

2. PROGRAM PLAN

A. Background

Introduction:

This is an application for renewal of grant T32MH15144, "Research Training in Mood and Anxiety Disorders: From Animal Models to Patients", that has been funded continuously since 1978. The primary goal of this proposal is to train postdoctoral (MD, MD/PhD, and PhD) fellows for careers as independent researchers in Affective, Anxiety and Related Disorders. Achievement of that goal is measured by how many fellows are continuing in a research-intensive trajectory after graduation, whether supported by a K award, the primary method, or other major sources of funding. An intensive three-year program is outlined in which fellows will learn how to identify key research questions, formulate hypotheses, and design and execute experiments that effectively test those hypotheses. Fellows will acquire skills relevant to research methodology, including expertise in experimental design and statistical analysis relevant to basic, translational and clinical research programs. Comprehensive training in the Responsible Conduct of Research is essential and begins early in the fellowship; fellows must maintain the highest standards of scientific integrity and understand the ethical issues relevant to human and animal experimentation, and the institutional review board or the animal care and use review process. Graduating fellows will be able to present clearly a project in both written and oral form as evidenced by publications and presentations. Fellows also develop an understanding of the administrative organization of a successful research enterprise, collaborating effectively with other researchers, and how to write grants that are successful in being funded by NIH, private foundations, and other sources.

In the last submission of this T32, reviewed on 11/18/2013, the committee concluded: "The environment for training, including the faculty and institutional research and training infrastructure, is clearly outstanding. The program has been remarkably successful in recruiting and training fellows, virtually all of whom have been productive in publishing their work and have remained in academic careers. In addition, the great majority has obtained grant funding to launch their careers as independent investigators, and almost two-thirds of fellows are MDs or MD/PhDs – a particular strength of this program. Despite some minor weaknesses, this is an outstanding training program."

The success of the training program is reflected in both the accomplishments of the trainees and in the diversity of the fellows. In the past 15 years, 48 fellows have received stipend support from the T32; 44% female, 42% MDs, 25% MD/PhDs and 33% PhDs. Overall, 41% of fellows graduated from the Columbia Psychiatric Residency program, and the remaining 59% of fellows came from outside the residency. 13% of the fellows are under-represented minorities; diversity beyond this is reflected by the fact that 27% of the fellows come from cultural or ethnic backgrounds that are either not Caucasian or not from North America or Europe. The graduation rate of the fellowship is 97% over the last 15 years including the 2 current third year fellows who graduate 6/30/18 (the remaining 6 fellows are still in the program or will be appointed to the program in June; the one fellow who did not graduate left after 1 year in order to pursue a tenure-track research faculty position at the Johns Hopkins School of Medicine and received a K-23 award). Currently, there are 6 fellows: 2 third-year, 1 second-year, and 3 in the first year of training; two fellows have been accepted to begin in June 2018, making a total of 48 fellows that will have been supported by the T32 in the last 15 years. Of the 42 fellows who have graduated the program in the last 15 years, 69% have received K awards (one received the equivalent of an R01 in France, where he holds a tenured position and has established his own research laboratory after graduation from the fellowship). Of the 21 fellows who have finished their K awards, 71% have already received an R series award. All 4 minority fellows in the last 15 years graduated and all 4 received K awards (all were MD/PhDs – there are 2 URMs currently in training). Two of these URMs have also received individual R01s. 52% of fellows received significant foundation grants (20 NARSADs, 2 American Foundation for Suicide Prevention, 1 Robert Wood Johnson). Seven fellows who did not receive a K received a foundation grant (6 NARSADs, 1 AFSP) so in total 86% of graduates have received independent funding. Of the 42 graduates in the past 15 years, 76% are in research-intensive positions and 12% are in research-related positions.

The challenge is how to maintain the best of the training program and also update the T32 continuously in response to evaluations and to evolving research strategies, methodologies, and realities. In the last submission we described the initiation of a program to recruit to the Psychiatric Residency at Columbia MD/PhDs whose work is focused on psychiatric disorders. This program has prospered and provides a very strong pipeline of M.D./Ph.D. physician-scientists for the fellowship. Another development that supports this effort is the opening of a Jerome L. Greene Science Center at Columbia, which is the home base for the Zuckerman Mind Brain Behavior Institute and the Department of Neuroscience. Thus, the training and job opportunities after graduation for fellows are significantly increased. Other changes include 1) the addition of six new mentors who strengthen

both the basic science and translational opportunities for fellows, 2) the didactic program continues to be revised in response to fellows' evaluations and in order to provide a more targeted approach to teaching of statistics, and now includes a fellow's seminar which provides scientific oral presentation experience as well as interactive discussions, and 3) additions made to the program to teach the Responsible Conduct of Research.

A continued emphasis for our program is the recruitment of minorities and psychiatrists. There are initiatives in place at the level of the University, Medical Center, Department of Psychiatry and this T32 that represent a sustained and multifaceted approach to increase the recruitment of minorities. These initiatives are outlined in the section on **RECRUITMENT AND RETENTION PLAN TO ENHANCE DIVERSITY**.

Rationale: The mission of this T32 is to train future leaders in psychiatric research focused on mood, anxiety and related disorders. The vision for the training program is built on the belief that transformative discoveries impacting the diagnosis and treatment of psychiatric disorders will result from research that elucidates the development, function, and dysfunction of specific neural circuits involved in cognition, emotion and emotional regulation. The characterization of these neural circuits must span from molecular and genetic markers, to anatomical connectivity, to physiological functions of neurons at the individual and population levels, to the causal role of circuit elements in cognitive and emotional behavior that becomes dysfunctional in psychiatric disorders. Ultimately, this understanding must be applicable to clinical populations. The focus on these neural circuits thereby spans level of investigations, from *in vitro*, to *in vivo* in animals, and all the way to humans with and without psychiatric illness.

For many years, fellows in this training program were focused primarily on clinical research related to the phenomenology and treatment of affective, anxiety or eating disorders. As research has changed, the fellowship has evolved. During the competitive renewal 10 years ago, we recognized that major contributions to understanding psychiatric disorders and to developing treatments are likely to come from different types of investigators. One type of fellow might be described as a "Clinical Neuroscientist", usually a psychiatrist or Ph.D. with clinical training and some research experience, who primarily executed clinical and laboratory studies of humans. The other type of fellow we termed Translational Neuroscientist; typically, either M.D./Ph.D. psychiatrists or with a Ph.D. in neuroscience. Translational Neuroscientists focused on the understanding of neural mechanisms related to affective, anxiety and related disorders. Our experience in the last 10 years, is that the terms Clinical and Translational Neuroscientist are outdated, and now we consider all of our fellows to be Translational Neuroscientists. Essentially, all of them focus on some aspect of brain function directly relevant to psychiatric disorders, whether it is in humans, animals or a dish.

Need for the Research Training Program: There is compelling need to train researchers who can develop novel research programs leading to transformations in the treatment of psychiatric disorders. Meeting this goal requires training psychiatrists and scientists to thrive in a multidisciplinary research environment. The breadth of work requires training programs that encourage and nurture cooperative and collaborative efforts between mentors and fellows with different types of experimental backgrounds, with theoretical and computational neuroscientists whose expertise is required to understand increasingly complex and rich datasets, and with psychiatrists who provide indispensable knowledge of clinical disorders and phenomenology. Our fellows perform research in a variety of areas, including: a) the development of neural systems related to psychiatric disorders in both animal models and humans; b) basic mechanisms of synaptic transmission and neural plasticity, especially in brain structures relevant to psychiatric disorders; c) rodent and non-human primate models of cognitive and emotional functions, including models that exploit targeted genetic and anatomical manipulations to understand brain circuit function and dysfunction; d) brain mechanisms in normal human populations; and e) studies of brain mechanisms in clinical populations, as well as how treatments may modulate brain functions in alleviating symptoms. The belief is that innovative, multi-dimensional collaborative research will lead to new and more personalized treatment for the patients that suffer from psychiatric illness. Trainees performing translational neuroscience research at a variety of levels take courses that relate neural mechanisms to clinical disorders, and they interact with clinicians studying disorders in formal and informal settings.

The description of the fellowship experience of three fellows, Drs. Bernardi, Miller and Schneck illustrates how this program facilitates the development of fellows from varied backgrounds.

B. PROGRAM PLAN

a. Program Administration

Program Director - Steven P. Roose, M.D. (2.4 CM) Dr. Steven Roose has been the Program Director for the last 13 years. T32 programs that develop researchers in psychiatry have been a core part of his career. For the 24 years before becoming program director, Dr. Roose was the training director of this T32 and participated in the development of every aspect of the program including the conceptual focus, curriculum design, mentor selection, fellow selection and recruitment, evaluation of mentors and fellows, and preparation of competitive renewals and yearly progress reports. Dr. Roose has been deeply involved with the development and careers of research fellows at Columbia for the past 35 years and prior to that was himself one of the first fellows enrolled in this T32. Dr. Roose is responsible for all components of the T32. He undertakes the recruitment of applicants and guides them through the application process. He is responsible for monitoring the quality of mentor/fellow relationships and meets formally and informally with fellows, often on a weekly basis at certain critical times such as when beginning the fellowship, applying for a K award or planning a third year of training. He assesses the progress of fellows as well as their morale and career plans. He meets with each fellow and mentor to review the Career Development Plan that is filled out by the fellow at 3, 12 and 24 months. He oversees financial administration and the coordination of the fellowship with other research and clinical fellowships at Columbia. Dr. Roose no longer takes on any new fellows in this T32 so that he has no conflicts in the selection of fellows or in the evaluation of mentors. In addition to being program director for this fellowship, Dr. Roose has been the program director of another T32, "Research Training in Late-Life Neuropsychiatric Disorders", from its inception 20 years ago; this also requires 2.4 CM effort. The administration of the two fellowships has many similar duties but the faculty and fellows have almost no overlap. In summary, Dr. Roose now spends 4.8 CMs being the PI of two T32s, 1 CM as Co-Investigator for the Educational Core of the Conte Center: "Neurobiological and Developmental Antecedents to Suicidal Behavior", 3 CM as the Principal Investigator of a PCORI funded study; "Optimum Study – Optimizing Depression Treatment in Older Adults". His research focuses on the phenomenology, psychobiology and treatment of late-life depression with a specific concentration on the relationship between vascular disease and depression.

Training Director - C. Daniel Salzman, M.D., PH.D. (1.8 CM) Dr. Daniel Salzman assumed the role of training director 11 years ago, and this enhanced the training in translational neuroscience related to anxiety and affective disorders. Dr. Salzman received his M.D. and his Ph.D. in neuroscience from Stanford University, where he also completed his internship and residency in psychiatry. He and Eric Kandel are the only psychiatrists who maintain academic appointments in both the Department of Neuroscience and the Department of Psychiatry at Columbia University. Dr. Salzman was recruited to Columbia 17 years ago by Dr. Kandel in collaboration with the Department of Psychiatry to help strengthen Columbia's research and training programs in the neurobiology of brain systems involved in psychiatric disorders. Dr. Salzman maintains an active research program with NIMH support. His lab focuses on understanding the role of the amygdala, pre-frontal cortex, hippocampus and related brain structures in mediating reinforcement learning, emotion, emotional regulation, and social processing. He also has played an active role in training Ph.D. students in neuroscience, as well as in training postdoctoral fellows, both within his lab, and beyond. For example, 9 Ph.D. students have successfully graduated within the last 10 years from his lab. Students have had first author publications in high profile journals such as Nature, Nature Neuroscience, Neuron, and Cell. He maintains leadership roles in the Ph.D. program in Neuroscience at Columbia, serving on the steering and admissions committees. He has extensive background in the educational mission at Columbia, with a broad experience in teaching students and residents about the neuroscience of emotion and psychiatric disorders including: 1) courses in the Department of Biology geared towards advanced undergraduate and graduate students; 2) graduate seminar courses taught in the Department of Neuroscience on the Neural Basis of Neuropsychiatric Disorders, on Neuropsychopharmacology, and on Systems and Cognitive Neuroscience; 3) courses taught to residents in Psychiatry focused on the Neuroscience of Psychiatric Disorders; and 4) courses taught to fellows in Child Psychiatry. He also participates in interviewing MD/PhD applicants to Columbia's medical school. Within the Dept. of Psychiatry, he is the Director of the Leon Levy Fellowship program which selects and recruits MD/PhDs into the Psychiatry residency program. These clinician-scientists-in-training are a key part of the pipeline for future trainees in this T32 program. Finally, Dr. Salzman is very involved in helping build neuroscience at Columbia. He chairs the search committee for new faculty in the Dept. of Neuroscience, and he serves on a committee to develop programs that bridge basic neuroscience research conducted within Columbia's Zuckerman Mind Brain Behavior Institute and ongoing research in the Dept. of Psychiatry. Dr. Salzman oversees the didactic curriculum. He is responsible for the scheduling and

effective implementation of the courses on statistics, research design, and grant writing. He and Dr. Roose conduct evaluation of these courses, providing feedback to the instructors when needed. He also meets regularly with fellows, helping direct them to additional courses specific to their research training, such as seminars, journal clubs, and other courses offered within the Departments of Psychiatry and Neuroscience. Finally, Dr. Salzman participates on the Selection and Advisory committees and is very involved in trainee selection, recruitment and advising.

Administrative Structure: Drs. Roose and Salzman meet monthly to review every aspect of the T32. Dr. Roose is ultimately responsible for all program decisions, decisions that are invariably made after consultation with Dr. Salzman and with the members of the Selection and Advisory committees as needed.

The Advisory Committee, consisting of Drs. Roose, Salzman, Melissa Arbuckle (Vice-chair of Education in the Dept. of Psychiatry), Blair Simpson (Vice-chair of Research and mentor), Javitch and Stroup (PDs of the schizophrenia T32 and Dr. Stroup is also Vice Chair of Faculty Affairs within the Dept. of Psychiatry) meets at least once a year (more if Dr. Roose feels it necessary). The topics discussed include the recruitment of fellows, the quality of mentoring, fellows' progress, the didactic program, the addition and deletion of preceptors, the administrative structure and the synergy of the fellowship with the research strategic plan of the department. Decisions to add or delete faculty from the training program are made after consultation with the Advisory Committee. Additions are made when it is clear that a faculty member brings relevant expertise to the training mission and is well qualified to be a preceptor. Deletions are made when faculty leave Columbia, no longer has a sufficient research portfolio, or if evaluations indicate that faculty are not meeting the goals of the training program. In addition, Dr. Roose has a personal relationship with the PDs of the other T32s at Columbia who meet formally once a year and who maintain a continuous dialogue about research training problems and innovations, the program to recruit underrepresented minorities, and the didactic program. Any improvement or opportunity developed by other T32s can be adapted and used to enhance this T32.

b. Program Faculty

The members of the mentoring faculty are in the Departments of Psychiatry and/or Neuroscience and/or Psychology at Columbia University (**Table 1**). The mentoring faculty serve as primary mentors for research fellows and each contribute 0.5 CM effort to the T32 (when they have a fellow). Some faculty have specific administrative responsibilities (e.g. Dr. Arbuckle serves on the Advisory committee) (**Table 2**). Since the last submission 5 years ago, 11 mentors have left Columbia (1 to become a department chair, 3 to take positions at the NIMH, and 7 to take research positions at other universities), and 2 have retired. Six new mentors were added: additions to the faculty include mentors for fellows interested in 1) neurodevelopment; 2) mouse models of psychiatric disorders; 3) functional neuroimaging to understand brain function related to psychiatric disorders; and 4) theoretical approaches for understanding neural circuit function and dysfunction that is related to cognition, emotion and psychiatric illness. The new faculty are additions to a faculty that comes from diverse research backgrounds including a strong clinical research tradition. At Columbia, as in most other centers, research has become increasingly interdisciplinary. Consequently, it is not uncommon for faculty members to pursue diverse research directions within their labs, for faculty members to have more than one academic appointment, and for faculty members to draw trainees to their lab from multiple programs. The 8 T32s currently funded in the Dept. of Psychiatry are quite distinct in terms of focus and they draw from a very different applicant pool. Some of the faculty for this T32 also serve as faculty in other T32s (**Table 3**). The faculty's current grant and contract support, trainees for the past 10 years and publications of research completed by trainees are presented in **Tables 2, 4, and 5**.

Representative Collaboration by the Training Faculty and its Impact on Fellows

Faculty members interact and collaborate extensively with faculty in the training program, as well as with other faculty at Columbia and beyond. Collaborations create a rich interactive environment for our fellows who benefit from the formal or informal co-mentorship that comes from collaborations. Mentor collaboration activities include joint lab meetings, journal clubs, co-sponsored seminar series, grants, research projects, and publications. 100% of our training faculty have been or are involved in collaborative research projects with at least one other faculty member. Below, we describe briefly some of these collaborative projects and/or publications, but this list is by no means complete.

Dr. Jay Gingrich has ongoing collaborations with Dr. Rene Hen, among others; these collaborations span basic to translational to clinical neuroscience. His lab also hosts a weekly seminar where trainees from various

labs present their work. Dr. Blair Simpson is involved in clinical research on OCD and has active collaborations with Yuval Neria and Rene Hen. In addition, she has jointly mentored with Dr. Rene Hen two graduated fellows, Drs. Rodriguez and Ahmari. Dr. Barbara Stanley has authored numerous papers with other faculty, including papers on PTSD, major depression, borderline personality disorder, and suicide with Drs. John Mann and Steven Roose. Drs. Stanley and Mann also co-mentored Eric Fertuck who received a K-award to study social cognition in BPD using fMRI. Dr. Rutherford collaborates on the study of aging in PTSD with Neria and also collaborates with Jonathan Posner. Dr. Alan Brown collaborates with Drs. Weissman and Gingrich, among others. Dr. Abby Fyer collaborates with Dr. Myrna Weissman on the epidemiology and genetics of anxiety disorders, as well as with Drs. Simpson and Monk. Dr. Myrna Weissman also collaborates with Drs. Gingrich, Mann, and Stanley on studies related to depression. Dr. Daniel Salzman collaborates with Dr. Fusi on a project trying to understand the mechanisms underlying the regulation of emotion; he also collaborates with Drs. Richard Axel and Charles Zuker to examine the functional architecture of the amygdala, a key brain structure for emotional processes. Finally, Dr. Salzman collaborates with Dr. Daphna Shohamy to extend his work in non-human primates into human subjects (with and without psychiatric illness) using fMRI; this collaboration was initiated by 2 fellows supported by this T32, Drs. Silvia Bernardi and Daniel Kimmel. In addition, Dr. Fusi collaborates with Dr. Rene Hen on modeling neurogenesis in the hippocampus, and they co-mentor a postdoc on this project, as well as with Dr. Attila Losonczy, where they work with a former T32 fellow. Dr. Kandel has numerous collaborations, such as with Hen, and Sulzer, investigating the role of dopamine in mouse knock-out models. Dr. Siegelbaum collaborates with Dr. Kandel on studies concerning synaptic plasticity in the hippocampus. Dr. Kevin Ochsner collaborates with Drs. Shohamy to study empathy, social learning, emotion regulation and how social factors impact fear and anxiety. In addition, Dr. Ochsner is the co-mentored with Dr. John Mann for Dr. Jeff Miller's K-award, and he collaborates with Dr. Barbara Stanley to study borderline personality disorder.

c. Proposed Training

The 8 T32s currently funded in the dept. of Psychiatry are quite distinct in terms of focus, and they draw from a very different applicant pool. Some of the core faculty for this T32 also serve as faculty in other T32s (**Table 3**). At Columbia and most other places, research has become increasingly interdisciplinary. However, there are certain skills that all research fellows need to learn, such as research design, grant preparation and the responsible conduct of research. Moreover, all programs must have an effective process to evaluate fellows, mentors and the program as a whole. Perhaps most important is the development and effectiveness of the mentor/fellow relationship, from the application process to the submission of a K-award, and how that relationship is cultivated, monitored and, in the infrequent times when the relationship is problematic, what intervention is taken. The Program Directors of the T32s in the Department of Psychiatry have worked closely together to address these issues. Thus, Columbia T32s, though distinct, understandably have in common some components with respect to research training, the evaluation procedures and the didactic program. Common didactics enhances training, as fellows interact with and learn from fellows in other programs. This commonality is readily apparent in the two T32s directed by Dr. Roose, which are both being submitted for competitive renewal this year (this one, and "Research Training in Late-Life Neuropsychiatric Disorders"). In addition, there are initiatives at the level of the Department of Psychiatry, the Medical School and the University that focus on the recruitment of minority applicants that transcend any one program.

Components of Training: The training program includes six major components: (1) relationship with the mentor; (2) participation in research, including the execution of the fellow's own studies; (3) the submission of scientific papers and grants; (4) didactic courses in research design, statistics, special topics, grant writing; (5) attendance at the fellow's seminar (6) instruction in the responsible conduct of research.

Mentoring The relationship between fellow and mentor is the core component of research training. This relationship is established during the application process when the applicant and mentor select each other (see application process). To complete an application, they must effectively work together to (1) identify an area of independent investigation, including developing a research proposal, (2) describe the fellow's involvement in the ongoing research of the mentor, including identifying data sets that the fellow can analyze and specifying papers and reviews that can be written. Thus, before an applicant is accepted into the fellowship, the effectiveness of the fellow-mentor relationship has already been tested.

The mentor has the primary responsibility for fostering the fellow's development to become an independent researcher. Over the past 3 years, Drs. Roose and Salzman have interviewed the most successful mentors to

get their perspective on the most important mentoring tasks to develop a young researcher. The consensually held view was that most of all it is a relationship that requires time. Submitting to the IRB or IACUC, the design and execution of a protocol, constructing an oral presentation, writing the first empirical paper and responding to journal reviews all require that the mentor have considerable experience, patience and time. Successful mentoring takes time away from the mentor's own research. However, successful mentors believe that training research fellows is a responsibility to the field and also opportunity to grow their own research division. We have new mentors spend time talking to successful mentors about being a mentor, the tasks of mentoring and the relationship between mentor and fellow. Being a successful researcher does not necessarily correlate with being a successful mentor. Mentors are selected not only on the basis of their research productivity and accomplishments, but also on their commitment to develop fellows into independent investigators.

Each mentor is also the head of or a member of an extended research group. Consequently, the fellows will not only have a relationship with the mentor but will work closely with other senior and junior investigators. Some of the junior investigators were recently fellows themselves (at Columbia or elsewhere), creating a multi-layered set of teaching and mentoring relationships. Mentors in this T32 share research collaborations and have frequent scientific and personal interchange with each other. Drs. Roose and/or Salzman monitor the mentor/fellow relationship throughout the fellowship and, individually or together, meet with the fellow, the mentor, and/or both together to ensure a successful relationship. Dr. Salzman is an active mentor and he and Dr. Roose obviously work closely together. Therefore, Dr. Timothy Walsh, one of the most successful and experienced mentors in our program, is responsible for monitoring of the fellow-mentor relationship of Dr. Salzman's fellows. The attention paid to the mentoring relationship is one of the reasons that in the last 15 years this T32 has a 97% graduation rate, 69% of fellows have received K-awards, and 86% independent funding.

To help introduce new fellows into the program, and to each other, in the beginning of July there is a meeting for all the fellows and Program Directors of the 8 T32s at Columbia that is chaired by Dr. Roose. Dr. Roose reviews the components of the training program and talks about the didactic, cognitive and emotional growth needed to become a successful fellow, representatives from the business office talk about funding sources and grants that fellows can apply for, and the director of the IRB talks about studying the ethics of research. Then all the PDs leave the room so that the second- and third-year fellows can candidly discuss with the incoming fellows what has worked for them and what has not in terms of their mentoring relationships.

Research Activities Over the years fellows have always told us that it is often a difficult transition for them to go from a very structured program, e.g., Psychiatric residency, to a program where for the most part they make their own schedule – often for the first time in their academic life. Although each fellow has their own roadmap for development, we have constructed a timetable for fellowship training that includes both mandated activities and serves as a guide for fellows and mentors (see **Fellowship Schedule**). The mentor is expected to outline a comprehensive reading program with the goal that the fellow can write a review paper or chapter in the fellow's proposed area of independent research. For researchers working with clinical populations, the beginning fellow is normally provided a previously collected data set and assumes primary responsibility for its statistical analysis and manuscript preparation. In addition to the formal statistics courses, all fellows are oriented to services provided by the Division of Biostatistics in the Dept. of Psychiatry. These services make statistical consultation and assistance readily available to fellows and mentors, beginning with study design, and carrying forward through data collection, analysis, and manuscript preparation. Significant emphasis is placed on fellows developing competence in statistical analysis. The faculty believes that to effectively become an independent translational researcher – no matter the level of investigation - one must have a solid understanding of standard univariate and multivariate statistical techniques and experience with their application to data sets. A second major task in the induction phase is to introduce the fellow into the mentor's research group or lab, integrate the new fellow into the research team, and introduce the fellow to key support staff and collaborators. Over the years, we have recognized that all of our trainees essentially are performing translational neuroscience, and what differs across trainees is the level of investigation (e.g. *in vitro*, *in vivo* in animal models, human subjects, patient populations, etc.). As such, our goal for each fellow is three-fold: 1) to foster their development of expertise in the specific methodology and analytic techniques in their own specific area of translational research, and 2) to ensure sufficient exposure of all trainees to the range of methodologies used across the spectrum of levels of investigation in translational neuroscience, and 3) to encourage and nurture the development of collaborative investigation that cuts across levels. For researchers performing experiments in animal models, or in novel cognitive neuroimaging or related areas, we encourage fellows to dive into the lab, learn all relevant techniques, become well-versed in the literature, and begin to develop the analytic expertise specific to their area of research.

Learning how to develop collegial relationships that are professionally effective and personally satisfying is an important part of the fellow's education and is often neglected. To become a functioning member of the research team, the fellow often requires tutorials on commonly used research techniques, e.g. structured interviews, physiological methods, behavioral assays, neuroimaging methods, etc. All of the mentors share the strong conviction that before a fellow delegates a task to a research assistant or lab tech, the fellow must know how to conduct the procedure themselves; only in this way can the fellow sufficiently appreciate the relevant strengths and limitations of the technique. The tasks in the second year are the continued execution of the fellow's research project, the writing of scientific manuscripts, presentation at a scientific meeting (usually a poster session), and most importantly the first eight months are primarily devoted to the preparation of a K-Award. Given that it is unusual for a K award to be funded on the first submission and there is only one resubmission now allowed, it is critical that the first submission be of excellent quality so that it is scored. In the third-year independent research continues as does submission of manuscripts, and most importantly the resubmission of the K award application if necessary. Although all fellows are initially directed towards a K submission, this may not always be appropriate or possible, and even if a K award is submitted it has been increasingly difficult to get funded. Therefore, mentor and fellows, with the help of the Columbia Medical Center Development Office, systematically search out all appropriate funding sources and applications are submitted.

Development of Independent Research Projects The development of an area of research associated with the mentor's expertise, but one that is sufficiently differentiated to allow the fellow to develop a unique research program and identity is the most critical task for the fellow. Work on this critical goal begins during the application process through the preparation of a research proposal submitted to the selection committee. There is pressure in the first 18-24 months to generate pilot data for a K award, so it is important to "hit the ground running" at the beginning of the fellowship.

Clinical Responsibilities: A critical feature of the fellowship program is that no revenue generating or clinical service is required of fellows. All the facilities described in the resource section are exclusively dedicated to research. 100% of the fellow's effort is focused on research. The Department of Psychiatry provides psychiatrist fellows a significant salary supplementation (\$50,000) to the T32 stipend during the fellowship so that their salary approximates their PGY level as if they were still in clinical training. Therefore, fellows are not required to provide clinical services to generate revenue and will not be distracted from their focus on research. Some fellows do have responsibility for the care of patients participating in research protocols. The "clinical" work with these patients involves learning necessary clinical research skills such as how to recruit a patient into a protocol, how to obtain informed consent, the development of the therapeutic alliance in a research context, and the use of structured interviews and rating scales. Since many research questions are originally generated through patient contact, the fellows are taught not only how to execute the protocol at hand, but also, equally importantly, how to observe what is new and unexpected. Furthermore, the participation of the fellow in the mentor's protocols helps the fellow develop relationships within the research group that will subsequently facilitate execution of the fellow's own work.

Grant writing: The career of an independent researcher depends on the ability to secure research support. Fellows often begin with a small grant proposal (\$17,500) to departmental funding sources such as the Pisetsky Award which supports young investigators at the rank of Assistant Professor or below who are within 5 years of completing clinical or research training; fellows are particularly encouraged to apply. The mentor helps the fellow overcome any inhibitions about grant preparation and also teaches the fellow that a well-constructed small proposal is a template for subsequent more developed grant submissions. At the end of the first year most fellows are in a position to submit a grant application to an external foundation (e.g., NARSAD). The fellows are told of all the foundations and organizations in their area of research that give grants, e.g. the American Foundation for Suicide Prevention. A large number of our fellows successfully compete for these foundation awards. The fellows are always thinking about the K award and take the K award course in their second year.

Didactics: The didactic courses described below are open to research fellows in the Dept. of Psychiatry if appropriate given the year of fellowship, previous training and subject matter. Some are required for all fellows in this T32 and the Schizophrenia and Late-Life Neuropsychiatric Disorders T32. This means that every research fellow interacts with a substantial cohort of fellows and learns about research areas and strategies beyond the ones being pursued by their own research groups. Required didactics are listed first.

Research Design and Statistical Analysis I (required): The course emphasizes understanding proper study design and statistical analyses. The course also prepares fellows for embarking upon their role as investigators in upcoming research projects by: 1) identifying and discussing the fundamental principles and procedures for the design of clinical research; 2) identifying and implementing appropriate statistical techniques in the analysis of data; and 3) requiring second year fellows to present their research projects to the first-year fellows. Faculty members with expertise on the same topic are present to provide feedback to the second-year fellows. This process assists the second-year fellows, as well as exposes first year fellows to ongoing research projects. Statistics I introduces or reacquaints fellows with the language of statistics by presenting the concept of distributions, measurement, and sampling. The basic statistics that are commonly used in the medical literature, including t-tests, ANOVA, nonparametric procedures, odds ratio and risk ratios, as well as the general linear model are covered.

Research Design and Analysis II (required): This follow-up course to Research Design and Analysis I continues to present statistics that are routinely used in professional and peer review journals, such as the general linear model, longitudinal models, survival analysis, meta-analysis, item-response theory, and relevant concepts including power, validity and, reliability. A set of practical lectures is designed to help fellows work with their own data (i.e., how to set up their data sets, how to look at distributions, outliers, how to think about coding, etc.). Most importantly, 3 sessions are devoted to the reading and writing of result sections, where fellows are presented with a set of data and asked to write a Results section, as well as to read and describe results from published papers. This practical, active approach helps fellows integrate the material that has been covered in Research Design and Analysis I and II.

If a fellow has adequate statistical training, they can skip some sessions in Statistics I and II and pursue further statistics training either through courses sponsored by the CTSA and the School of Public Health such as the intensive week-long, non-credit courses for faculty, students, and healthcare professionals seeking advanced skills in statistical software and analysis, data visualization, modeling, and focused epidemiological topics. For some fellows, depending on previous training and research project, the course "Statistics for Basic Sciences" given in the neuroscience program is more appropriate.

Grant Preparation: One of the responsibilities of the mentor is the identification of funding sources and in-depth involvement in every phase of grant preparation. The mentor instructs the fellow on how to develop an effective working relationship with the program staff at the funding agency.

In addition to the mentor's instruction, fellows take two courses:

Funding and Grantsmanship for Research and Career Development (required): This is a seven-session given by the CTSA faculty and attended primarily by post-doctoral scientists, and new investigators. Topics include: 1) Types of support and review processes for research and training activities: Government Agencies, 2) Types of support and review processes for research and training activities: Voluntary Health Organizations, Foundations, Industry, Clinical Trials Development, 3) Planning and Organizing a Fellowship/Career Development Proposal - NIH F30/F31/F32 and K01/K07/K08/K23/K25/K99(R00) applications, 4) Experiences of a peer reviewer and an "Inside Look" at an extramural grant review panel.

The K Award (required). Dr. Harold Pincus, Vice Chair of the Department of Psychiatry and Co-director of the Irving Institute for Clinical and Translational Research at Columbia University leads the very popular K award course. The K Class Seminars are designed to assist research fellows in preparing a successful proposal for a NIH Research Career Development Award (or similar grant from CSTA - or external sources). Each seminar has a faculty presenter or panel and focuses on a component of the K Award application. Submission of draft sections from course participants is required and group and individual feedback is provided. At least two of the seminars are mock reviews where fellows volunteer to have their applications reviewed by senior faculty and the class experiences a simulated study section meeting.

The Biology of Neurological and Psychiatric Diseases (required): Rene Hen PhD, Prof of Neuroscience and Pharmacology

Stephen Rayport MD/PhD, Professor of Neurobiology in Psychiatry

Scott Small MD, Professor of Neurology:

This one-semester 16 session course is taught every other year for graduate students and postdoctoral fellow. This course examines brain mechanisms underlying neuropsychiatric disorders. Topics covered include animal models, development, brain imaging, brain recovery, neurodegeneration, motor neuron disorders, epilepsy, Parkinson's disease, attention disorders, Alzheimer's disease, affective disorders, genetics of complex disorders, schizophrenia, addictive disorders, and anxiety disorders. A major effort is made to draw general principles from the material so that even topics outside the focus of this training grant benefit trainees. The course emphasizes strategic approaches to investigating the etiology, genetic transmission, and development of therapeutic approaches for brain diseases. Each disease is first introduced in a lecture by a faculty member and fellows present original research papers. The course is open to interested pre- and postdoctoral trainees from neuroscience labs throughout the medical school, and also attracts interested residents from Psychiatry and Neurology, as well as our fellows. This course provides a highly interactive environment for our trainees, exposing them to basic, translational, and clinical neuroscience, and challenging them to integrate concepts and knowledge across these areas. It has heightened our trainees' interests in and appreciation of the major issues in psychiatric and neurological research, leading to a broader perspective on the relevance of basic science research to clinical problems. Various faculty mentors in our training program participate, as do faculty from Psychiatry and Neurology.

T32 Third Year Fellow's Presentation (required); This is a required seminar for fellows in this T32 as well as fellows in the Schizophrenia and Late-Life Neuropsychiatric Disorders T32s. Third year fellows from these three T32s are the presenters. The emphasis of the seminar is study design, data analysis and fellow interaction. Fellows present the background and study design for 15 minutes and then there is 15-minute discussion. This is followed by fifteen-minute presentation of results and conclusions followed by discussion. The seminar is scheduled for 60 minutes but has never ended before 90 minutes. Anticipating that the discussions would be lively and go longer, the seminar is scheduled for monthly at 5 PM, i.e., a time where most people do not have further obligations afterwards thus allowing the discussion to continue beyond the nominal stopping time. One session is devoted to overall program evaluation and this has proved invaluable. This one of the key activities where fellows who are doing research at very different levels of investigation are brought together and interact with each other extensively. This helps bridge the gap across levels of investigation in our training program.

Other Course Available to Fellows: Both the medical center and the Department of Psychiatry offer a variety of courses that many of the research fellows find very helpful, for example:

The Department of Psychiatry MRI course - This is a course that teaches principles of MRI with emphasis on applications in neuroscience and psychiatry research. The course uses simple language to present the basic physics involved in creating an image, spectrum, or map by magnetic resonance technology. The use of this technology, specifically as it applies to the unique challenges of neuroscience will be discussed. It is offered in response to the increasing numbers and diversity of studies presently being carried out or planned by investigators. In the first six weeks, participants will learn topics such as basic physics, hardware, image formation, data quality assurance, k-space data, and image reconstruction. Special topics of fMRI, diffusion imaging (DTI), spectroscopy (MRS), high field MRI, and molecular imaging will be covered in the second half of the course reinforcing the theories learned in the first half. A number of seminal research papers on the use of MRI in neuroscience and psychiatry will be discussed as examples of topics covered in the course. The content of the course is updated every year to include the latest developments in magnetic resonance as it applies to neuroscience, such as the study of challenging anatomical regions and physiological processes in the brain. There are 16 classes, each 2 hours' duration.

fMRI Design and Analysis: This is a 5-day workshop designed for investigators having familiarity with the basic fundamental principles of fMRI measurement and design, with some experience in functional neuroimaging data acquisition and analysis. The first 4 days of class will be held at NYSPI and the last day of material will be given in a series of 2 hour on-line interactive sessions given over the following month. T32 fellows and K awardees in the Department of Psychiatry will be given priority for registration.

The highly interactive workshop will focus on using software and their extensions for statistical modeling, preprocessing, and the visualization of data associated with a range of clinical and basic fMRI experimental designs. Those participating in the workshop will learn the basics of analyzing both task-related and resting state data. In terms of the software being used to accomplish these ends, SPM12 and the Connectivity Toolbox will

be the primary focus of attention, although other software tools will be discussed and demonstrated. Other tools discussed will be relevant for fMRI quality assurance—through artifact detection—and data visualization methods which include, but are not limited to MRIcron, xjView and the CAT12 Toolbox.

Columbia CTSA: Columbia's CTSA has courses available to fellows conducting clinical and translational science. The CATSA goal is to broaden the scope of research and training efforts across Columbia, so courses have been designed to help trainees at multiple levels to conduct high quality clinical and translational research. In addition to the course of Funding and Grantsmanship and advanced instruction in statistics examples of other relevant activities are:

Building Interdisciplinary Research Models: This course will allow participants to build skills in interdisciplinary research by collaborating with scholars from various disciplines.

Advances in Precision Medicine: This monthly seminar series features leaders in Precision Medicine field from across the nation. These seminars highlight recent developments in implementation of “precision medicine” concept in everyday medical practice. Topics addressed this year include establishment of individualized programs for disease prevention and detection at academic medical centers, improvements in our understanding of the role of genomic factors in the individual response to drugs, progress in adaptive clinical trials exploring predictive algorithms and patient genomic data in oncology, mining of electronic health records to explore genotype and phenotype associations across diseases, and others

Additional Classes in Neuroscience: For fellows requiring or desiring more formal didactics in neuroscience, trainees are welcome (and encouraged) to attend a number of graduate courses offered at the medical center. These courses include (but are not limited to):

- 1) Systems Neurophysiology and Modeling
- 2) Molecular Mechanisms in Synaptic Transmission and the Control of Transmitter Release Structure and Function of Membrane Ion Channels
- 3) Neuropsychopharmacology (taught by Neuroscience and Psychiatry faculty).

Grand Rounds and Seminars: Columbia's Department of Psychiatry runs a weekly Grand Rounds. Most speakers come from outside Columbia. Many topics fall within the scope of this training grant, and our fellows attend regularly. In addition, the Department of Neuroscience runs a weekly seminar series, and some of those seminars are on brain systems related to psychiatric disorders. There are also a number of other seminar series, including ones run by individual divisions within the Dept. of Psychiatry such as the Brain Imaging Division the Lieber Center, and seminars in Theoretical Neuroscience. Many of the seminar series provide opportunities for fellows to interact with the outside speakers. The large array of seminars that span basic, translational and clinical neuroscience provide a rich environment for fellows' intellectual development.

Presentation at Meetings and Interchange with Investigators: Fellows are expected to present their research at scientific meetings as frequently as possible. Provision has been made in the budget of the T32 for fellows to attend at least one national scientific meeting each year. These meetings are often the ACNP, Society for Biological Psychiatry, the APA, or Society for Neuroscience. In addition, there is an annual Neuroscience poster-fest at Columbia, held after the Society for Neuroscience meeting.

Fellow Schedules: When fellows begin the fellowship, it is often the first time in many years for the MDs that their time is not scheduled. The consensual agreement among the mentors, based on years of experience, is that it is important to help the fellows structure the fellowship by setting specific goals to be achieved in 6-month blocks. The following schedule reflects this consensus.

FELLOWSHIP SCHEDULE RESEARCH ACTIVITIES	COURSE WORK
First Semester - First Year 1. Comprehensive review of the literature 2. Participation in preceptor's protocols 3. Begin fellow's research project	1. Research Design and Statistics I 2. Fellow's Seminar

4. Submission of a small grant (e.g. Pisetsky Fund) 5. Career Development Plan (CDP) at month 3	
Second Semester - First Year 1. Collect pilot data for research project 2. Author review paper or Chapter 3. Progress report, 2nd year research plan and 12-month CDP 4. Submit grant application (NARSAD)	1. Fellow's seminar 2. Responsible Conduct of Research 3. Biology of Psychiatric and Neurological Diseases (taught every other year) 4. Attend IRB subcommittee and full board meetings
First Semester - Second Year 1. Execution of fellow's research projects 2. Submission of empirical paper 3. Develop a plan and begin writing K award	1. The K-Award Course 2. Individualized Coursework in Neuroscience 3. Research Design and Statistics II 4. Fellow's seminar
Second Semester - Second Year 1. Presentation at scientific meeting (ACNP, APA, Biological Psych, Society for Neuroscience, ANA) 2. Submission of K-Award 3. 24-month CDP	1. Biology of Psychiatric and Neurological Diseases (taught every other year) 2. Individualized Coursework 3. Fellow's seminar 4. Funding and Grantsmanship Course
First Semester - Third Year 1. Independent Research 2. Submission of empirical papers from independent Research 3. Resubmission of K-Award	1. Individualized Coursework 2. Fellow's seminar
Second Semester - Third Year 1. Independent Research 2. Presentation of findings at scientific meeting 3. Submission of empirical papers from independent Research	1. Individualized Coursework 2. Fellow's seminar