PROGRAM PLAN

A. Program Background

UVA's decades-long commitment to epilepsy research and training

During the last 25 years, the NINDS has periodically assembled the world's leading epilepsy researchers to identify *Benchmarks for Epilepsy Research*. These benchmarks are intended to galvanize the research community into developing critically needed therapies for people with epilepsy, a disease that afflicts 50 million people worldwide. In 2021, the NINDS-hosted meeting highlighted the need to: **(1)** Identify cellular- and circuit-level mechanisms of seizure initiation and propagation; **(2)** Understand the neural circuits, cell types, and genetic factors that participate in different seizure types; and **(3)** Resolve the molecular, cellular, and circuit basis for current treatments and their side effects.

Training the next generation of epilepsy researchers is clearly necessary to ensure that we meet current and future *Benchmarks for Epilepsy Research*. The University of Virginia (UVA), with its rich and sustained history of epilepsy research—and of producing world-class epilepsy researchers—is poised to assume a leadership role in this responsibility. During the last 10 years, UVA's epilepsy research community has grown considerably and now boasts one of the largest groups of epilepsy researchers in the world; much of this research aligns with the NINDS-mandated goal of resolving cellular- and circuit-level mechanisms of epilepsy. Herein, we codify our practice of producing future leaders of epilepsy research with a formal training plan.

Fritz Dreifuss is largely credited for initiating UVA's long-standing commitment to epilepsy research. Dreifuss started his storied career at UVA in 1959 and ultimately retired from the university nearly 40 years later, after publishing more than 300 articles. Early in his career, Dreifuss pioneered the use of continuous EEG recordings to measure spike-wave discharges associated with absence epilepsy. He eventually advocated for the now widely accepted practice of using these discharges as an indispensable marker for evaluating the efficacy of anti-absence epilepsy drugs. Indeed, Dreifuss was among the very first epilepsy researchers to study the efficacy of ethosuximide, clonazepam, and valproate—three anti-seizure drugs used commonly today—in the treatment of epilepsy. Among his notable service contributions, Dreifuss served as President of the American Epilepsy Society, Chairman of the Professional Advisory Board of the Epilepsy Foundation of America, and President of the International League Against Epilepsy. Dreifuss trainees include several leaders in epilepsy today, including Robert Macdonald (past president, American Epilepsy Society), Greg Holmes (past president, American Epilepsy Society), and Simon Shorvon (Editor-in-Chief, Epilepsia).

A second foundational figure in the history of UVA epilepsy research is Eric Lothman. Lothman joined the faculty of UVA in 1983 and ultimately served as UVA's Chair of Neurology. Despite his death at the age of 48, Lothman's impact on epilepsy research was profound and still reverberates today. Altogether, he trained 29 pre- and postdoctoral students, some of whom are recognized leaders of epilepsy research today. Notable Lothman trainees include: (1) Edward Bertram, a pioneer clinician-scientist at UVA with expertise in the basic mechanisms of generalized seizures; (2) Scott Baraban, an internationally recognized epilepsy researcher at University of California, San Francisco who pioneered the use of zebrafish to identify novel anti-seizure drugs; and (3) Jaideep Kapur, the world's foremost expert on the devastating and often lethal condition of unremitting seizures known as status epilepticus. Lothman continues to be recognized today for his fundamental discoveries regarding the cellular- and circuit-level mechanisms of epilepsy.

UVA's commitment to epilepsy research continues today. Jaideep Kapur, a Lothman trainee, joined the university's Neurology Department in 1998 and continues to lead a productive and multifaceted epilepsy research program. Kapur's research extends from using rodent models to resolve the basic mechanisms of seizure generation, to developing and implementing clinical trials in search of effective treatments for status epilepticus. In addition to leading an NIH-supported comparative study of drugs to treat status epilepticus—an effort that includes 60 sites—Kapur has served as President of the *American Epilepsy Society* and currently serves as Chair of the Board of the *International League Against Epilepsy-North America*. He has also served on the editorial boards of many professional journals including *Neurology, Annals of Neurology, Experimental Neurology, Epilepsy Research, Epilepsy Currents*, and multiple NIH review panels. In 2021, Kapur received the Javits Neuroscience Investigator Award, an award that recognizes investigators with a track record of exceptional and preeminent scientific achievement.

In 2002, Howard Goodkin joined UVA's team of epilepsy researchers. Goodkin, a clinician-scientist with a specific interest in pediatric epilepsy, currently serves as UVA's Chair of Neurology and is credited for building UVA Children's Neurology Care into an internationally recognized program that is among the best in the country. Goodkin will serve as President of the *American Epilepsy Society* in 2025.

UVA's cadre of epilepsy researchers has expanded over the last two decades and includes scientists devoted to resolving the cellular- and circuit-basis of epilepsy. Manoj Patel (co-PI of this T32 training program) leads an NIH-funded research

program that aims to determine how patient-identified mutations in sodium channels cause devastating childhood encephalopathies. Using a range of electrophysiological tools and transgenic mouse models, Patel's work has provided key insights into how sodium channel mutations promote severe and often lethal seizures. Mark Beenhakker (co-PI) leads an NIH-funded lab motivated to identify neural circuits that initiate and propagate seizures associated with absence epilepsy, a common pediatric epilepsy. The Beenhakker lab uses electrophysiological and computational tools to identify key cellular components within thalamocortical circuits that promote the generation of absence seizures.

In summary, UVA's commitment to both conducting outstanding epilepsy research and training future epilepsy researchers stretches over six decades. With the relatively recent addition of new epilepsy researchers at UVA, we are now poised to formalize the epilepsy training environment we have cultivated during the last decade—for both *Epilepsy Training Program (ETP)* trainees and newly independent epilepsy researchers. Indeed, in the last 10 years, our *Epilepsy Interest Group* (Figure 1) has convened with our pre- and postdoctoral trainees every week to discuss developments within our respective research programs and to delve deeply into current discoveries in the broader field of epilepsy research. Our trainees—nearly 25 in all (16 in photo)—have benefitted enormously from this collaborative research environment and have carried their expertise to postdoctoral and faculty positions in academia, as well as positions within biotech. Formalizing our training environment with an NIH-sponsored training program will serve to strengthen our existing infrastructure, as well as to establish new training opportunities that will ultimately support NINDS's long-standing goal to fully realize current and future *Benchmarks for Epilepsy Research*.



Figure 1. UVA's Epilepsy Interest Group. Trainees pictured, in alphabetical order: Anastasia Brodovskaya, Selena Garcia DuBar, Ela Dulko, Madison Failor, Suning He, Aleksandra Maciejczuk, Maria Marlicz, Raquel Miralles, Soudabeh Naderi, Guzel Naik, Patrycja Oleniacz, Magdalena Pikus, Caeley Reever, Irene Sanchez-Brualla, Erica Slogar, AnnaLin Woo.

Faculty and Research Staff pictured, in alphabetical order: Mark Beenhakker, Edward Bertram, Alexis Boscia, Andrey Brodovskiy, Jennifer Burnsed, Tyler Deutsch, Ukpong Eyo, Zhongxiao Fu, Molly Gerding, Howard Goodkin, Nick Guagliardo, Marissa Incer, Suchitra Joshi, Jaideep Kapur, Alex Kuan, Manoj Patel, Edward Perez-Reyes, Racheal Spera, John Williamson.

B. Program Administration

The administrative structure of our *Epilepsy Training Program (ETP)* is shown in **Figure 2**. Drs. Patel and Beenhakker will serve as the program's directors and are ultimately responsible for programmatic administration and training activities. To ensure the vibrancy of our program and the success of our trainees, our administrative structure is organized upon four foundational pillars, each of which will be supervised by a designated mentor: **(1)** Research curriculum and mentoring (Dr. Jaideep Kapur); **(2)** Clinical curriculum (Dr. Ifrah Zawar); **(3)** Recruitment and retention (Dr. Ukpong Eyo); and **(4)** Professional development (Dr. Howard Goodkin). Collectively, this team of program directors and designated mentors constitute the program's *Executive Committee*.

The Executive Committee will meet once every three months to discuss our efforts in advancing our ETP objectives. Each meeting will focus on one of our four pillars, and we will rotate through all four pillars during the year (Figure 2C). This structure ensures that we fully evaluate the status of each pillar once a year and enables us to continually implement and advance our best practices. The program directors will each devote at least 2.5% of their effort toward the administration

of the program; UVA's School of Medicine contributes 5% toward PI salaries. This is in addition to the School of Medicine's 50% salary support provided to all basic science faculty to ensure that a robust and inclusive academic environment exists at the university. The *Executive Committee* will report to our *Internal Advisory Board* once per year. The *Executive Committee* will also provide a formal, annual report to our mentors and current trainees for feedback and suggestions for programmatic improvement. In addition, our annual retreat devotes time for open discussion among trainees and faculty on the findings of our annual report. Finally, the *External Advisory Board* will provide additional programmatic feedback in several ways. Below, we describe the training program's leadership roles, as well as how the qualifications of our identified leaders will support a robust training environment.

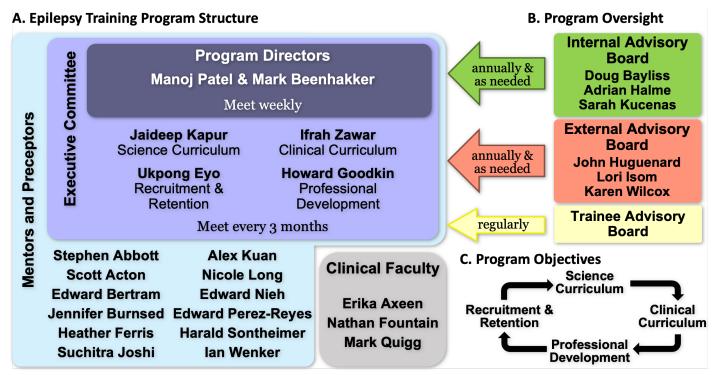


Figure 2. Structure and oversight of our Epilepsy Training Program. A. Structure. The Executive Committee is composed of the program directors and four faculty, each of whom is responsible for overseeing one primary programmatic objective. To ensure that we provide our trainees with a modern clinical perspective, we have also identified three clinical faculty to oversee our curriculum. **B.** Oversight. Three advisory boards will evaluate the administration of our training program. **C.** Each quarterly meeting of the Executive Committee will address our progress with advancing one of our four foundational pillars.

B1. Program Directors

Drs. Manoj Patel and Mark Beenhakker will serve as program directors of UVA's *ETP*. Their respective, independent research programs encompass a wide range of epilepsy research areas. Over their past 13 years together at UVA, Drs. Patel and Beenhakker have built an excellent working relationship and interact regularly as colleagues. Indeed, serving as co-directors of the *ETP* is a natural extension of the relationship Drs. Patel and Beenhakker have cultivated for many years.

Logistically, both co-directors will interface with UVA's research community in distinct ways to ensure that the *ETP* represents all epilepsy research disciplines at UVA. Both PIs have primary faculty appointments in departments housed within UVA's School of Medicine: Department of Anesthesiology (Patel) and Department of Pharmacology (Beenhakker); both PIs have secondary appointments with UVA's Department of Neuroscience (School of Medicine), Department of Biology (College of Arts & Sciences), and UVA's *Program in Fundamental Neuroscience* (College of Arts & Sciences). By virtue of having different primary departmental appointments—and by having secondary appointments across UVA's campus—Drs. Patel and Beenhakker will bring diverse perspectives to their respective co-director roles, and both will be able to leverage their distinct vantage points to ensure that the *ETP* recruits a diverse team of trainees. Finally, as described above, the program directors will not execute their respective responsibilities in isolation. Instead, the program directors will work with members of the *ETP Executive Committee*. Additional details regarding our dynamics and interactions are described in the Multi-PD/PI Leadership Plan.

<u>Manoj Patel, Co-Director</u> Dr. Patel is a Professor in the Department of Anesthesiology and is a past director of UVA's Neuroscience Graduate Program. He also serves as a faculty member of the Neuroscience Graduate Program's Executive Committee and was previously a member of the Neuroscience Graduate Program Strategic Advisory Committee.

- Current research areas. Research in the Patel lab focuses on understanding the role of voltage-gated ion channels, particularly sodium (Na), in the development of epilepsy. More recently, his lab has focused on *de novo SCN8A* (Nav1.6) mutations, how these mutations alter sodium channel activity, and their role in the development of epileptic encephalopathy (EE).
- Experience in research training. Dr. Patel is an active member of UVA's Neuroscience Graduate Program. He has mentored and graduated six PhD students (one underrepresented minority [URM] female and five males) and two postdoctoral students (one URM male). One of his previous postdoctoral researchers currently holds a faculty position at UVA. Many of his PhD students have obtained extramural fellowship funding (3-NRSA; 1-AES pre-doctoral award, 1-UNCF Merck Fellowship). Two have received recognition as the top students in the Neuroscience Graduate Program. He currently mentors three PhD students (three females; one URM and one LGBTQ+) and one European female postdoctoral researcher. One of his current PhD students was awarded a NIH NRSA award. Dr. Patel has also mentored over 50 undergraduate students.
- **Graduate teaching.** For the last 20 years, Dr. Patel has been involved in both PhD and medical school courses. His PhD teaching focuses on neurophysiology (NESC 8000), Molecular Characterization of Drug Targets and Anesthetics (PHAR 9002), and Tools for Neurobiology (Course director, NESC 9022). Dr. Patel's medical school teaching focuses on Mind Brain Behavior (Blood supply to Brain, Surface and Deep Structures of the Brain, Anti-emetics and Synaptic Plasticity), Foundations of Medicine (Osmosis and Diffusion), and Musculoskeletal-Integument (Cellular Electrophysiology and Neuromuscular Junction).
- Commitment to diversity. Dr. Patel is deeply committed to enhancing the diversity within the UVA graduate program. Patel's current lab personnel consist of three female graduate students (one being a URM of Cuban decent) and a European female postdoctoral student. Dr. Patel has previously mentored an African American female for her PhD and trained an African American male postdoctoral student. Patel is of Indian descent, and although not considered a minority, he has experienced many difficulties and obstacles throughout his training, both within the UK and the US and understands the importance of having a diverse scientific lab.
- Executive experience related to graduate training. Dr. Patel was the director of UVA's Neuroscience Graduate Program from 2013 to 2016. He is a member of the Neuroscience Graduate Program Executive Committee and was a previous member of the Neuroscience Graduate Program Strategic Advisory Committee.

Mark Beenhakker, Co-Director Dr. Beenhakker is currently an Associate Professor in the Department of Pharmacology and is the director of UVA's Neuroscience Graduate Program. He also serves as a faculty member of Neural Systems & Behavior, an intensive summer course held at the Marine Biological Laboratory. In 2021, Dr. Beenhakker was inducted into UVA's Academy for Excellence in Education.

- Current research areas. Research in the Beenhakker lab focuses on thalamocortical circuits and their contribution to
 common childhood forms of epilepsy. His lab seeks to resolve how physiological states—metabolism and respiratory
 function—modulate thalamocortical circuits to drive seizures.
- Experience in research training. At UVA, Dr. Beenhakker is an active member of both the Neuroscience and the Pharmacology Graduate Programs. He has mentored and graduated four PhD students (two women and two men). He currently mentors three PhD students, one postdoctoral researcher, and one research scientist. Dr. Beenhakker has also mentored 43 undergraduate students.
- **Graduate teaching.** For the last decade, Dr. Beenhakker has taught in both PhD and medical school courses. His lectures focus on neurological disease (NESC 8250), neuropharmacology (PHAR 9002), mechanisms of opiates and sedatives/hypnotics (MedEd 90-903), and drug discovery (PHAR 9004). Dr. Beenhakker also serves as a co-director for the Cell Signaling block in the Core Course in Integrative Biosciences (BIMS 6000). In addition to providing didactic lectures, the Cell Signaling block also includes a lab demonstration on electrophysiological recording techniques and individualized neurophysiological simulations that reinforce the material presented during lectures. For the last five years, Dr. Beenhakker has taught a course he developed called Synapses and Circuits (NESC 9020).
- Commitment to diversity. Dr. Beenhakker is involved in several efforts that seek to increase diversity in the UVA neuroscience community. UVA's Neuroscience Graduate Program recently formalized their commitment to diversity, equity, and inclusion (DEI) by creating a student-led committee charged with enhancing the presence and voice of historically underrepresented communities at the university. As director, Dr. Beenhakker works directly with this committee to accelerate the full realization of their stated goals. These efforts recently culminated in the recruitment of an incoming cohort (2023), wherein 50% identify as URM.
- Executive experience related to graduate training. Dr. Beenhakker now serves as the director of UVA's *Neuroscience Graduate Program*. Prior to serving as the director, Dr. Beenhakker led efforts to revitalize the program's curriculum in 2018.

B2. Executive Committee

Jaideep Kapur, Research Curriculum & Mentoring Dr. Kapur is a clinician investigator whose laboratory studies the neurobiological mechanisms underlying status epilepticus, a devastating condition of unrelenting, continuous seizures. Dr. Kapur has been at the forefront of research that aims to understand how seizures modulate the trafficking of GABA and AMPA neurotransmitter receptors. Recently, Dr. Kapur's discoveries regarding receptor trafficking prompted interest in a large-scale, NIH-funded clinical trial called the *Established Status Epilepticus Treatment Trial* (ESETT) that defined treatment strategies for status epilepticus when benzodiazepines fail. Notably, if administered early enough, benzodiazepines can treat status epilepticus. However, if benzodiazepine treatment occurs too late, then patients often die. Dr. Kapur's study found that the three primary drug treatments for benzodiazepine-insensitive status epilepticus are similarly effective, a conclusion that contrasts with previous, largely observational reports.

Dr. Kapur's appointment as supervisor of our research curriculum stems from his expertise in both basic science and translational research. Indeed, Dr. Kapur's recent clinical trial reflects a true realization of the expression "Bench to Bedside." Moreover, as co-director of the UVA Brain Institute, an institution devoted to promoting the neurosciences throughout UVA—and that recently received \$75 million from the university—Dr. Kapur is in the optimal position to identify curricular opportunities throughout UVA for the trainees of our *ETP*. Moreover, from his vantage point, Dr. Kapur will be able to identify new UVA faculty whom we can recruit into our program to ensure that we maintain a vibrant curriculum that reflects state-of-the-art scientific advances. Dr. Kapur's proximal role in supervising our research curriculum includes working with our workshop faculty (**Section H2a**) to ensure that recent biomedical research advances relevant for the epilepsy field are addressed. Dr. Kapur has trained four NIH K-awarded faculty, nine postdoctoral researchers, and seven graduate students.

Ifrah Zawar, Clinical Curriculum Dr. Zawar is a clinician scientist with double board certification in neurology and epilepsy. She has extensive clinical training in the field of epilepsy from one of the world's renowned epilepsy centers, the Cleveland Clinic. Her current research, funding, history of dissemination, and prior mentoring collectively demonstrate her ability to execute innovative, impactful research and provide training in the field of epilepsy. Dr. Zawar has received several research awards in epilepsy, including the American Neurological Association Research Award, the American Epilepsy Society Grass Foundation Young Investigator Award, and the Epilepsia Open Clinical Prize in 2022 for the single best article from all 2022 publications in Epilepsia Open, the official journal of the International League Against Epilepsy. Her research has been covered by several media outlets, including US News and World Report in both 2022 and 2023. During Dr. Zawar's 2.5 years as Assistant Professor, she has received multiple research grants and has authored several first- and senior-author peer-reviewed articles and book chapters. She also serves on the editorial board of the official journal of the American Epilepsy Currents, and as an associate editor for Journal of Alzheimer's Disease.

As a clinician scientist, the breadth of Dr. Zawar's mentoring ranges from the clinical to research world. During her fellowship at the Cleveland Clinic, she served as the mentoring chief epilepsy fellow because of her dedication to training. At UVA, she has developed the surgical epilepsy curriculum for epilepsy and clinical neurophysiology fellowships and epilepsy teaching curriculum for neurology residency. Dr. Zawar was recognized with an *Excellence in Teaching Award* for her dedication to training when she served as a Clinical Instructor of Medicine at the Lerner School of Medicine at the Cleveland Clinic from 2017 to 2021. She is also actively involved in research mentoring for residents, fellows, graduate students, and postdoctoral fellows in her relatively new independent research lab. Under her co-mentorship, her graduate student was awarded the Presidential Fellowship Award in Collaborative Neuroscience for innovative neuroimaging research in dementia and epilepsy.

<u>Ukpong Eyo, Recruitment & Retention</u> Dr. Eyo is an Associate Professor at the UVA School of Medicine. His current goal as an independent researcher is to combine both his graduate training in developmental glial biology and postgraduate training in microglial-neuronal interactions in adulthood to study microglial contributions in development, maturity, and pathology. His research currently aims to elucidate microglial contributions to brain injury paradigms such as seizure disorders and interrogating microglial involvement in neurodevelopmental disorders like autism spectrum disorder (ASD) and neurodegenerative disorders like Alzheimer's Disease (AD). Since opening his independent lab in 2018, Dr. Eyo has contributed to over 20 published papers including in *Nature*, *Nature Communications*, *Neuron*, *GLIA*, and *Cell Reports*.

In the six years since opening his lab, Dr. Eyo has trained/is training four graduate students (75% women, 75% underrepresented minorities, and 50% international). Dr. Eyo is committed to ensuring DEI, as exemplified in the individuals represented in his lab. Of the 17 trainees (12) and staff (5) that have come through Dr. Eyo's lab, 53% have been women, 41% have been URM including Black, Hispanic, and Native American individuals. Furthermore, Dr. Eyo instituted our School of Medicine's *Diversity Symposium* in 2022, as well as completed and facilitated formal mentor training provided by the *Center for the Improvement of Mentored Experiences in Research* (CIMER). In 2023, with the

support of the HHMI Gilliam Award, his lab has been instrumental in establishing the Society for Black Biomedical Scientists and Engineers. Finally, trainees in Dr. Eyo's lab have been successful in securing positions on institutional training grants, an institutional postdoctoral fellowship from the UVA Brain Institute, and an HHMI Gilliam Award to advance diversity and inclusive activities on campus.

Howard Goodkin, Professional Development Dr. Goodkin currently serves as UVA's Chair of Neurology. In 2025, he will also serve as President of the *American Epilepsy Society*. Both capacities provide Dr. Goodkin with an exceptional perspective on the professional opportunities available to our trainees. Not only are his national and international professional networks well-established and far-reaching, but they also include experts in both the realms of basic research and clinical practice. Thus, Dr. Goodkin will be able to connect our trainees with individuals across the globe, so that they can fully realize their professional aspirations, irrespective of possible constraints placed on where they can work.

Codifying Dr. Goodkin's role in our *ETP* as supervisor of Professional Development provides a truly unique opportunity for our trainees. We will take specific advantage of our direct access to Dr. Goodkin by establishing annual professional development workshops, wherein he will lead discussions that highlight how epilepsy-related PhD research can be leveraged to achieve success in a wide range of career paths, including those in academia, biotech, and patient advocacy.

B3. Internal Advisory Board

The Internal Advisory Board (IAB) will be responsible for providing formal oversight of the ETP in collaboration with the External Advisory Board. Three UVA faculty members (Drs. Kucenas, Halme, and Bayliss) have agreed to serve as our IAB and will meet annually with our ETP Executive Committee, during which we will review trainee progress and formal evaluations (Section J and Figure 2). IAB members will also meet as needed with the program directors and Executive Committee to provide guidance on pressing or unexpected matters. The IAB will also meet annually with all trainees in a town hall-style format to gather informal feedback.

Sarah Kucenas, Professor of Biology Dr. Kucenas is a Professor in the Department of Biology and has secondary appointments in the Departments of Neuroscience and Cell Biology. She is also the co-director of the Brain, Immunology, and Glia training grant. Dr. Kucenas also helps lead neuroscience research and education efforts at UVA by serving as the inaugural Director for UVA's Program in Fundamental Neuroscience and co-director of the UVA Brain Institute. In her research program, Dr. Kucenas uses zebrafish to resolve the roles of glia and neurons during nervous system development, maintenance, and disease/injury. Her lab combines genetic perturbation, single-cell manipulation, laser ablation/axotomy, small molecule drug screening, single-cell RNAseq, and in vivo time-lapse imaging to observe glial cell origins, behaviors, and interactions directly and continuously in an intact vertebrate system.

Dr. Kucenas has graduated nine trainees (seven women, one man, one transgender woman) and is currently mentoring six students (four women, two men). The nine graduated PhD students have gone on to either postdoctoral fellowships, industry, science writing, scientific outreach, or non-tenure track teaching professor positions. Additionally, she has mentored three previous postdoctoral researchers who have all started independent careers as tenure-track faculty, with two recently being awarded tenure. Finally, Dr. Kucenas has mentored over 50 undergraduate students (>95% women), all of whom have gone on to pursue additional professional training in medical and/or graduate school.

Adrian Halme, Assistant Dean for Graduate Research & Training Halme is an Associate Professor in UVA's Department of Cell Biology and also serves as the Assistant Dean for UVA's umbrella Biomedical Sciences (BIMS) graduate program. Using the *Drosophila* model system, Halme's lab aims to resolve the molecular pathways involved in regenerative growth following tissue damage. Thus, Halme is a scientist interested in fundamental biological processes and is also a graduate program administrator who oversees the larger graduate training ecosystem at UVA.

For several reasons, Halme's perspective as Assistant Dean for Graduate Research & Training will be invaluable to our *Internal Advisory Board*. First, as one who is in part responsible for PhD training at UVA, Halme is keenly aware of national trends driving best practices in graduate education. His insights will ensure that our *ETP* remains aligned with modern teaching and mentoring standards. Second, Halme will keep us abreast of any changes to coursework provided to our PhD students in their first and second years of graduate school, thereby enabling us to adjust our curriculum accordingly. Finally, as described above, most of our students will enter our *ETP* as members of UVA's *Neuroscience Graduate Program*. However, as our BIMS umbrella program welcomes ~50 new PhD students per year, Halme will be able to identify prospective trainees who may be initially overlooked during our recruiting efforts.

<u>Doug Bayliss, Chair & Professor of Pharmacology</u> Dr. Bayliss has a broad background in physiology, with a longstanding interest in understanding mechanisms of ion channel regulation and consequences for physiology and behavior. His laboratory studies cellular and ionic mechanisms that regulate brain function, with a particular interest in the receptors,

signaling pathways, and ion channel effectors that underlie neurotransmitter/neuropeptide modulation of brainstem neurons involved in cardiorespiratory control. Another area of interest is in understanding biophysical properties and activation mechanisms of Pannexin ion channels, which are widely expressed and release ATP and other metabolites for intercellular signaling in multiple (patho)physiological contexts.

Dr. Bayliss has been primary mentor for seven graduate students, including two PhD students currently working in his laboratory (one URM). One MD/PhD graduate just matched for his residency of choice, and another recently completed her residency. The three remaining graduated PhD students had successful postdoctoral experiences and moved on to gainful employment (at NIH, Pfizer, and ASPET). To date, all PhD students have obtained extramural fellowship funding (6-NRSA; 1-AHA). Among the five graduated students, four received recognition as the top students in their respective programs, with one selected as runner-up (Hungerford Award) and another as the overall top graduate student (Peach Award) across all biomedical graduate programs. Dr. Bayliss has served on >60 thesis committees for PhD students and hosted >25 undergraduates in the laboratory, many of whom were themselves mentored by graduate students. Dr. Bayliss is committed to training scientists from diverse backgrounds and has hosted four summer students from the SRIP program at the University of Virginia. He has received two awards recognizing his mentoring: Distinguished Mentor Award for Undergraduate Independent Research and Robert J. Kadner Award for Outstanding Graduate Teaching.

Dr. Bayliss has also directly supervised the activities of 15 postdoctoral fellows, two of whom are currently in the laboratory. Among these, seven now hold academic faculty positions, four are in research positions at pharmaceutical companies or other universities, and one works for the FDA. NRSA postdoctoral fellowships were obtained by three of four eligible postdoctoral fellows; two fellows held transitional grant/fellowships from the AHA, and one obtained a Parker B. Francis fellowship. He also served as K08 mentor for a clinician-scientist who is now a well-funded Professor of Anesthesiology and for another who was recently promoted to Associate Professor in Anesthesiology. As Chair of Pharmacology, he has recruited and mentored 10 junior faculty members who established productive, NIH-funded laboratories.

B4. External Advisory Board

Our External Advisory Board (EAB) provides an additional source of programmatic oversight for our ETP. We have recruited three internationally recognized epilepsy research and training experts — Drs. Isom, Wilcox and Huguenard — to provide outside perspectives on the implementation of our ETP. Each year, the Executive Committee will provide our External Advisory Board with reviews collected from our established feedback mechanisms (Section J), as well as a summary of trainee progress. The EAB will formally meet with our Executive Committee once per year (Figure 2).

Lori Isom, Chair of the Department of Pharmacology, University of Michigan Dr. Isom aims to resolve how variants in ion channel genes can lead to neurological or cardiovascular diseases called channelopathies. Her work focuses on human variants in genes encoding voltage-gated sodium channel α and β subunits that lead to a devastating pediatric epileptic encephalopathy called Dravet syndrome, a disease with a high risk of Sudden Unexpected Death in Epilepsy (SUDEP). Dr. Isom has proposed that SUDEP arises from simultaneous arrhythmias of the brain and heart due to the expression of mutant sodium channel genes in both organs. Her lab aims to discover novel targets for epilepsy therapeutics and to identify biomarkers for SUDEP risk.

Dr. Isom has trained many PhD students and postdoctoral researchers during her career, and many of them have ultimately achieved great success in academia and the biotech industry. Dr. Isom has received numerous awards for research and mentoring, including her current NINDS Javits R37 MERIT award and the University of Michigan Rackham Distinguished Graduate Mentoring Award. Dr. Isom's achievements in epilepsy research were recently recognized when she was awarded the 2023 Basic Science Award from the *American Epilepsy Society*. In 2021, Dr. Isom was elected to the prestigious *National Academy of Medicine*. As the PI of Michigan's Pharmacological Sciences Training Program T32 grant, Dr. Isom will be in an excellent position to provide guidance to our *Epilepsy Training Program*.

Karen Wilcox, Chair of the Department of Pharmacology & Toxicology, University of Utah The Wilcox laboratory is interested in understanding basic mechanisms underlying epileptogenesis, seizure generation, and therapy-resistance to anticonvulsant drugs. The Wilcox lab uses electrophysiological, calcium imaging, pharmacological, behavioral, genetic, immunoblot, and immunohistochemical techniques in a variety of *in vitro* preparations and animal models of epilepsy. In 2019, Dr. Wilcox was awarded an R37 NINDS Javits Neuroscience Investigator Award for her work on the role of microglia in temporal lobe epilepsy.

Dr. Wilcox has successfully mentored 11 post-doctoral fellows, as well as 13 current and former neuroscience, biological chemistry, biomedical engineering, and pharmacology, and toxicology graduate students. Of those trainees, six were URM, several have disabilities, several are openly from the LGBQT community, and 13 are women. In addition, she has mentored

numerous undergraduate and high school students in her laboratory. Dr. Wilcox's commitment to training is also reflected in her roles as chair of the curriculum committee for Utah's Interdepartmental Program in Neuroscience, chair of Utah's Graduate Training Committee for the Department of Pharmacology & Toxicology, and as a member of Utah's Graduate Admissions Committee and the Graduate Council at the University of Utah. Nationally, Dr. Wilcox served as co-chair of the Fellows/Junior Investigators Professional Development Committee for the *American Epilepsy Society* (AES) from 2016 to 2018. This committee is responsible for developing content and mentoring activities for clinical and postdoctoral fellows at the AES annual meeting. Finally, Dr. Wilcox serves as MPI on a recently awarded T32 training grant in Neuroimmunology, as well as an R35 postbaccalaureate training program for underrepresented groups in neuroscience. Collectively, Dr. Wilcox's experiences will establish an important resource for evaluating and advising our *ETP*.

John Huguenard, Professor of Neurology, Stanford University Dr. Huguenard's lab aims to resolve the neuronal mechanisms that underlie synchronous oscillatory activity in the thalamus and the cortex, particularly those oscillations associated with cognitive processes and certain forms of epilepsy. The Huguenard lab is also interested in comorbidities in epilepsy, such as ASD, and whether the circuit abnormalities in ASD may overlap with those of epilepsy. For his research accomplishments, Dr. Huguenard has been recognized with (1) An R37 Javits Merit Award; (2) The Research Recognition Award from the American Epilepsy Society; and (3) Induction as a Fellow of the American Association for the Advancement of Science (AAAS) in 2015.

In addition to his epilepsy research accomplishments, Dr. Huguenard is also a staunch advocate for trainee development. He has served on the Professional Advisory Board for the *American Epilepsy Society* and directed Stanford's Neuroscience Graduate Program for seven years. Dr. Huguenard also served as co-director of Stanford's longstanding *Postdoctoral Training Program in Epilepsy Research* (T32). His expertise in the basic mechanisms of seizure generation—coupled with his demonstrated commitment to training future epilepsy researchers—will enable him to provide important evaluations and recommendations for our *ETP*.

B5. Trainee Advisory Board

Our *Trainee Advisory Board* (*TAB*) will represent the trainee perspective and consists of two *ETP*-funded trainees and one predoctoral student working in an *ETP* mentor's lab who is not necessarily funded by the *ETP*. For instance, this third *TAB* member could be a trainee who has rolled off *ETP* funding or is training grant ineligible. This perspective is valuable because nearly all *ETP* activities are open to all trainees participating or interested in epilepsy research to benefit the larger UVA epilepsy research and training community. The program directors will meet with the *TAB* as needed by either group, and the *TAB* will join for part of the quarterly *Executive Committee* meetings to provide input to each of the *ETP* objectives, discuss any timely issues or topics, and review evaluations (**Section J**).

C. Primary Mentors

Trainees of the *ETP* will carry out their PhD research in labs managed by the program's *Primary Mentors* (**Table 1**). Junior faculty members who have not yet graduated a PhD student are designated as preceptors. *ETP* preceptors will be assigned a senior advisor to facilitate with trainee mentorship (see **Section E2**). In addition to the members of the *Executive Committee* described above, *Primary Mentors* include:

Stephen Abbott, Assistant Professor of Pharmacology Dr. Abbott is an Assistant Professor in the Department of Pharmacology. Using animal models, his lab aims to improve the treatment of cardiovascular disease and respiratory disorders in humans by elucidating the neural systems that are required for the homeostatic reflex-control of respiratory and cardiovascular function. Dr. Abbott's work also provides information that is pertinent for understanding why patients with epilepsy experience autonomic dysfunction, blood pressure instability and respiratory arrest, which in the most severe circumstances can result in Sudden Unexpected Death in Epilepsy. To achieve this, the Abbott lab uses a combination of neurophysiology and neuroanatomy combined with genetic and inducible models of human disease.

Training in the Abbott lab focuses on developing a sound understanding of functional neuroanatomy, as well as providing trainees with the skills needed to be successful in whatever career they choose. To date, he has advised two predoctoral trainees and one postdoctoral trainee, who are all currently pursing research careers in academia and industry.

Annual Research Support			
Mentor	Direct Costs		
Abbott	\$425,000		
Acton	\$299,500		
Beenhakker	\$322,050		
Bertram	\$275,000		
Burnsed	\$70,000		
Eyo	\$941,431		
Ferris	\$362,241		
Goodkin	\$183,493		
Joshi	\$217,000		
Kapur	\$637,395		
Kuan	\$1,342,618		
Long	\$285,000		
Nieh	\$225,256		
Patel	\$781,604		
Perez-Reyes	\$579,219		
Sontheimer	\$1,103,003		
Wenker	\$325,000		
Zawar	\$128,333		
AVERAGE \$472,397			
Table 1. FTP Mentors and			

Table 1. *ETP* Mentors and Preceptors Research Support

Scott Acton, Professor of Electrical and Computer Engineering Dr. Acton has 30 years of experience in image analysis research. His best-known work is in segmentation and tracking of biological objects from microscopy. Dr. Acton has two books on these subjects: *Biomedical image analysis: tracking* and *Biomedical image analysis: segmentation*. He has been named Fellow of the Institute of Electrical and Electronics Engineers (IEEE) for "contributions to biomedical image analysis." His laboratory, Virginia Image and Video Analysis, is fully capable of producing high-quality, open-source software that can be used in scientific laboratories and imaging centers. During the past year, his group has been investigating automated analysis techniques for super-resolution microscopy. Recent machine learning methods have included diffusion networks and transformer networks.

In the last few years, Acton's biologically oriented research has concentrated on problems in microscopy for the analysis of bacteria and neurons. His group has pioneered new methods of segmenting cells and matching/comparing cells using a combined morphological, graph-theoretic approach. Their 2011 paper on neuron matching won a best paper award. Acton's group demonstrated the first fully automated algorithm for 3D neuron segmentation and provided the first solution to morphological neuron matching. Most recently, Dr. Acton's group has demonstrated the ability to segment individual bacteria in a 3D biofilm.

Dr. Acton has been primary mentor for 25 PhD students and 35 MS students. Several of the PhD students are in academic positions such as MIT, University of Alberta, Nanying University, and the University of Vermont. Several are in top industry positions at Microsoft, Meta/Facebook, Dupont, KLA Tencor, and Amazon. Acton has also mentored eight postdoctoral researchers who are now in academic positions across the world including Middlebury, Özyeğin University, University of Western Carolina, and the Indian Statistical Institute.

Edward Bertram, Professor of Neurology Dr. Bertram is a clinician scientist who uses animal models of epilepsy to identify treatment targets in seizure circuits and to determine how those targets can be modulated to suppress seizures. His emphasis is on the thalamocortical interactions that support seizures. Dr. Bertram is also developing novel models for epilepsy that will provide new insights into the circuitry of different types of epilepsy. Collectively, Dr. Bertram's studies make use of *in vivo* physiology in anesthetized and awake animals so that his lab can understand circuit interactions. Many of their studies draw from clinical experience with the primary purpose of tying his lab's work to the human condition to maximize clinical applicability. Another major theme of interest in Dr. Bertram's lab is drug resistance in epilepsy. About one third of people with epilepsy have incomplete control of their seizures. Dr. Bertram's lab has documented therapy resistance in a rat model of chronic limbic epilepsy, and their goal is to use this model to study possible mechanistic contributors to treatment failure.

Jennifer Burnsed, Associate Professor of Pediatrics (preceptor) Dr. Burnsed is a neonatologist and clinician investigator. Her lab studies neonatal hypoxic-ischemic (HI) encephalopathy, the most common cause of neonatal seizures and a common cause of neurodevelopmental deficits, including cerebral palsy. The Burnsed lab uses a well-established mouse model to investigate the effects of neonatal HI seizures on neuronal activity and on cognitive and behavior outcomes. In addition, she uses this model to investigate the potential neuroprotective effects of lactate receptor, HCAR1. Her lab uses techniques such as tissue clarification, multiphoton microscopy, rodent electroencephalography, electrophysiology, and behavioral assays. Dr. Burnsed founded and co-directs the UVA NeuroNICU Program. Her clinical research interests include neonatal neurocritical care, early intensive therapies in high-risk preterm infants, and outcomes of infants with hypoxic-ischemic encephalopathy. Dr. Burnsed has trained two neurology fellows, one pediatric resident, four medical students, four visiting graduate students, and 12 undergraduate students.

Heather Ferris, Assistant Professor of Medicine Dr. Ferris holds appointments in both the Division of Endocrinology and Metabolism and the Department of Neuroscience; her lab is located within the Department of Neuroscience. Her lab is also a member of UVA's Brain, Immunology and Glia (BIG) Center. She also maintains a strong relationship with the Endocrine Division, which has a long history of active basic science research in both diabetes and neuroendocrinology; her trainees have access to both of these pools of talent. Dr. Ferris serves as a mentor for students in both the pharmacology and neuroscience graduate programs, and she has sponsored medical students in her lab for summer research projects and undergraduates through a diabetes summer research experience. Although her lab is still relatively new, Dr. Ferris has already mentored students at all levels of training. To date, she has mentored two postdoctoral researchers, three graduate students, three medical students, and 13 undergraduates. Of these 21 trainees, 13 are women and four are from URM groups. She has received significant training through both clinical and basic science departments in bias reduction to help support and grow this diverse talent pool.

<u>Suchitra Joshi, Research Associate Professor of Neurology (preceptor)</u> Dr. Joshi aims to resolve how female reproductive hormones regulate neuronal activity and brain function. The cyclic changes in the levels of these hormones occurring

during reproductive years impact seizures in women with epilepsy. These seizures, called catamenial seizures, represent the most common form of drug refractory seizures, affecting up to a third of women with epilepsy. Dr. Joshi's research aims to understand the ways progesterone regulates neuronal activity and seizures and determining the changes occurring in epilepsy that could affect progesterone's efficacy. Using transgenic mice and electrophysiology, biochemistry, molecular biology, and imaging techniques, her research has revealed that progesterone likely exerts opposing actions on neuronal activity occurring at distinct times. Through its metabolite allopregnanolone, progesterone rapidly potentiates GABAergic inhibition and suppresses seizures. However, through the direct activation of progesterone receptors, the hormone mediates a slowly emerging increase in glutamatergic transmission and promotes seizures. These contrasting effects may impact progesterone's therapeutic potential.

Women are also disproportionately affected by chronic pain and migraines relative to men. Dr. Joshi's recent studies have uncovered the role of progesterone receptors in regulating pain sensitivity and migraine. Going forward, she aims to obtain insights into molecular mechanisms regulating these effects using tissue and single-cell RNA sequencing and an indepth elaboration of alterations in the network activity. Dr. Joshi has mentored seventeen undergraduate students, three of which have co-authored research papers.

Alex Kuan, Professor of Neuroscience Dr. Kuan was trained as a developmental neurobiologist and, since 2001, has maintained an independent research program that studies normal neurodevelopment, developmental brain disorders, and ischemic brain injury. He has published over 90 research papers and has trained over 20 postdoctoral researchers or graduate students. He has also served as a regular member for two NIH study sections (Neurogenesis and Cell Fate; Developmental Brain Disorders). More recently, Dr. Kuan has expanded his research to include the "aging brain." His lab specifically studies the neurotoxicity of hyperphosphorylated tau oligomers, which appear to serve as the driving force for neurodegeneration and cognition decline in Alzheimer's Disease. He also investigates the roles of microglia in neurovascular coupling and purinergic signaling in the aging brain. Finally, his lab also studies seizures triggered by cerebral ischemic stroke or neuronal senescence.

Nicole Long, Assistant Professor of Psychology (preceptor) The aim of Dr. Long's research program is to establish the core neural mechanisms that support memory encoding and memory retrieval. Identifying these mechanisms is central not only to our basic understanding of how memory processes operate but also to determining how memory mechanisms interact with other cognitive functions and how these mechanisms go awry in healthy aging and disease. She has a broad background in psychology with focused training in the cognitive processes and neural mechanisms that support memory formation and memory retrieval. Complementing her conceptual expertise, Dr. Long has technical expertise in the collection and analysis of scalp electroencephalographic (EEG), intracranial electroencephalographic (iEEG), and functional magnetic resonance imaging (fMRI) data. She also has specific expertise in univariate and multivariate analysis of high dimensional brain data, including the use of machine learning algorithms to decode memory brain states.

Dr. Long has direct mentoring experience with brain recording and analysis techniques and has trained undergraduate students, research assistants, and graduate students to collect and analyze neural data to test theoretical questions about memory function. She has also received direct training in mentoring, as a scholar in the integrated Translational Health Research Institute program (2020-2022), through a two-day mentoring workshop facilitated by the Associate Dean of Graduate and Medical Scientist Programs at the University of Virginia (Spring 2022) and through the NIH's Raising a Resilient Scientist series (Spring 2024).

Edward Nieh, Assistant Professor of Pharmacology (preceptor) Dr. Nieh is an Assistant Professor in the Pharmacology department at the UVA. His general research goals focus on studying neural population dynamics in neuropsychiatric disorders, especially those involving the brain's reward processing systems, such as drug addiction, and those involved in stress and anxiety, such as post-traumatic stress disorder. Dr. Nieh is also interested in understanding the neural mechanisms underlying epilepsy, with a spotlight on predicting and tracking seizures through the brain. Dr. Nieh has a broad background in biomedical engineering, computational neuroscience, and systems neuroscience. His research program currently uses simultaneous two-photon cellular-resolution stimulation and imaging, one-photon head-mounted miniscopes for freely moving behavior, *in vivo* electrophysiology, computational techniques for extracting population neural codes, and complex behavioral assays in both controlled and naturalistic environments.

Dr. Nieh is deeply committed to teaching and mentorship. As a graduate student at MIT, he served as a teaching assistant for the flagship Introductory Neuroscience course and was awarded the Angus MacDonald Award for Excellence in Undergraduate Teaching. His teaching and mentorship style focuses on individualized relationships; the specific needs of each mentee dictates his interactions. Dr. Nieh focuses on teaching students to question science, aiming to help students understand why we believe a fact to be true rather than the fact itself. To this end, Dr. Nieh focuses on experimental methods and helping students learn how to design experiments to tackle difficult questions. Dr. Nieh started his lab at

UVA less than two years ago and is already training three PhD students, one postdoctoral trainee, and six undergraduate students. While a postdoc at Princeton, Dr. Nieh trained three PhD students and several undergraduate students.

Edward Perez-Reyes, Professor of Pharmacology Dr. Perez-Reyes's PhD studies were in Neuropharmacology, and his postdoctoral studies included both molecular cloning and electrophysiology. His early career built on these interests, leading to cloning and characterization of the biophysical properties of the low voltage-gated T-type calcium channel family. A pivotal moment in his career was when he studied how the effects of mutations in the Cav3.2 channel might contribute to absence epilepsy. Since then, he has devoted his efforts to developing cures for the epilepsies. Major contributing factors to this career change were the incredible human and physical resources dedicated to epilepsy at UVA and the spirit to train and collaborate with each other. Dr. Perez-Reyes's current research focuses on developing a gene therapy for focal epilepsy, developing animal models that mimic the human disorder and are amenable to screening campaigns (few are!), and deciphering the roles of astrocytes and microglia in focal epilepsies. Dr. Perez-Reyes has trained three PhD students, seven international Master's students, nine postdoctoral trainees, and 12 undergraduate students.

Harald Sontheimer, Chair & Professor of Neuroscience The Sontheimer lab has been studying the physiology of astrocytes in a number of disease processes for over 25 years. Initially, his focus was on the role of astrocytes in acquired epilepsy, and these studies revealed changes in glutamate transporters and gap junctions in mesial temporal lobe epilepsy. These findings then turned his attention to malignant astrocytes in glioma, and he discovered that glutamate transporters are entirely dysregulated to the point that these tumors release glutamate rather than remove it. He identified the system XC transporter (SXC) as the culprit and showed that glutamate release via this antiporter is a major driver for tumor-associated epilepsy. As a result, his lab is now studying the role of SXC in other forms of epilepsy. In another line of research, Dr. Sontheimer is studying the interactions of astrocytes and brain vasculature in normal aging and in Alzheimer's disease. These studies use *in vivo* two photon imaging extensively.

Regarding training, Dr. Sontheimer has trained 35 PhD students, including 13 MSTP students, and 27 postdoctoral researchers, many of who run successful research laboratories today. He also mentors countless undergraduates, and his lab typically has between 8-10 students working in the lab next to graduate students and postdocs. Many of these undergraduates have gone on to doctoral or medical training. Dr. Sontheimer's trainees have all completed their PhD research in 4-5 years and have all published well. He trains students to be rigorous and unbiased in their experimental design, methodology, analysis, interpretation, and reporting of results. He has a track record of supporting trainee's participation at conferences and workshops in various areas of alternate career paths. As chair of the Department of Neuroscience, Dr. Sontheimer also works hard to ensure everyone's success and to make sure he provides an inclusive training and mentoring environment.

lan Wenker, Assistant Professor of Anesthesiology (preceptor) Dr. Wenker has a background in neurobiology and physiology, with a longstanding interest in understanding how the brainstem controls automatic processes, such as breathing and cardiovascular function. Within this context, his research program currently investigates the role of brainstem neural circuitry in the respiratory, cardiac, and vascular disruptions during seizures and sudden unexpected death in epilepsy (SUDEP). SUDEP is the unexpected and unexplained death of a person with epilepsy, accounts for approximately 14% of all deaths of people with epilepsy, and, of all the neurological disorders, is second only to stroke in the number of life years lost. Dr. Wenker's lab made the novel observations that the tonic phase apnea and postictal hypotension that occur during seizures cause mortality. Current work aims to understand how aberrant seizure activity affects brainstem neural circuitry to produce these fatal complications.

Dr. Wenker began his faculty position in June of 2023; thus, his official mentor roles are limited. However, during his graduate studies at the University of Connecticut, he mentored several undergraduate students who have pursued careers in science and medicine, including Erin Poss (PhD, University of California, San Francisco), Jarelys Michelle Hernández Jiménez (MD, San Juan Bautista School of Medicine), Irene Cheng (PhD, University of Virginia), and Andrew Goldsmith (MD, University of Connecticut School of Medicine). Many of these mentees were from underrepresented backgrounds in the research community. As a postdoc at UVA, Dr. Wenker mentored Abrar Idrissi, Panchal Payal, Beth Blizzard, and Priyanka Saraf, all now enrolled in medical school. Under his mentorship, Abrar Idrissi and a current undergraduate mentee, Miranda Sculimbrene, were awarded competitive summer research fellowships at UVA. As an independent investigator, Dr. Wenker currently mentors a postdoctoral researcher in his laboratory, Dr. Selena Garcia DuBar. Together, they have already submitted a Diversity Supplement and plan to write a transition award for her to study the connection between epilepsy and Alzheimer's Disease, the focus of her PhD studies.

D. Clinical Faculty

 \mathbf{T} rainees appointed to the ETP are PhD students. However, the ETP is guided by the philosophy that impactful clinical

research is best achieved when basic scientists have a deep understanding of the clinical landscape. Therefore, our program includes faculty with extensive clinical training so that *ETP* trainees acquire a strong clinical perspective. Our clinical faculty are not mentors per se but will establish a robust clinical training experience by facilitating the development of our *Epilepsy Research Today* course and workshops (see **Section H2**). These faculty include:

Nathan Fountain, Professor of Neurology Dr. Fountain has the expertise, leadership, training, and motivation necessary to successfully implement the training plan of our *ETP*. His research interest is in experimental therapeutics related to epilepsy. As director of the UVA *Comprehensive Epilepsy Program*, Dr. Fountain created a clinical research infrastructure that has successfully completed many research projects across NIH-, foundation-, and industry-supported programs since its inception in 1997 (see >100 PubMed publications). Dr. Fountain has been involved in the development of almost all approved drugs and devices for epilepsy. His insights on drug development are also informed by his prior role as chair of the FDA Advisory Committee on Peripheral and Central Nervous System Drugs and as founder and co-chair of the Research Roundtable for Epilepsy. Dr. Fountain has directed the two-year clinical epilepsy fellowship at UVA since 1997, which has 3-6 fellows at a time. He has trained 49 fellows, 25 of which have pursued academic positions. For the *ETP*, Dr. Fountain will serve as an advisor to provide insight, guidance, and advice to mentees so that they are ultimately successful. As *ETP* clinical faculty, Dr. Fountain's administrative role will be to promote and support the interaction of T32 participants with the research and educational aspects of the Comprehensive Epilepsy Program and clinical epilepsy fellows.

Mark Quigg, Professor of Neurology Dr. Quigg is the TR Johns Professor of Neurology at UVA. His clinical responsibilities include Medical Directorship of the Clinical EEG, Intensive Monitoring, and Evoked Potential Laboratories. He is also the founder of the UVA Neurological Sleep Laboratory (now part of the multidisciplinary Sleep Center). His research work focuses on the interactions among sleep, epilepsy, and circadian regulation, and the methods of epilepsy surgery and surgical evaluation with a history of NIH, industry, and foundation funding as PI or site PI. His work in education is extensive. He serves as the Education Chair for the NIH-NINDS NeuroNEXT consortium and is responsible for network fellowship training and programming. He is also a member of the Executive Committee for the NIH-NINDS Clinical Trial Methodology Course and is co-PI of a proposed continuation of this rigorous program of training early-phase faculty. He is former co-chair of the Research and Education Council of the American Epilepsy Society (AES) and the current co-chair of the Clinical Neurophysiology Section of the American Board of Psychiatry and Neurology's Examination Committee. He is the founding chair of the Sleep and Epilepsy Workgroup of the AES. Local education activities include his founding of the Virginia Brain Institute-sponsored Neuroscience Clinical Research Interest Group, a peer-based grant review service. He and his colleagues have trained more than 50 fellows in neurophysiology and epilepsy.

Erika Axeen, Assistant Professor of Neurology Dr. Axeen is an Assistant Professor in Neurology and pediatric epileptologist at UVA. She specializes in evaluating and managing seizures and epilepsy in children. She has a particular interest in the clinical diagnosis and management of genetic epilepsies, including brain malformations. In the inpatient setting, Axeen sees children as part of the pediatric neurology team, and she cares for both children and adults as part of the inpatient epilepsy team. In addition, she is associate program director for UVA's epilepsy fellowship and director of the journal club for our pediatric neurology residency. Through her clinical duties, she works regularly with undergraduate student observers, medical students, child and adult neurology residents, and epilepsy fellows. She has served as a longitudinal mentor for nearly 15 child neurology residents and epilepsy fellows, providing career advice during their transition to attendings, since 2017.

E. Mentorship Oversight

E1. Criteria for Mentorship

With the substantial growth of the UVA neuroscience research community during the last 10 years, the *ETP* remains selective, but not exclusive, when aligning training faculty with the program. Participation in the *ETP* is open to graduate faculty who: (1) Express an interest and willingness to participate in the academic activities of the *ETP* (Section H); (2) Maintain active research programs that can support the research of a PhD candidate in neuroscience; and (3) Qualify to serve as a thesis advisor for *ETP* PhD trainees by virtue of training and academic activity. Tenure-track/tenured or research faculty are invited to apply to become members of the *ETP* by submitting their CV, a description of their epilepsy-related research and grant support, and a mentorship statement. Applicants are evaluated by the *Executive Committee* with decisions made based on epilepsy-relatedness of research, publication record, and grant/research support. Mentoring history with an explicit record of promoting and enhancing diversity, teaching in neuroscience-related courses, and participation in epilepsy program activities are also considered when evaluating more senior faculty.

The current *ETP* faculty (**Data Table 4**) are in one of two groups: **(1)** Faculty who have "R01-like research funding" as defined by the NINDS, have a clear record of having successfully trained predoctoral trainees, and are designated as *mentors* who can nominate their trainees for appointment to the *ETP* T32; and **(2)** Faculty who have R01-level funding or

are pre-tenure (supported with start-up funds) but lack evidence of having successfully trained graduate students and are designated as *preceptors*. The latter group can nominate trainees to the *ETP* T32 but require an *ETP* faculty member with prior training experience to serve as a senior advisor for the trainee and preceptor. These advisors are chosen from a list of *ETP* mentors and ensure that the preceptor is following best training practices and that their trainee is making sufficient progress. To identify the most appropriate person to pair with a preceptor, the *Executive Committee* will consider the stage of the preceptor (e.g., is this their first student?) and their research area. In almost all cases, a senior advisor suggested by the preceptor is chosen. The advisory process includes close monitoring and evaluation by the *ETP* program directors, *Executive Committee*, and the trainee's thesis advisory committee. Finally, (3) we anticipate the need for another, *affiliated faculty* status that includes members whose funding has lapsed, thereby making them ineligible to nominate trainees for appointment to the *ETP* T32. However, these faculty still have much to offer to the *ETP* in terms of co-mentorship, teaching, membership on thesis advisory committees, recruitment and retention of trainees, and involvement in programmatic activities. Importantly, these designations are dynamic, and faculty can quickly transition between these designations based on the required criteria.

Based on these criteria, we have assigned mentor or preceptor designations to ETP faculty based on their mentoring experience (Data Table 2). Each year, the designation of each ETP faculty member will be evaluated through careful review by the program directors and remainder of Executive Committee prior to the call for nominations of ETP trainees. The Executive Committee will evaluate: (1) Contribution to high quality mentorship by assessing the success of mentor/preceptor trainees and exit survey information provided by recent graduates; (2) Attention to robust experimental design and statistical and experimental rigor, assessed by the quality of their publications and comments related to reproducibility and rigor that are provided in student committee meeting reports; (3) Promotion of quantitative literacy by assessing the work of their trainees in papers and aptitude in committee meetings; and (4) Commitment to creating an inclusive environment that welcomes varied perspectives of all trainees and faculty. Once all mentors and preceptors have been evaluated, faculty will be provided feedback and will be informed of their standing as participating faculty in the ETP. Importantly, faculty who demonstrate weaknesses in any of these areas will be advised by a member of the Executive Committee or a program director during the next year to help them achieve their goal of excellent mentorship in all areas related to graduate training. Faculty nominations to become mentors (or reinstated) in the ETP will be accepted on a rolling basis upon receipt of a CV, description of their epilepsy-related research and grant support, and mentorship statement with an explicit requirement to address promoting diversity and inclusion in their labs and the broader ETP and UVA communities. The Executive Committee will review mentor eligibility on an ad hoc basis.

E2. Mentoring Junior Preceptors

Mentoring assistant professors is vital to their success and career development. Even when an *ETP* preceptor is not actively training a student, they will be assigned a mentorship committee, led by an *ETP Executive Committee* member and two other senior mentors. The mentorship committee will meet with the junior faculty member twice per year to discuss all aspects of career success, including mentorship, grantsmanship, teaching advice, conversations on how to build a supportive and inclusive lab environment, and leadership development. Every two years, a preceptor colloquium will be held to exchange insights, discuss best practices, and cultivate a supportive community.

E3. Removal of Preceptors & Mentors

The Executive Committee will review all ETP mentors once per year. Mentors or preceptors will be removed from the program, or transitioned to affiliated faculty, based on a combination of factors: (1) No student training for five or more years; (2) Prolonged loss of funding; or (3) Lack of participation in programmatic activities. These measures are designed to protect ETP trainees. In the unlikely event that a mentor has insufficient funds to support the research of a trainee, several institutional measures are in place to ensure that funding lapses do not prevent trainee progress. These measures include interim funding mechanisms that award up to \$100k for one year when individual research grants have lapsed. Additionally, before a student can join a lab, the home department of the host lab commits to supporting students in the event of a funding lapse. In all cases, the ETP co-directors and Executive Committee will closely monitor our mentors to ensure that every ETP trainee can complete their degree without disruption.

Finally, UVA has several formal guidelines for researchers suspected of misconduct. Should an *ETP* mentor be formally suspected in misconduct, we will immediately remove them from all training responsibilities until a verdict is reached. Once reached, the *Executive Committee* will consider what steps, if any, can be taken for mentor remediation. Any consideration of remediation will be driven by the best interests of all *ETP* trainees. We will also consult with UVA's *Research Integrity Officer*, David Hudson, while formal remediation options are considered.

F. Trainee Outcomes

The primary goal of our ETP is to train scientists. The mentors of our ETP have trained many pre- and postdoctoral

researchers who have garnered much professional success. Most of our predoctoral trainees (i.e., the trainee population relevant for our *ETP*) enter postdoctoral research programs upon graduation. In the last 20 years, many of our predoctoral trainees have continued with postdoctoral positions at research intensive institutions, including Johns Hopkins, MIT, Texas A&M, University of Delaware, Stanford, University of Michigan, UCSF, UPenn, University of Cincinnati and the NIH. Several of these trainees have ultimately earned academic posts ranging from research/senior scientist positions to tenure-track faculty positions. Many of our trainees have also established careers within the biotech industry. **Data Table 8A** enumerates the outcomes of recently graduated trainees associated with the mentors of our *ETP*.

F1. Summary of Current Trainees

Currently, the mentors of our *ETP* collectively train 31 PhD students (**Data Tables 1, 2**). These students formally belong to UVA's Graduate Programs in Neuroscience (73%), Pharmacology (17%), and Biology (10%), and are approximately evenly distributed across years 1 to 5 of their respective programs. Most of our current trainees identify as female (68%). Importantly, 31% of our trainees are members of an underrepresented community (e.g., African American, Latinx). Nearly all of our senior trainees are currently identifying academic postdoctoral labs to join or have already formally accepted a postdoctoral position in their future lab. Importantly, this demographic snapshot not only reflects trainees in UVA epilepsy-related labs as of 2024 but also reflects trainee demographics during the last decade, a period wherein our *ETP*

sustained much growth. Thus, these metrics are predictive of the trainee pool from which our *ETP* will draw in the future.

F2. Summary of Participating Faculty & Departments

A defining feature of UVA's ETP is the strength of the research environment and faculty. Our mentors have primary appointments in eight departments (Data Table 1). The basic science departments have degree-granting programs that are oriented to their specific disciplines and complement this training program (Data **Table 1**). Faculty with primary appointments in clinical departments in UVA's School of Medicine typically also hold secondary appointments in basic science departments. Each department participating in our ETP includes disciplines consistent with traditional scientific foci while also including specialized areas of interest relevant to neuroscience research. Also, several research centers connect faculty with common interests, including UVA's Program in Fundamental Neuroscience, the Center for Brain Immunology and Glia (BIG Center), and UVA's Brain Institute. Although neuroscience research at UVA is largely driven by graduate students, a robust undergraduate, postbaccalaureate postdoctoral research community also exists (20 among mentors, Data Table 1).

Many of our mentors also participate in other institutional training programs (Data Table 3), reflecting the collaborative spirit of our institution and the breadth of expertise and talents of the faculty. In fact, co-participation of our faculty across multiple programs is a strength of our ETP and a great benefit to our trainees. The collaborative spirit endemic throughout UVA's campus ensures that our

PI	Department	Collaborations	
	-	(Publication, Grant, Trainee)	
Abbott	Pharmacology	Beenhakker ^{P,G,T} , Patel ^G , Quigg ^G	
Acton	Electrical & Computer Eng.	Eyo ^P , Kapur ^{P,G,T}	
Axeen ^C	Neurology	Bertram ^T , Fountain ^T , Goodkin ^{P,G,T} , Kapur ^{G,T} , Quigg ^{P,G,T} , Zawar ^T	
Beenhakker	Pharmacology	Abbott ^{P,G,T} , Eyo ^T , Joshi ^P , Kapur ^T , Kuan ^G , Nieh ^T , Patel ^T , Perez-Reyes ^{P,G,T} , Quigg ^P ,	
Bertram	Neurology	Axeen ^T , Kapur ^{P,G,T} , Patel ^{P,G,T} , Perez- Reyes ^{P,G} , Quigg ^{P,T} , Zawar ^T Goodkin ^P , Joshi ^P , Kapur ^{P,G,T} , Kuan ^{P,T} ,	
Burnsed	Pediatrics	Goodkin ^P , Joshi ^P , Kapur ^{P,G,T} , Kuan ^{P,T} , Quigg ^P	
Eyo	Neuroscience	Acton ^P , Beenhakker ^T , Kapur ^G , Kuan ^{P,G} , Perez-Reyes ^{P,G} , Sontheimer ^P	
Ferris	Medicine	Kapur ¹ , Perez-Reyes ^G	
Fountain ^c	Neurology	Axeen ^T , Kapur ^{P,G,T} , Quiga ^{P,G,T} ,	
Goodkin	Neurology	Goodkin ^{P,T} , Zawar ^T Axeen ^{P,G,T} , Burnsed ^P , Fountain ^{P,T} , Joshi ^P , Kapur ^{P,G,T} , Patel ^G , Quigg ^{P,T} , Zawar ^{P,T}	
Joshi	Neurology	Beenhakker ^P , Burnsed ^P , Goodkin ^P , Kapur ^{P,G} , Kuan ^G , Perez-Reyes ^P	
Kapur	Neurology	Acton ^{P,G,T} , Axeen ^{G,T} , Beenhakker ^T , Bertram ^{P,G,T} , Burnsed ^{P,G,T} , Eyo ^G , Ferris ^T , Fountain ^{P,G,T} , Goodkin ^{P,G,T} , Joshi ^{P,G} , Kuan ^G , Patel ^T , Perez-Reyes ^{P,G} , Quigg ^{P,G,T} , Wenker ^{P,G} , Zawar ^{P,G,T}	
Kuan	Neuroscience	Beenhakker ^G , Burnsed ^{P,T} , Eyo ^{P,G} , Joshi ^G , Kapur ^G , Perez-Reyes ^G , Sontheimer ^{G,T}	
Long	Psychology	In-progress	
Nieh	Pharmacology	Beenhakker ^T	
Patel	Anesthesiology	Abbott ^G , Beenhakker ^T , Bertram ^{P,G,T} , Goodkin ^G , Kapur ^T , Perez-Reyes ^{P,G} , Wenker ^{P,T}	
Perez- Reyes	Pharmacology	Beenhakker ^{P,G,T} , Bertram ^{P,G} , Eyo ^{P,G} , Ferris ^G , Joshi ^P , Kapur ^{P,G} , Kuan ^G , Patel ^{P,G}	
Quigg ^C	Neurology	Abbott ^G , Axeen ^{P,G,T} , Beenhakker ^P , Bertram ^{P,T} , Burnsed ^P , Fountain ^{P,G,T} , Goodkin ^{P,T} , Kapur ^{P,G,T} , Zawar ^{P,G,T}	
Sontheimer	Neuroscience	Eyo ^P , Kuan ^{G,T}	
Wenker	Anesthesiology	Kapur ^{P,G} , Patel ^{P,T} ,	
Zawar	Neurology	Axeen ^T , Bertram ^T , Fountain ^T , Goodkin ^{P,T} , Kapur ^{P,G,T} , Quigg ^{P,G,T}	

Table 2. Existing Collaborations among *ETP* Faculty; ^CClinical Faculty

trainees not only derive benefits from our specialized *ETP* but also through the cultivation of an academic environment outside our laboratories that is both synergistic and comprehensive in all aspects of neuroscience research and training. The commitment of mentors to our trainees is underscored by the number of faculty who teach in neuroscience courses (**Figure 3A**), serve on thesis or postdoctoral advisory committees, serve in leadership positions, attend seminars, and comentor students (**Table 2**). *Importantly, other institutional training grants at UVA are completely distinct from our ETP in their training goals, administration, trainees, and programmatic requirements.* Thus, although our *ETP* is the only training program at UVA focused on predoctoral training for careers broadly in epilepsy research, our trainees nevertheless benefit from UVA's vibrant and expanding neuroscience community.

G. Diversity Efforts

Our ETP promotes and celebrates diversity at every level, a commitment that is reflected in our mentee recruitment and retention efforts (Section I), as well as in the equitable inclusion among our Executive Committee (Section B2, Figure B2), Internal (Section B3) and External Advisory Boards (Section B4), and our Training Program Evaluation efforts (Section J). Like many R1 universities, UVA is working to build a STEM faculty that is representative of its local and national communities, and our administration is deeply invested in righting historical wrongs. Therefore, we have included programmatic (Section E1) and university-wide plans to develop parity among our STEM faculty (Section I2), and we will leverage this T32 mechanism to formally drive these changes. We also recognize that diversity goes beyond ethnicity, race, and gender, and extends to experience, perspective, socioeconomic factors, and disability. We fully uphold the belief that supporting these unique perspectives enhances the richness and creativity of our research environment.

G1. Recruitment of Students

All trainees enter the graduate program either through UVA's Biomedical Sciences Graduate Program (BIMS) or Biology and Psychology graduate programs. BIMS is an umbrella program that recruits students into several graduate programs defined as clusters (Neuroscience, Biochemistry and Molecular Genetics, Cell Biology, Microbiology, Immunology, and Cancer Biology, Biomedical Engineering, Molecular Physiology and Biophysics, Pharmacology, and Pathology). Thus, *ETP*-eligible students enter UVA through diverse mechanisms. Nonetheless, irrespective of their programmatic affiliation, all students broadly interested in the neurosciences take the same courses during their first two years of graduate school (Section H1). If we identify a strong *ETP* recruit who is nonetheless deficient in neuroscience fundamentals, we will then require that this recruit enroll in courses established by UVA's Neuroscience Graduate Program.

Regarding student support, UVA's School of Medicine fully funds graduate students in their 1st year. During the spring semester of their 1st year, students enter into their specific PhD degree-granting programs. Funding for year 2 is provided by training grants, other internal fellowships such as those available from the Brain Institute, or funding through graduate mentors. Trainees who are committed to epilepsy research will apply to the *ETP* in the spring of their 2nd year so that selected candidates can start their epilepsy-related training at the start of their 3rd year of graduate training (see **Section 11** for trainee recruitment). We anticipate that most trainees will receive two years of support (Years 3 and 4 of their PhD training). However, a trainee's second year of support is contingent upon a favorable evaluation of their progress during their first year of funding.

H. Epilepsy Training Program

H1. Initial Training: Developing a Strong Foundation in Years 1 & 2

Our training program targets 3rd and 4th year PhD students and, first and foremost, aims to produce excellent scientists. We believe that epilepsy research establishes many training opportunities to support this aim. However, fully realizing our goal of producing strong scientists relies on a robust training experience provided to our students in their 1st and 2nd years of graduate school. Importantly, both PIs of this *ETP* have served (Patel) or are serving (Beenhakker) as the Director of UVA's *Neuroscience Graduate Program*. Dr. Beenhakker also serves on the steering committee for UVA's *Pharmacology Graduate Program*. Therefore, both PIs have extensive knowledge of UVA's biomedical PhD training environment, and both have helped to develop the curriculum established for our 1st and 2nd year PhD students.

All students entering UVA's various biomedical PhD programs—UVA has eight such programs—are required to take a comprehensive cellular and molecular course (BIMS 6000) during their first semester of graduate school (Figure 3). Neurocentric PhD students in Biology and Psychology also take BIMS 6000. UVA's umbrella program for the biomedical sciences (i.e., BIMS) administers this course. Soon after completing BIMS 6000, each student will have also completed their three required lab rotations and will have identified a lab for their PhD work. Although students who enter BIMS programs have identified a primary research interest (e.g., neuroscience), they are free to rotate with any BIMS-affiliated lab. Thus, the flexible nature of UVA's biomedical training environment affords first-year PhD students the ability to ultimately identify a mentor and lab that best serves them. This environment also ensures that our ETP will draw from a

diverse pool of biomedical research students at UVA. Thus, although it follows logically that neuroscience will serve as the primary interest of most trainees for this *ETP*, some students will enter the training program as part of UVA's Biology or Pharmacology graduate programs. Although the *ETP* will accept the curricular requirements established by these other degree-granting programs, our training program's *Executive Committee* will identify any neuroscience deficiencies among our *ETP* recruits and identify additional course work to address these deficiencies.

The selection of a PhD lab by a first-year student largely defines their future course trajectory. Students joining neuroscience research labs will naturally enroll in courses administered by UVA's *Neuroscience Graduate Program*. The flagship, graduate-level neuroscience course is NESC 8000 (**Figure 3A**) and is provided to all PhD students interested in the neurosciences, irrespective of their specific sub-field interests. This course provides students with foundational knowledge in a broad collection of disciplines ranging from developmental neuroscience to systems- and circuit-level neuroscience. Immediately following completion of NESC 8000, students enter one of three focused tracks: (1) Developmental and Molecular Neuroscience; (2) Systems and Circuit-Level Neuroscience; or (3) Neuroimmunology. Each track includes a foundational course wherein fundamental concepts are taught, and a methods course wherein the implementation of modern techniques is described. Finally, by the time a UVA biomedical PhD student has completed their 2nd year of graduate school, they will have also taken required courses in statistics: (1) *Practical Biomedical Statistics I* (BIMS 8380) and (2) *Practical Biomedical Statistics II* (BIMS 8382). Although some UVA biomedical PhD programs require only the first statistics course, *ETP* trainees are required to take both. Finally, students completing their 2nd year of graduate school will have also taken an ethics course (BIMS 7100) and will have successfully defended their written and oral qualifying exams. Therefore, the first two years of biomedical graduate education at UVA provides trainees of our *ETP* with a strong foundation to achieve their next training milestone: establishing a specific expertise in epilepsy research.

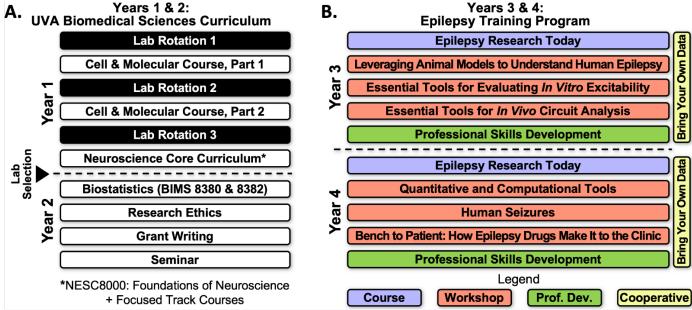


Figure 3. Overview of trainee curriculum. **A.** During their 1st year of graduate school, UVA students enrolled in biology/biomedical graduate programs at UVA enroll in foundational courses and rotate in labs. During their 2nd year, students enroll in statistics, ethics and writing courses. **B.** Our *ETP* proposes to support PhD students in their 3rd and 4th years. During this period, *ETP* trainees enroll in our weekly, comprehensive *Epilepsy Research Today* course (NESC 8050) and our brief, concentrated workshops (four per year). We also maintain a bi-weekly informal programming cooperative staffed by faculty who provide hands-on training in modern, computationally-intensive analysis tools.

H2. The Epilepsy Training Program: Developing Scientific Expertise in Years 3 and 4

A student's research progress during their 3rd and 4th year is often the most critical for ensuring that a student can complete an impactful body of PhD-level work within a reasonable timeframe. Thus, our *ETP* is designed to establish scientific expertise and ensure that students complete their PhD within the nationally defined average of ~5.5 years. Therefore, we have designed the *ETP* around a core curriculum (Figure 3B) that includes: (1) A weekly *Epilepsy Research Today* course; (2) An informal, bi-weekly programming cooperative called *BYOD* (Bring Your Own Data); and (3) Brief, concentrated workshops. This core curriculum (Section H2a) is supplemented by several additional, *ETP*- and UVA-sponsored training opportunities (Section H2b). Finally, as we ultimately aim to train scientists with strong quantitative and statistical skills, we also describe how the development of these skills are integrated throughout our *ETP* (Section H2c). We also highlight how trainees will leverage our *ETP* for the development of their future professions (Section H2d).

Below, we describe this comprehensive, ETP-sponsored training experience in detail.

H2a. Core Training in Epilepsy Research Epilepsy Research Today (ERT)

Our trainees are required to participate in our weekly course entitled *Epilepsy Research Today* (NESC 8050). The course occurs each spring and fall semester and includes a combination of formal didactic lectures, literature highlights, and research progress updates. Topics covered by this course include: (1) Seizure classification and treatment; (2) Animal models of epilepsy; (3) Cellular hyperexcitability; and (4) Modern tools of epilepsy research. In addition to formal lectures, the course also highlights student presentations of recent literature and research progress. *ETP* faculty who regularly attend the weekly course include Drs. Patel, Beenhakker, Kapur, Goodkin, Sontheimer, Eyo, Perez-Reyes, Burnsed, Zawar, Kuan, Bertram, and Wenker.

Epilepsy Research Today is also attended by our ETP-appointed and UVA staff biostatistician, Dr. Marieke Jones. Dr. Jones provides our students with an expert perspective on how to best evaluate biological data. To ensure that our students

derive the most from this perspective, we encourage students to explicitly describe the statistical approach (e.g., power analysis, effect size, statistical tests) they employ when evaluating their data. For example, when providing the audience with an update on their research progress, students devote several slides to describing *only* their statistical approach. Likewise, when highlighting recent literature, students do the same: describe the statistical approach in great detail. By doing so, Dr. Jones can provide concrete feedback regarding best statistical practices. This T32 mechanism will support Dr. Jones with 10% effort for this weekly statistical perspective.

Each hour-long lecture of the course is followed by 30 minutes of a student-run discussion. To ensure that our students have a comfortable atmosphere for this discussion, most faculty are not present. However, Dr. Jones remains for the duration so that our students have additional, more informal access to a biostatistician for follow-up questions. **Figure 4** provides the *Epilepsy Research Today* schedule for Spring 2024.

Spring 2024 - Epilepsy Research Today Schedule

DATE	TITLE	PRESENTER(S)
January 31	Mortality in older adults with epilepsy	Ifrah Zawar, MD, Neurology
February 7	Lactate neuroprotection via HCAR1 in neonatal HIE	Jen Burnsed, MD, Neurology
February 14	Mechanisms and Treatment of Status Epilepticus	Jaideep Kapur, MBBS, PhD, Neurology
February 21 (trainee session)	Epilepsy basics: neurobiology of seizures & epileptogenesis	Raquel Miralles (trainee)
February 28	Clinical Seizures Semiology	Erika Axeen, MD, Neurology
March 13	Trainee presentations to Sydney Cash, MD, PhD, Professor of Neurology, Harvard Medical School	Trainees
March 20	Understanding patch-clamp electrophysiology in	Raquel Miralles (trainee)
(trainee session)	an epilepsy context	Paper: Spratt et al., 2021
March 27	Post-stroke seizures in mice: some pilot data in	Kuan Lab, MD, PhD,
	search of collaboration	Neuroscience
April 3	Neuron Subtype Roles in DNM1 Mouse Models of	Matthew Weston, PhD, Fralin
	Developmental Epileptic Encephalopathy	Biomedical Institute, Virginia Te
April 10	Post-traumatic epilepsy	Ed Bertram, MD, Neurology
April 17	Postoperative delirium is an epigenetic disorder of	Nadia Lunardi, MD, PhD,
	cognitive and circadian function	Anesthesiology
May 1 (trainee session)	Genetic tools for epilepsy treatment	Caeley Reever (trainee)
		Paper: Lenk et al., 2020
May 8	Neural populations activated during seizure- induced apnea	Ian Wenker, PhD, Anesthesiolog
May 15	SCN8A epileptic encephalopathy – role of inhibitory neurons in seizures	Manoj Patel, PhD, Anesthesiolo

Location: MR-4, 3rd Floor Conference Room

Figure 4. Spring 2024 Epilepsy Research Today schedule.

Bring Your Own Data (BYOD): A Data Cooperative

In our experience, programming skills are best learned when students have a vested interest in acquiring these skills. Therefore, we maintain a bi-weekly, informal programming cooperative wherein our students learn how to use programming languages (e.g., Python, Matlab) to quantify and analyze their data. Students bring their data to these sessions, and our mentors with extensive programming experience (e.g., Drs. Beenhakker, Nieh, and Wenker) provide one-on-one guidance for data analysis. PhD students and postdoctoral researchers with strong programming skills are also encouraged to attend to provide guidance. Although informal, these sessions establish a strong community of programmers that our trainees can rely on to learn modern, sophisticated skills to analyze data. We refer to this community as a data cooperative as the informal group is unified by a common purpose: to analyze data with modern computer programming skills. We have included funds in our budget to provide refreshments/snacks for these late afternoon sessions.

Epilepsy Workshops

Our core *ETP* curriculum includes seven formal workshops that address topics ranging from <u>Leveraging Animal Models to Understand Human Epilepsy</u> to <u>Bench to Patient: How Epilepsy Drugs Make it to the Clinic</u>. Each specialized workshop addresses a specific topic relevant for epilepsy research and will last five consecutive days (two hours/day). Each year, three biyearly workshops are provided, and alternate with the three biyearly workshops provided in the previous year (**Figure 3B**). By contrast, our annual *Professional Skills Development* workshop is provided every year. Therefore, our *ETP* sponsors six biyearly workshops and one annual workshop. Notably, each workshop is designed to function independently of all other workshops. Therefore, the order in which a student enrolls in the workshops is not critical. Finally, because we have designed our workshop-based curriculum so that trainees take one five-day, concentrated workshop every three months, we feel that our trainees will still be able to devote a significant amount of time and energy to their primary responsibility: their PhD research.

Our *ETP*-sponsored workshops include:

Workshop #1: Leveraging Animal Models to Understand Human Epilepsy

<u>Summary</u> This workshop begins by providing a strong understanding of both human and mouse neuroanatomy. Trainees visit the cadaver lab to study the structure and organization of the human brain. Trainees learn to identify key surface features and deep brain structures of the human brain, with the goal of identifying key structures involved in the circuit mechanisms of temporal lobe epilepsy (TLE), absence epilepsy, and frontal lobe epilepsy. *ETP* faculty (Drs. Patel, Kapur, Wenker, Beenhakker, Kuan) teach this workshop.

Since most epilepsy research involves the use of rodent models, trainees also learn how to identify key structural areas involved in temporal lobe epilepsy, absence epilepsy, and frontal lobe epilepsy in both mouse and rat models. During this workshop, trainees are also exposed to different rodent models of epilepsy, including the chronic hippocampal stimulation model of TLE, kainic acid seizure model, pilocarpine model of epilepsy, and the genetic absence model of epilepsy. Special attention is paid to the advantages and limitations associated with each model.

<u>Trainee Outcomes</u> Following this workshop, trainees will have a strong neuroanatomical foundation to understand the structural underpinnings of seizure initiation and propagation. Trainees will also learn how mouse and human brains differ, thereby providing trainees with an understanding of how rodent models inform (or don't) the human condition.

Workshop #2: Essential Tools for Measuring In Vitro Excitability

Summary At its core, epilepsy is a disease of neural circuit excitability. The gold-standard for evaluating neuronal excitability is patch clamp electrophysiology. Therefore, in this workshop, trainees learn how to prepare viable brain slices from both rats and mice and how to visualize neurons using infrared microscopy. Participants gain hands-on experience in: (1) Recording from individual neurons in acute brain slices and measuring neuronal excitability; (2) Recording and analyzing evoked, spontaneous, and miniature synaptic currents; and (3) Recording voltage-gated and ligand-gated ion channels and analyzing their biophysical parameters. Training is provided by Drs. Patel, Wenker, Beenhakker, and Kapur. In addition to learning electrophysiological techniques, trainees will learn how various electrophysiological measurements inform our understanding of seizures.

<u>Trainee Outcomes</u> Following this hands-on workshop, trainees will understand how to evaluate neuronal excitability using electrophysiological techniques. Trainees will also understand how to interpret electrophysiological data.

Workshop #3: Essential Tools for In Vivo Circuit Analysis

<u>Summary</u> Seizures, the hallmark of epilepsy, result from the rapid and pathological organization of hyperexcitable neurons within neural circuits. In this workshop, trainees learn how to measure and manipulate neural circuits using multiple *in vivo* techniques:

- (1) EEG. Trainees learn how to measure the electrical activity produced by the brain using electroencephalography (EEG), the standard approach to measure seizures. Trainees learn how to design and manufacture recording headsets and cables for the detection of EEG signals. Trainees are instructed how to analyze EEG recordings using LabChart software for the detection of seizures. Training will be provided by Drs. Wenker and Kapur.
- (2) Cellular Techniques for *In Vivo* Circuit Analysis. Trainees learn how calcium and voltage sensors, fiber photometry, and GRIN lens-coupled optical approaches are used to evaluate neural circuit activity. Trainees also learn how to leverage head-fixed mouse systems and two-photon microscopy to resolve the activities of single neurons. In addition to imaging techniques, trainees learn how to implement and analyze data derived with modern, high-density recording electrodes (e.g., Neuropixels). This training will be provided by Drs. Nieh and Beenhakker.
- **(3) Opto- and Chemo-genetic Manipulation.** Optogenetic and chemogenetic techniques are essential for resolving how specific neural circuit elements promote the onset and propagation of seizures. Trainees are introduced to topics including the use of channelrhodopsin, archaerhodopsin, and DREADDS to activate or inhibit neural circuits. Trainees also receive hands-on training on how to construct and surgically implant optogenetic stimulation probes. The effects of optogenetic control of seizures are observed in the lab. Training is provided by Drs. Wenker and Beenhakker.

<u>Trainee Outcomes</u> Following this workshop, trainees will understand how seizures are measured and how cutting-edge tools are used to resolve the cellular and circuit components of seizure initiation and propagation.

Workshop #4: Quantitative and Computational Tools

<u>Summary</u> This workshop introduces trainees to modern programming languages used to analyze complex datasets. Unlike our BYOD data cooperative, the goal of this workshop is to provide trainees with a broad understanding of the modern approaches to handle and analyze large, complex datasets. In addition to the programming platforms generally used to process complex signals and evaluate time-series data (e.g., Matlab & Python), trainees will also learn modern approaches

to evaluate genomic and single cell data. Trainees also learn the skills and conventions commonly utilized by programmers to ensure convenient and robust code and data sharing. Drs. Wenker, Beenhakker and Perez-Reyes will lead this workshop.

<u>Trainee Outcomes</u> Following this workshop, trainees will understand how to leverage different programming languages for the quantitative evaluation of data.

Workshop #5: Human Seizures

Summary This workshop focuses on clinical presentations of common and rare epilepsies and the tools used to diagnose and manage epilepsies. Drs. Quigg, Fountain, and Axeen – the *ETP*'s clinical faculty – will lead this workshop.

- (1) Drug and surgical treatment of epilepsy. We review the broad description of epilepsy drug classes, definitions of drug refractory epilepsy and its treatments with surgery, laser ablation, neurostimulation, and vagal nerve stimulation.
- **(2) Scalp and intracranial EEG recordings in human focal epilepsy.** We will introduce trainees to scalp EEG recordings of focal seizures, as well as intracranial EEG using stereo-EEG techniques, subdural electrodes, and traditional hippocampal depth electrodes. We will end with a demonstration of human responsive neurostimulation to terminate seizures.
- **(3) EEG in generalized epilepsies.** We will review EEG findings in generalized epilepsies, such as childhood absence and juvenile myoclonic epilepsy. We will also review interictal patterns in developmental epileptic encephalopathies and Lennox-Gastaut syndrome. Finally, ictal EEG patterns during various generalized seizures will be discussed.
- **(4) Imaging in epilepsy.** Classical MRI findings in mesial temporal sclerosis and focal cortical dysplasias will be reviewed. Principles of PET scans and applications in epilepsy, as well as the role of fMRI in language mapping, will be discussed.
- **(5) Neuropsychology of epilepsy.** This portion will address memory and cognitive deficits associated with epilepsy, and symptoms of anxiety and depression in epilepsy patients.

<u>Trainee Outcomes</u> Following this workshop, trainees will have a better understanding of the clinical landscape and the challenges and barriers faced by clinicians and patients.

Workshop #6: Bench to Patient: How Epilepsy Drugs Make It to the Clinic

<u>Summary</u> The goal of this workshop is to learn how seizures are treated in the modern era, and how scientists are developing novel approaches to treat epilepsy in the future. The workshop covers current pharmacological approaches to treat epilepsy, as well as how deep brain stimulation can be used to suppress seizures. The workshop also highlights the development of gene therapy-based strategies to treat epilepsy.

- (1) Anti-Seizure Medications (ASMs). Lectures highlight how ASMs work at the molecular and cellular levels to control neuronal excitability associated with seizures. Information on the benefits and drawbacks of each type of ASM are also discussed, and clinicians provide their perspective on how they ultimately decide upon the medications used to treat patients with epilepsy. Trainees also learn how clinical trials work and how end points are evaluated. The session is led by Dr. Kapur.
- (2) Genetic Therapies. Trainees learn how current genetic therapies aim to leverage modern gene editing techniques—CRISPR-Cas9, base editing, and prime editing technologies—to treat patients with epilepsy. Instruction will cover the fundamentals of AAV viruses and designing viral vectors. Cell-specific promoters and available viral vector resources are also discussed. The session will be led by Drs. Patel and Perez-Reyes.

<u>Trainee Outcomes</u> Following this workshop, trainees will understand how epilepsy is treated today. This understanding is essential for maximizing the therapeutic potential of pre-clinical models. Trainees will also understand how scientists envision effective treatment strategies of the future.

Workshop #7: Professional Skills Development

<u>Summary</u> To successfully integrate into the professional landscape after graduate school, trainees must learn important written and oral communication skills. This workshop is provided every year and is designed to foster professional skills within our trainees, including:

- (1) Effective Grant Writing. Although all *ETP* trainees are required to enroll in UVA's Grant Writing course (CELL 8450) in their 2nd year of school, this workshop will provide trainees with practical resources for effective grant writing. Lectures will highlight effective approaches for writing grants, as well as help trainees identify grant mechanisms that support their professional goals. This workshop is led by Dr. Patel, who served on the NIH/ZRG1 F01-F study section from 2014 to 2021. Therefore, he has extensive experience with evaluating F31 grants. Guidance is also provided to trainees who wish to apply for the Diversity Specialized Predoctoral to Postdoctoral Advancement in Neuroscience (D-SPAN) F99/K00 award.
- (2) Formal and Informal Presentations. The ability to effectively communicate scientific concepts and justify proposed experiments are essential skills for biomedical researchers. Therefore, the goals of this workshop include how to practice

effective forms of communicating their science to the public and peers. Trainees are instructed how to communicate their science through "Chalk Talks" and "Elevator Pitches" wherein trainees describe their research question and experimental findings without using prepared slides. Drs. Patel and Beenhakker will lead this session, along with other ETP faculty.

Trainee Outcomes Following this workshop, trainees will understand how to write effective grants and how to identify grant mechanisms that best suit their goals. Trainees will also understand standard approaches to effectively communicate their research and findings to both lay and expert audiences.

H2b. Supplemental Training Opportunities

 ${f T}$ he core of the ETP curriculum includes the aforementioned Epilepsy Research Today course, our BYOD cooperative, and our workshops. ETP trainees are required to participate in this core curriculum. In addition to this core curriculum, the ETP also supports supplemental training opportunities that include: (1) A quarterly Experimental Epilepsy Group meeting; (2) An Epilepsy Shadowing Program; and (3) Epilepsy and neuroscience seminars. Trainees are strongly encouraged to participate in at least one supplemental training opportunity per year. These supplemental training opportunities are described below.

Experimental Epilepsy Group

 ${f T}$ he full realization of impactful translational research requires a thorough understanding of the clinical landscape. To ensure that our trainees recognize important clinical circumstances wherein treatment strategies remain unsatisfactory, we have established our quarterly Experimental Epilepsy Group (EEG) meetings (Figure 5). Every three months, UVA's basic epilepsy research scientists convene with UVA clinicians—residents and attendees—to discuss the clinical manifestation of a specific form of epilepsy and current research devoted **Figure 5**. Previous Experimental Epilepsy Group to developing a mechanistic understanding of that form of epilepsy.



meeting with neurology clinician presentations.

Each 1.5-hour meeting begins with a 30-minute lecture by a clinician wherein clinical features of the disorder are detailed. A portion of this clinically oriented lecture is also devoted to current therapeutic strategies and, if pertinent, how such strategies fail. Next, an ETP trainee provides a 30-minute lecture that highlights recent scientific literature that aims to resolve a mechanistic understanding of the disorder. Following the two formal lectures, the meeting is open for discussion and questions. Howard Goodkin, Chair of Neurology and member of our ETP Executive Committee, is responsible for identifying clinicians to present the 30-minute clinical lecture, whereas the ETP PIs are responsible for selecting a PhD student for the accompanying research lecture. This session will be led by Drs. Kapur, Patel and Beenhakker. Clinical features will be presented by ETP clinical faculty and members of UVA's Department of Neurology.

Epilepsy Shadowing Program: A Window into Clinical Epilepsy

Training in the clinical aspects of epilepsy is critical if trainees are to better understand the clinical condition they hope to treat. A well-informed clinical perspective also enhances the translational potential of their research. Clinical faculty from the Department of Neurology (Section D) will direct training in clinical epilepsy. Each ETP trainee is encouraged to take part in our Epilepsy Shadowing Program once during their two-year appointment; the program is designed to accommodate only one trainee at a time. Trainees are exposed to the Epilepsy Monitoring Unit (EMU) and to surgical conferences wherein treatment strategies are identified.

 ${f T}$ rainees are individually paired with an epilepsy clinician (attending physician) for a one-week rotation in the EMU. Trainees will attend morning rounds from 9 to 11 AM on weekdays. The attending physician reviews the history, physical exam, and MRI of each patient admitted to the EMU. The attending physician reviews baseline EEG, awake and sleep recordings between seizures, and then the recordings of epileptic seizures, all of which facilitate in the classification of seizures and the determination of potential seizure onset zones. Trainees also have the opportunity to observe patients undergoing intracranial recording. Trainees are then invited to attend epilepsy surgery conferences, wherein patients they observed in the EMU come up for discussion.

 ${f T}$ he epilepsy surgery conference involves several medical experts, including neurologists who record seizures, outpatient neurologists, neuroradiologists specializing in MRI and/or PET scans, neuropsychologists specializing in epilepsy, and psychiatrists. The conference illustrates the multidimensional approach used to treat epilepsy. Trainees are therefore exposed to the different types of epilepsy surgeries that are used to treat certain types of seizures, including focal resection, temporal lobe resection, extratemporal resection, and neurostimulation devices used for vagus nerve and deep brain stimulation. These programs will be organized by our ETP clinical faculty.

Seminars Hosted by the ETP and Neuroscience Graduate Program

- (1) ETP Retreat. ETP faculty participate in an off-campus retreat. At the retreat, the morning session is reserved for the trainees only. Trainees use this time to meet with our invited outside speaker and to discuss strategies to enhance professional development. The afternoon session of the retreat is attended by both basic science and clinical faculty and involves 3-minute data blast sessions and 10-minute data presentations. Figure 6 shows an example program from 2023. The retreat is organized by Dr. Patel with administrative support from the UVA Brain Institute.
- (2) Neuroscience Graduate Program (NGP) Retreat. The NGP holds an annual retreat off-campus. The retreat is organized by the trainees and the Director of the NGP (Dr. Beenhakker). The retreat provides opportunities for scientific exchange and informal interactions among faculty and students. The retreat consists of a series of faculty and trainee presentations as well as trainee poster sessions. External, student-invited speakers are also invited to present their research. The retreat also hosts a career panel where previous UVA graduates are invited to talk about their career development.
- (3) Neuroscience Seminars. UVA's Neuroscience Graduate Program holds its own weekly seminar series where they bring in experts from academia, industry, and government to present their research and insights into current issues affecting neuroscience. ETP trainees will be invited to meet and have lunch with the speakers. All trainees in the ETP will be expected to attend NGP seminars.

EPILEPSY INTEREST GROUP RESEARCH RETREAT 2023 RESEARCH PRESENTATIONS :05 - 1:15 IAN WENKER, PHD, PATEL LA 1:15 - 1:20 IENNIFER BURNSED, MD, DEPT, OF PEDIATRICS 1:20 - 1:25 DARIA SKWARZYNSKA, PHD, KAPUR LAB 1:25 - 1:35 SUCHITRA JOSHI, PHD, DEPT. OF NEUROLOGY 1:35 - 1:40 ERICA SLOGAR, PATEL LAB 1:40 - 1:50 ANDREW SCHOMER, MD, DEPT. OF NEUROLOGY 1:50 - 1:55 NATHAN FOUNTAIN MD DEPT OF NEUROLOGY 1:55 - 2:00 MADISON FAILOR, PEREZ-REYES LAB 2:00 - 2:10 MARK BEENHAKKER, PHD. DEPT. OF PHARMACOLOGY 2:10 - 2:15 MARK QUIGG, MD, DEPT. OF NEUROLOGY 2:15 - 2:25 BHANU TEWARI, PHD, SONTHEIMER LAB 2:25 - 2:30 RAQUEL MIRALLES, PATEL LAB 2:30 - 2:35 ANASTASIA BRODOVSKAYA, PHD, KAPUR LAB 2:35 - 2:50 BREAK! 2:50 - 3:00 ZHONGXIAO FU, PHD, KUAN LAB 3:00 - 3:05 IFRAH ZAWAR, MD, DEPT, OF NEUROLOGY 3:05 - 3:10 IRENE SANCHEZ BRUALLA, PHD, PATEL LAB 3:10 - 3:20 ED PEREZ-REYES, PHD, DEPT, OF PHARMACOLOGY 3:20 - 3:25 CAELEY REEVER, PATEL LAB 3:25 - 3:35 ED BERTRAM, MD, DEPT. OF NEUROLOGY 3:35 - 3:40 ANNALIN WOO. SONTHEIMER LAB 3:40 - 3:45 ERIKA AXEEN, MD, DEPT. OF NEUROLOGY November 9, 2023 THE FORUM HOTEL AT DARDEN

Figure 6. ETP (formerly called the Epilepsy Interest Group) Retreat Program 2023.

(4) UVA Brain Institute Symposium. The UVA Brain Institute hosts a three-day symposium on numerous neurosciencefocused topics including clinical and translational neuroscience, neurodegeneration, neurodevelopment, and neuroimmunology. Figure 7 lists the external and internal speakers during the Epilepsy session at the 2024 symposium.

Finally, in addition to local retreats and seminars, ETP trainees will be encouraged to submit abstracts for presentation to the American Epilepsy Society annual meeting, the Society for Neuroscience annual meeting, and the biennial Gordon Conference on the Mechanisms of Epilepsy and Neuronal Synchronization. Attendance at these meetings will expose ETP trainees to the most innovative and cutting-edge research currently being undertaken.

H2c. Rigorous Experimental Design and Statistical Methodology

All ETP trainees are expected to master fundamental knowledge in the rigor of modern experimental design and quantitative reasoning. To achieve this mastery, we have formalized training in quantitative and statistical techniques in our ETP. Formal methodology lectures occur once per month at our Epilepsy Research Today course. We have recruited

Dr. Marieke Jones, a staff biostatistician at UVA, to provide formal lectures on general statistical approaches. As noted above, Dr. Jones attends all Epilepsy Research Today lectures. We have also identified specific lectures wherein she will lead the discussion. For these collective responsibilities, our ETP will support Dr. Jones with 10% effort. Following each lecture, a detailed rubric is used to evaluate student comprehension; the rubric will be filled out by attendees and then provided to the presenter. The 30 minutes established after the formal hour-long lecture provides the opportunity to discuss the rubric with the presenter. Dr. Jones' lectures include:

- (1) Experimental Design and Quantitative Literacy. This lecture focuses on fundamental aspects of Scientific Rigor of experimental design, including the use of appropriate experimental controls, sources of bias, sample size determination, and blinding/randomizing practices.
- (2) Statistical Methodology. This series of lectures introduces advanced statistical methods used in contemporary epilepsy research (e.g., longitudinal data analysis, spatial data analysis).
- (3) Statistical Approaches: In the Trenches. In conjunction with Dr. Jones, ETP faculty present the statistical approaches they have used to evaluate



Figure 7. 2024 UVA Brain Symposium – Epilepsy-focused Keynote and Epilepsy Session

their own data. Unlike a conventional scientific talk, these lectures emphasize statistical approaches to evaluate real data.

In addition to Dr. Jones, the *ETP* will invite three external presenters per year to deliver seminars on quantitative data analysis, experimental design, or statistical principles. The *Executive Committee*, *IAB*, and *EAB* will collate a list of potential presenters who fit logically into the upcoming year's programming (particularly workshops, which alternate each year). Each external presenter will focus on a specific topic related to quantitative skills and approaches to neuroscience research, for example, the meaning of a p-value or statistical significance vs. biological relevance. Each visit will be scheduled so the presenter can attend an *Epilepsy Research Today* weekly course meeting and at least one other regularly scheduled *ETP* programming event (e.g., BYOD or workshop). All trainees will be expected to attend, and the entire epilepsy and neuroscience research community will be invited. Each external presenter will have dedicated time to meet with *ETP* trainees in small groups to discuss specific quantitative issues faced by the trainees.

H2d. Professional Development: Leveraging the Epilepsy Training Program for Career Opportunities

For all our trainees, we assemble a "career mentoring team" that introduces the trainee to networking, professional development, and training opportunities specifically tailored to their scientific interests. The teams are developed in consultation with the trainee, program directors, appropriate members of the *Executive Committee*, and the trainee's primary mentor. Teams are composed of *ETP* faculty, current/past neuroscience trainees, and alumni. Together, these professional development teams are not only designed to promote retention of our trainees but also to encourage trainees to feel positively about their future scientific careers.

The ETP also provides a clear conduit for trainees to explore career options during their later years of graduate school. To this end, the ETP interfaces with PhD+, a UVA-wide program established by versatile academics who are deeply engaged with society's needs to nurture influential professionals in every sector. Striving to integrate professional training for PhD students at appropriate points in their student careers, the program is designed to introduce self-reflection, intentionality in training, and iteration into professional development and career-related activities. Trainees can leverage individual career advising sessions and attend the "PhD+ Career Design" course wherein they learn strategies to explore career sectors that align with their core values, skills, and professional interests, as well as build development plans toward career transition in those sectors.

Trainees are also exposed to various career paths via career panels at annual retreats sponsored by the *Neuroscience Graduate Program* and our *Epilepsy Training Program*. Recent retreat panelists include: Dr. Mark Mattson from NIH and Johns Hopkins University; Dr. Robert J. Koestler from the Museum Conservation Institute; Dr. Geoffrey Horwitz from Decibel Therapeutics; Dr. Carolina Ramôa from the FDA; and Dr. Lucia Tejada from the Endocrine Society.

I. Recruitment & Retention of Trainees

I1. Recruitment

The ETP will draw from training grant eligible (TGE) students within BIMS, Biology, Biomedical Engineering, and Psychology (**Data Table 6**). As described above, the ETP will accept the curricular requirements established by these other degree-granting programs. Nonetheless, our ETP's Executive Committee will identify any neuroscience deficiencies among our ETP recruits and identify additional course work to address these deficiencies. Collectively, over the last five years, these UVA programs average 81 TGE matriculants per year with an average GPA of 3.6. TGE new entrants had, on average, 22.9 months of prior research experience, and 27% were from underrepresented groups. Roughly 10% of new entrants select epilepsy-focused labs. This is sufficient to ensure a successful and competitive training program.

Once students have selected their thesis advisor, we will ask *ETP* mentors to nominate their best and brightest matriculants to become ETP-funded trainees. The program directors and *Executive Committee* will review these nominations and make final decisions about which students to appoint to the T32-supported *ETP*. The most important considerations for appointment include: (1) Commitment to epilepsy research; (2) Evidence of promise as a productive scientist; (3) Past academic performance; and (4) Letters of recommendation from current and former mentors. We anticipate 2- to 3-fold more nominees (~12 to 18) than training positions.

12. Program Diversity

Within UVA, the Office of Graduate and Postdoctoral Diversity Programs, led by Dr. Jasmine Crenshaw, spearheads many initiatives to diversify and enhance the graduate student experience. Initiatives include: (1) The annual Diversity Retreat that brings together students, staff, faculty, and administrators; (2) The Mentoring Institute, an interdisciplinary, interethnic mentoring program; and (3) Student affinity groups. Also, a student-led initiative at UVA called the Graduate Recruitment Initiative Team (GRIT) works to build a more robust community of inclusion around STEM students underrepresented in their fields. GRIT's mission is to enhance diversity and inclusion across the graduate programs within

the Biomedical Sciences Program at the School of Medicine, the Department of Biology in the Graduate School of Arts and Sciences, and the School of Engineering and Applied Sciences. Through GRIT, students and faculty work together to achieve this mission through increasing efforts to improve the recruitment and retention of students with disabilities, women, underrepresented minorities (URMs), and LGBTQ+ students in doctoral programs at the UVA.

Diversity at the level of both our faculty and trainees is essential for the strength and success of the proposed training program, and our program leadership reflects our strong commitment to diversity and equity. The program directors are committed to enhancing the diversity among the mentors of this *ETP* and of the broader neuroscience community at UVA. Nonetheless, although all associated *ETP* professors are proven mentors and successful scientists, the gender and racial gap at the senior level is a painful reminder of the implicit biases of our past, and remedying these injustices and training a diverse and empowered scientific workforce for the future remain explicit goals of this training grant.

Importantly, recruiting and retaining a diverse faculty is a major institutional goal that is being addressed at the highest level of administration at UVA. Thus, as the diversity of the overall faculty improves, so will the diversity of our *ETP* faculty (See Institutional LOS and LOS from Provost Baucom). To immediately provide our trainees with diverse perspectives, we will invite and champion neuroscientists of diverse backgrounds through our *ETP* seminar series. We invite speakers that not only represent ethnically and culturally distinct backgrounds but also gender and professional rank. Our trainees will also ensure that final decisions on speakers reflect the perspectives of our students.

Although UVA's administration is actively enhancing diversity among our faculty, the program directors of this training program are leading efforts to immediately augment our students' experience by establishing a network of diverse mentors outside UVA. In conjunction with UVA's *Neuroscience Graduate Program, ETP* co-director Mark Beenhakker invited Dr. Ulises Ricoy (University of Arizona) and Dr. Gerald Downes (University of Massachusetts, Amherst) in 2024 to give scientific lectures at UVA. In addition to maintaining active research programs, Drs. Ricoy and Downes are also heavily committed to diversity and scientific outreach. Dr. Ricoy serves as the Director of *Outreach Initiatives for the Grass Foundation*, whereas Dr. Downes serves as the Co-Director of the *Summer Program in Neuroscience, Excellence and Success* (SPINES) maintained by the Marine Biological Laboratory in Woods Hole, MA. As part of their UVA visit, we allotted time for our trainees to talk to Drs. Ricoy and Downes to discuss best practices for maintaining a vibrant and diverse scientific workforce. At least one external *ETP*-invited speaker per year will be from a historically underrepresented group and will have dedicated time to speak and connect with trainees.

13. Retention

A goal of the *ETP* is to ensure that our trainees are successful and elect to remain in scientific careers, particularly those focused on epilepsy or neuroscience once they complete training. Because of the critical relationship between mentor and trainee, all *ETP* mentors are expected to complete the Mentor Training program hosted by the School of Medicine, which is already an expectation for all faculty actively training graduate students. This eight-hour workshop (divided over two days) is based on the curriculum developed through NIH-supported projects by the Center for the Improvement of Mentored Experiences in Research and the National Research Mentoring Network. One of the modules covered in this training is "Addressing Equity and Inclusion" that, when combined with essential topics such as "Effective Communication" and "Aligning Expectations," will provide a firm foundation for our faculty to approach their mentoring relationships. Trainees will also be strongly encouraged to complete and maintain an Individual Development Plan (IDP) using tools available through Office of Graduate and Postdoctoral Affairs, as well as avail themselves of other institutional offerings for graduate students (see **Section H2d** and LOS from Dr. Jasmine Crenshaw). Additionally, every *ETP* trainee will meet with one of the program directors at least once annually to ensure that trainees remain in a safe, productive research environment and are making progress toward their goals.

J. Training Program Evaluation

As with any training program, mechanisms must be established to evaluate the extent to which the *ETP* is achieving its goals. Assessment of the program will occur every six months by the co-directors and *Executive Committee*. Each of these groups will scrutinize course evaluations and trainee progress/outcomes. Additionally, input from current trainees and *ETP* faculty will be collected in town halls, written questionnaires, and informal interactions at retreats and symposia. Annual assessments of the program will result from internal and external board meetings that will examine suggestions from past and present trainees and identify any deficiencies. Trainees are encouraged to make suggestions about courses or other programmatic issues to the program directors, members of the *Executive Committee*, and/or *ETP* faculty. Our *Trainee Advisory Board* (Figure 2) formalizes this process. Trainee input will be received as follows:

J1. Soliciting Evaluations from Current Trainees

• Trainee Advisory Board. Trainees who serve on this Board will have numerous opportunities to provide the Executive

Committee with input into the program including, but not limited to, joint Executive Committee/Trainee Advisory Board meetings and as-needed meetings with the program directors.

- **Course Evaluations.** A web-based student evaluation system is in place to gather feedback for all workshops and courses of the curriculum. It includes questions that are answered using a standard five-point scale as well as open response questions for which the students can provide unstructured narrative comments. The program directors, the *Executive Committee*, and the *Trainee Advisory Board* review the evaluations. This valuable feedback will be used to make iterative improvements in our coursework.
- Quantitative Training. With the growing prevalence of large-scale neuroscientific data sets and novel quantitative approaches for tackling neuroscience problems, it is important that we constantly evaluate whether the statistical training is sufficiently rigorous. As such, once a year, the ETP curriculum committee will survey the variety of computational and statistical techniques used by ETP trainees to determine whether our current quantitative training is sufficient. Thus, the statistics and methodology courses presented in Section H2c will likely evolve every year according to these surveys. Statistical literacy will also be evaluated with a mastery rubric to determine if students are employing the appropriate statistical methods and that they can articulate why those methods are the most suitable for their research.
- **Retreats and Symposia.** Annual *ETP* retreats and symposia provide opportunities to solicit input from trainees about the training program.
- Informal Input. All program faculty are available to meet with trainees one-on-one to address individual problems, concerns, and ideas. Student-faculty interactions are of a sufficiently relaxed and frequent nature that most of these discussions occur on an ad hoc basis. When necessary, ETP faculty bring issues to the attention of the program directors and/or Executive Committee.
- **Town Hall Meetings.** We also hold annual town hall meetings with all *ETP* trainees to specifically brainstorm and solicit input from students on the direction of the program.

J2. Soliciting Evaluations from Past Trainees

Once per year, the *Executive Committee* will send questionnaires to trainees who have completed the training program. In addition to gathering specifics of the former trainee's current position and basic information about career trajectory, the questionnaire will assess the extent to which the *ETP* prepared them for their chosen career path and solicit suggestions for additional preparation that may have been helpful. These questionnaires will be emailed each year to trainees who are two and five-years post-training to allow trainees time to acclimate to their new positions and reflect on their past training experience. The responses will be tabulated, discussed, and acted upon by the program directors and *Executive Committee*. Additional input will be solicited from past trainees on an *ad hoc* basis.

J3. Soliciting Evaluations from Faculty

ETP faculty will meet at annual retreats and symposia to more formally discuss policies and new programmatic initiatives. This meeting will also serve as a venue to evaluate the existing program.

J4. Soliciting Evaluations from the External Advisory Board

The External Advisory Board will receive: (1) The most recent NIH progress report; (2) A 2-page addendum provided by the program directors that outlines the challenges and accomplishments of the prior year; and (3) A list of specific objectives for external board review. During these meetings, members of the External Advisory Board will interact with trainees, the Executive and Trainee Advisory Boards, faculty, administrators, and community leadership. At the conclusion of the meeting, the External Advisory Board will provide an evaluation to the program directors. Additionally, External Advisory Board members will be informed of program progress and evaluation outcomes through email and/or teleconference and will be available throughout the grant period to address potential concerns and share experiences.

J5. Trainee Outcomes

Ultimately, the success of our training program is reflected by the outcomes of current and former trainees. Specifically, we will assess: (1) The productivity, including the quality and number of publications, of trainees and continually work to ensure that it is appropriate for an outstanding training program; (2) The time-to-degree completion is at or better than the national average; (3) Post-graduation positions reflect the ability of our trainees to continue toward independent scientific careers; (4) Successful attainment of individual extramural fellowships and awards; and (5) Invitations of scientific presentations and invited talks at national and international conferences. This information will be reported annually to the *Executive Committee*. We will also develop a matrix to enable comparison from year to year, with the goal of improving each of these outcomes during the current and the next grant period.

K. Institutional Environment Commitment to Training

The most important resource available to ETP trainees is the outstanding scientific environment and the collection of