:38 PM
To: [redacted]
Cc: Chandler, Peggy [redacted]
Subject: Re: Draft Gift Agreement for Greengard/Heintz OCD/Depression Project

Dear Debra:

As promised, I am sending you an agreement for the OCD/Depression initiative for your review.

I am happy to work with your attorney/advisor on this and help in any way.

With very best regards,

Marnie

DRAFT

THE ROCKEFELLER UNIVERSITY

GIFT AGREEMENT

We, Debra and Leon Black (the "Donors"), do hereby pledge a gift of ten million dollars ($10,000,000) to The Rockefeller University (the "University"), upon the following terms and conditions:

1. This gift will be used to support research on Obsessive-Compulsive Disorder (OCD) and depression conducted at the University by Professor Paul Greengard, head of the Laboratory of Molecular and Cellular Neuroscience, and Professor Nathaniel Heintz, head of the Laboratory of Molecular Biology. These funds are specifically directed toward a new research initiative to apply the most modern molecular and genetic approaches available to development of new therapeutic strategies for the treatment of OCD and depression, as described in the proposal entitled "Toward Development of New Treatments for Obsessive-Compulsive and Comorbid Disorders", dated September 2014 (Attachment A).

2. This contribution of $10 million shall be fulfilled over a five-year period, in accordance with Schedule A (attached). Payment will commence during fiscal year 2015 (defined as July 1, 2014 through June 30, 2015).

3. We may at any time, and at our sole discretion, accelerate payment of the above-referenced funds. Should we predecease fulfillment of this pledge, we have made contingency provisions, through our wills, such that the fulfillment of this pledge will be binding upon our estates.

IN WITNESS WHEREOF, we have executed this Gift Agreement this 1 day of October, 2014.

By: Debra F Black

DEBRA BLACK

By: [signature]

LEON BLACK

ELIZABETH IRENE
Notary Public - State of New York
No. 01IR6224637
Qualified in New York County
My Commission Expires ~~July 6, 2014~~ Sept 4, 2018

The agreement is hereby accepted upon the terms and conditions set forth above.

THE ROCKEFELLER UNIVERSITY

By: _____

MARC TESSIER-LAVIGNE
PRESIDENT

SCIENTIA · PRO · BONO · HUMANI · GENERIS
The Rockefeller University
1901

The Rockefeller University
1901
SCIENCE FOR THE BENEFIT OF HUMANITY

Marc Tessier-Lavigne, Ph.D.
President
Carson Family Professor
p: 212-327-8080
f: 212-327-8900
e: marctl@rockefeller.edu

Confidential

MEMORANDUM OF UNDERSTANDING

To: Debra and Leon Black

From: Marc Tessier-Lavigne
President

Date: September 24, 2014

Subject: **New Research Initiative in OCD/Depression at The Rockefeller University**

Dear Debra and Leon:

The Rockefeller University is deeply grateful for your generous commitment to the new research initiative in Obsessive Compulsive Disorder and Depression being launched by Professors Paul Greengard and Nat Heintz. As agreed, this is a five year project, and I wanted to address our plans for the robust continuity and completion of this project should Paul Greengard cease to lead a Rockefeller laboratory either through death, retirement, or an incapacitating event at any point during the time period of the grant. First, I should note that Paul Greengard is healthy now and has one of the most productive laboratories, not only at Rockefeller, but in the world today. The new discoveries he has made in recent years have been published in the very top scientific journals, and Paul still give lectures on his work around the world.

Nonetheless, I want to state in this Memorandum how we would proceed if Paul were to cease leading an RU laboratory at any time during the grant period. First of all, Paul and Nat have collaborated on research projects for over a decade. Nat is an outstanding scientist who is highly recognized in the community, and would be fully capable of carrying on this project by himself, with the personnel and the resources in his laboratory. Moreover, when a tenured professor passes away, his or her laboratory does not shut down immediately. It usually takes several years for the members of the laboratory team to either migrate to other laboratories within Rockefeller or join new research groups at other institutions. Paul Greengard has seasoned scientists and superb postdoctoral fellows who could stay on for the duration of the project.

I can assure you that there would be no interruption, drift, or hiatus in such a case. Importantly, the intellectual leadership that both Paul and Nat provide could be carried on by Nat alone or by Paul alone. Paul and Nat have teamed up because they have developed a revolutionary technology that allows definition of all of the proteins expressed in any cell type or circuit (known as TRAP translational profiling). This technology has met with enormous success in the identification of novel therapeutic targets for a variety of CNS disorders—including Parkinson's disease, schizophrenia, and age-related cognitive decline—which have already led to clinical development programs within the pharmaceutical industry.

Nat would be entirely capable of completing this project and delivering the preclinical data that can be evaluated by potential pharma partners for the development of new drugs for OCD/Depression.

I hope this provides you with the reassurance you need to move forward with this promising initiative.

MT-L:mr

DRAFT

SCHEDULE A

Debra and Leon Black

Payment Schedule for Gift in Support of Research on Obsessive-Compulsive Disorder and Depression

Fiscal Year 2015 (payable on or before June 30, 2015)	$2,000,000
Fiscal Year 2016 (payable on or before June 30, 2016)	$2,000,000
Fiscal Year 2017 (payable on or before June 30, 2017)	$2,000,000
Fiscal Year 2018 (payable on or before June 30, 2018)	$2,000,000
Fiscal Year 2019 (payable on or before June 30, 2019)	$2,000,000
	$10,000,000

ATTACHMENT A

Toward Development of New Treatments for Obsessive-Compulsive and Comorbid Disorders

Molecular dissection of the cortico-striatal-thalamo-cortical (CSTC) circuits controlling obsessive compulsive, depressive, and anxious behaviors in mammals

September 2014

Paul Greengard, Ph.D., and Nathaniel Heintz, Ph.D.

Although the precise causes of obsessive-compulsive disorder (OCD) are still not known, a great deal of progress has been made over the last two decades in identifying brain circuits that are aberrant in this disorder. The consensus view that has emerged from functional imaging studies of OCD patients is that abnormal patterns of activity in circuits involving the cerebral cortex, the basal ganglia, and the thalamus are characteristic features of OCD. This conclusion has been supported by deep brain stimulation studies that, although quite variable, indicate that stimulation at several nodes in these circuits can have a positive therapeutic effect in OCD. Additional support for the CSTC model has come from recent rodent studies of OCD, where it has been demonstrated that artificial stimulation in CSTC pathways can elicit persistent OCD-like behaviors, and that cortico-striatal synaptic defects cause similarly aberrant behaviors.

Taken together, the available clinical and experimental data allow the conclusion that novel therapies that result in specific modulation of CSTC circuits should be developed, and that such therapies would have significantly increased efficacy and fewer side effects than current OCD therapies. Furthermore, one might reasonably infer that the generation of pharmacologies specific for different elements of this circuitry should result in effective therapies for even those OCD patients who are refractory to currently available treatments (e.g., Zoloft, Paxil, Anafranil, Prozac, etc.). While these studies of "core circuitry" and cell types altered in OCD are fundamental for progress in OCD treatment, it is clear that studies of the comorbidities associated with OCD (e.g. major depression (MD), anxiety disorders (AD)) will be required to fully understand and treat OCD.

It has become clear in recent years that brain areas implicated in OCD, MD and AD overlap substantially. However, little is known regarding the molecular disturbances that occur in the cell types and circuits affected in each case, and whether these molecular signatures predict common, complementary or combinatorial approaches to treatment. In the opinion of Drs. Greengard and Heintz, the most powerful approach toward investigation of OCD is to characterize the molecular properties of cell types comprising the CSTC circuits in mouse models of OCD, to expand these studies to include additional circuit elements implicated in comorbid disorders, and to perform detailed comparative analyses of the molecular phenotypes occurring in these cell types in the context of distinct but overlapping disorders.

The Heintz and Greengard laboratories at Rockefeller University are uniquely positioned to lead the effort to develop novel therapies for OCD. Dr. Greengard has had a longstanding interest in the striatum and other basal ganglion circuit elements (his 2000 Nobel Prize was awarded in part for his pioneering research in this area). Dr. Heintz has led modern efforts to define each of the cell types in the complex circuitry of the brain, and to accelerate studies (such as those mentioned above) to identify specific cell types

mediating complex behaviors in mammals. Their laboratories are presently engaged in state-of-the-art molecular and genetic studies of depression, autism spectrum disorders and drug addiction.

Over the last decade, the collaborative efforts of these laboratories have led to a revolutionary experimental technology that allows definition of all of the proteins expressed in any cell type or circuit (TRAP translational profiling). This methodology is the only available approach for comprehensive molecular characterization of brain-cell types, and for the identification of novel therapeutic targets that can be used to develop new treatments for complex central nervous system diseases and disorders. The TRAP profiling approach has been employed by the Greengard and Heintz laboratories for comparative analysis of nearly 100 CNS cell types, including many of those that comprise the CSTC circuitry relevant to OCD. These studies have resulted in identification of novel therapeutic targets for a variety of CNS disorders—including Parkinson's disease, schizophrenia, and age-related cognitive decline—that have already led to clinical development programs within the pharmaceutical industry.

To address the pathophysiological molecular mechanisms operant in OCD, MD, and AD and develop effective, new therapeutic strategies for their treatment, the Greengard/Heintz team propose a comprehensive program to:

1. define at the molecular level each of the cell types present in the CSTC and associated circuits
2. profile each of these cell types in select mouse models of OCD, MD and AD
3. identify specific pathways that are altered in key cell types in each disorder
4. employ advanced bioinformatics for comparative analysis of these pathways and formulation of testable hypotheses regarding circuit manipulations that would result in beneficial therapeutic effects for OCD, MD, and AD
5. identify cell-specific molecules whose activity could be pharmacologically targeted to compensate for the disturbances evident in CSTC and other cell types in OCD
6. test genetically the roles of these putative therapeutic targets in modulation of OCD-like behaviors in mice.

Completion of these studies will result in a complete package of preclinical data that can be evaluated by potential pharmaceutical partners for the development of new drugs for treatment of these related and debilitating disorders.

Although the objectives stated above are well within the unique capabilities of the Heintz/Greengard laboratories, they involve complex mouse molecular genetics, state-of-the-art and expensive high throughput sequencing methodology, and advanced comparative bioinformatics analysis of the large, complex datasets that will issue from the planned experimentation. Consequently, this initiative will require both a significant, long-term commitment from each of the laboratories and substantial financial support. Given these conditions, it is certain that this program will advance tremendously our knowledge of the molecular pathophysiology associated with OCD, MD and AD. We believe this new knowledge will provide a rational basis for development of new and more effective treatments for these difficult and debilitating conditions.

Budget Outline for Heintz and Greengard OCD/Depression/Anxiety Proposal

The revised budget on the following page reflects the intent of the Heintz and Greengard laboratories to establish a comprehensive program to apply the most modern molecular and genetic approaches available to development of new therapeutic strategies for the treatment of OCD, depression and anxiety. Expansion of the comprehensive OCD research program described in our original proposal to include the comorbid disorders depression and anxiety will require additional resources. It is important to note, however, that we are enthusiastic regarding inclusive studies of these conditions because this strategy will add intellectual depth to our analyses and reveal insights into molecular mechanisms of disease that cannot be obtained from studies of OCD alone. While this revision of our project will necessarily encompass additional brain circuits and cell types, these are overlapping with those affected in OCD and there is an economy of scale that will be achieved by concurrent studies of the disorders.

The technologies that will be employed within the program to define the relevant circuitry at the molecular level require preparation of specialized engineered mouse strains, sophisticated genetic and behavioral analysis, and an entire suite of molecular and bioinformatics techniques that are state-of-the-art and costly. The revised budget presented here outlines the combined costs that are required for the Heintz and Greengard laboratories to initiate these studies, to complete the molecular profiling experiments described in the proposal, and to identify target molecules that can serve as candidates for development of novel therapies for OCD, depression and anxiety (Aims 1-5 in the revised proposal). The preclinical studies required for validation of these new therapeutic targets (Aim 6) will be initiated but cannot be completed within the 5 year time frame presented herein.

Since the major driving forces for this program are both to pursue OCD, anxiety and depression from an advanced basic science perspective and to generate clinically relevant data that will lead to novel treatments, Drs. Greengard and Heintz are committed to creating a program that will in the future include the necessary translational research components required for therapeutic development.

Estimated Yearly Budget for Entire Program: $2,000,000

Projected Budget

Personnel	
4 Postdoctoral Associates	$260,000
4 Research Assistants: Molecular Biology	$180,000
2 Research Assistant: Animal Behavior	$80,000
2 Animal Technicians	$60,000
1.0 Bioinformatics Specialist	$65,000
Fringe Benefits @ 40%	$258,000
Materials and Supplies	
Anatomical Services (from Neuroscience Associates)	$40,000
BAC Modification Supplies	$25,500
General Lab Supplies	$30,500
General Molecular Biological Reagents	$35,000
RNAseq reagents	$38,500
Genotyping Supplies	$45,500
HTS Sequencing services	$365,000
Animal Costs	
Maintenance (Cage charges, CBC Charges, etc.)	$335,000
Purchase (includes surrogates for IVF)	$64,500
Cryopreservation	$32,500
In Vitro Fertilization (IVF) Services	$29,000
Computation	
IT Services (maintenance costs, backup services, etc.)	$44,000
Cloud Storage for HTS data	$12,000
Total Yearly Cost	**$2,000,000**