

## 6. PROGRESS REPORT

**6A. Period Covered: July 1, 2007 - May 21, 2012**

### **6B. Accomplishments of the Training Program**

**Trainees:** Over the last five years, **8 postdoctoral and 6 predoctoral trainees** have been supported, typically for two years of their training program, with all but 1 of 14 continuing in biomedical research and training (2 with academic faculty positions, 1 with a Facility Director position at UAB, 1 in Medical School, and 9 currently continuing various training paths at UAB). **Our trainees in this five-year period have been gender balanced (57% male and 43% female) and have included 22% under-represented minorities.**

Over the same time period, our trainees have trained with **10** different primary and co-mentors from **7** departments (Cell, Developmental and Integrative Biology; Pediatrics; Surgery; Neurology; Neurobiology; Radiology and Radiation Oncology). We believe this interdisciplinary breadth provides a rich investigative training experience for trainees and faculty alike. This is highlighted by the fact that **95%** of the Program Faculty have published with at least one other Program Faculty, illustrating the highly collaborative and interdisciplinary nature of our Training Program.

**Over the period covered, these trainees have published 48 peer-reviewed manuscripts (TABLES 6A and 6B),** with an additional **11** under submission. These manuscripts were published in journals such as *Clinical Cancer Research*, *GLIA*, *Journal of Immunology*, *Nature Medicine*, *Journal of Biological Chemistry*, *Molecular Cancer Research*, *Molecular Cancer Therapeutics*, *Cancer Research*, *Journal of Neuro-Oncology*, *New England Journal of Medicine*, *Trends in Immunology*, *Molecular Cell Biology*, *Neurotherapeutics*, *Journal of Virology*, *PLoS One*, and *Cancer Gene Therapy*. Of the 6 predoctoral trainees, 5 have published at least one first-author publication, 6 have published at least one co-authored publication, and 1 has several first-author manuscripts in preparation. Of the 8 postdoctoral fellows, 6 have published at least one first-author paper, 7 have published at least one co-authored publication, and 3 have first-author or co-author manuscripts under review. We are very pleased with the publication record of our trainees.

All our trainees have been encouraged to submit grants seeking extramural, independent research support. Three of the 14 trainees have received independent funding, and 3 have submitted grants that will be reviewed in the next few months.

**Mentors:** The 5 faculty added as new mentors (Drs. Bredel, Cassady, Fiveash, Griguer, and Willey) support new and enhanced areas of emphasis within the field of brain tumor biology, reflecting our commitment to rigorous research training in these areas (cancer stem cells, transcription factors, signal transduction pathways, bio-energetics, oxidative stress, systems biology, bioinformatics, genomics, kinomics, innate immune response, clinical trials). The newly recruited faculty have provided increased programmatic emphasis on interdisciplinary research, which is of great benefit to the trainees. Our expanded faculty have facilitated the **opportunity for co-mentorship of the trainees**, which we will continue to encourage during the next training period. Examples include co-mentorship of David Gaston by Drs. R. Whitley and K. Cassady, Crystal Wheeler by Drs. B. Nabors and P. King, and Dr. George Dobbins by Drs. D. Curiel and Y. Gillespie.

### **6C. Benefits of Training Related Expenses**

Training-related expenses have been instrumental in enabling our trainees to attend meetings, workshops and off-campus courses to present research and network with leaders in their field. In our program evaluations, multiple trainees have pointed to these opportunities, not only as a highlight but also as seminal activities, in their career development. Examples include the following: partial support for Angel Alvarez to attend the Keystone Symposium on Stem Cells, Cancer and Metastasis (March 2011); partial support for David Gaston to attend the ASCI/AAP Joint Meeting, Chicago, IL (April 2012); partial support for Dr. Susan Buckingham to travel to the Dudek lab at the University of Utah to learn surgical and EEG techniques, which were instrumental for her first-author publication in *Nature Medicine* (2011); partial support for Dr. James Cody to attend the AACR Special Conference on Tumor Microenvironment Complexity, Orlando, FL (November 2011); and partial support for Dr. Braden McFarland to attend the Society for Neuro-Oncology meeting, Anaheim, CA (November 2011). In addition, these funds have been used to defray the cost of health insurance for the trainees, provide honoraria/travel expenses for guest lecturers in the Brain Tumor Biology Advanced Course, and partially defray the salary of Ms. Rene Eubank, who is responsible for assistance in the administration of the training program, in the coordination of meetings for both trainees and program faculty, and in the preparation of the annual reports.

## 6D. Training Supported During the Previous Project Period (Years 1-5)

It should be noted that this Training Grant is in no-cost extension (07/01/2012-06/30/2013). There were several reasons for the delay in submitting the competitive renewal, which include the following: 1) many of our Program Faculty (Benveniste, Bredel, Buchsbaum, Fiveash, Gillespie, Nabors, Sontheimer, Whitley and Zinn) were highly involved in the competitive renewal of the UAB CCC Support Grant NIH P30 CA13148, which was successfully renewed in 2011, and 2) many of the Program Faculty (Benveniste, Bredel, Buchsbaum, Cassady, Fiveash, Gillespie, Griguer, Markert, Nabors, Roth, Whitley and Willey) were involved in the successful competitive renewal of the UAB Brain SPORE Grant (P20 CA151129) in 2011. As stated earlier in the text, this training grant is intimately related to these two entities, and it was critical to ensure the success of the CCC and Brain SPORE Grant, which in turn provide invaluable resources for this training program. Because of the NCE, we were not able to appoint any new trainees in the last year of the grant.

The trainees/research projects supported by this training grant are briefly summarized below. See **Tables 6A and 6B** for publications by the trainees (abstracts not included).

### Postdoctoral Trainees:

#### 1. David Bauer, M.D.                      07/01/2007-06/30/2009                      Mentor: Jim Markert, M.D.

We developed an anti-glioma vaccine using an IL-12 expressing version of G207, a selectively replicating, oncolytic human HSV-1. The vaccine was evaluated with flow cytometry, *in vitro* cytotoxicity, and two murine models of intracranial malignant tumor. During the time of this training grant, Dr. Bauer was also a Neurosurgery Resident at UAB. **Eleven** publications have resulted from Dr. Bauer's research and clinical training, and he has given oral presentations at the American College of Surgeons (2009, 2010), Southern Neurosurgical Society (2009, 2010, 2011), CNS/AANS Joint Section of Pediatric Neurosurgery (2009, 2011), and at the UAB Postdoctoral Research Day (2009). Poster presentations on the oncolytic virus vaccine were at the Congress of Neurological Surgeons (2008), Society of Neuro-Oncology (2008, 2009), American Society of Gene Therapy (2009), and the UAB CCC Research Retreat (2008).

**Dr. Bauer has obtained a position as Assistant Professor, Department of Surgery, Dartmouth, effective July 2012.**

#### 2. Susan Buckingham, Ph.D.                      09/01/2007-06/30/2009                      Mentor: Harry Sontheimer, Ph.D.

Seizures affect more than 50% of patients with brain tumors and these seizures can be highly resistant to management by anti-epileptic medications. The hypothesis is that peritumoral seizures result from glutamate released by glioma cells in exchange for cystine via the  $\text{Na}^+$ -independent, electronegative cystine-glutamate exchanger, system  $x_c^-$ . Dr. Buckingham's research focus is to characterize spontaneous seizures in human glioma cell bearing-mice and treating them with sulfasalazine to determine whether blocking glutamate release through system  $x_c^-$  minimizes or prevents spontaneous seizure activity. Peritumoral seizures had not yet been identified in rodent models of human glioblastoma, however, with the use of continuous EEG and video monitoring of tumor-implanted animals, Dr. Buckingham can record spontaneous activity. These seizures could only be detected with EEG as they have a more subtle phenotype compared to characteristic convulsions. Because the implanted tumor cells express green fluorescent protein, she can identify the location of these cells and electrically stimulate the peritumoral brain. Together, these techniques provide a better understanding of seizure foci location and whether neurons are being kindled by repeated exposure to high levels of glutamate. Peritumoral astrocytes are also being studied to find out if glutamate-uptake mechanisms in these cells are failing. This work was presented at the Society for Neuroscience Annual Meetings in 2009, 2010 and 2011, at the Gordon Conference on Glial Biology in 2011, and resulted in a first-author publication in *Nature Medicine*, 2011.

**Dr. Buckingham has obtained a position as Director, EEG Core Facility, UAB Intellectual and Developmental Disabilities Research Center.**

#### 3. Susan Campbell, Ph.D.                      07/01/2010-present                      Mentor: Harry Sontheimer, Ph.D.

Malignant gliomas are fast growing tumors whose mass often results in seizures which are resistant to treatment with antiepileptic drugs. Glioma cells may contribute to epileptic seizures by releasing glutamate from the tumor mass via the  $\text{Na}^+$ -independent, electronegative cystine-glutamate exchanger, system  $x_c^-$ , onto the peritumoral region. Results from our lab have shown that the peritumoral region is hyperexcitable and this excitability can be inhibited by blocking glutamate release with sulfasalazine (Buckingham et. al., *Nature*

*Medicine*, 2011). We reported that glutamate is elevated in the interstitial space around the malignant glioma, and that tumor-implanted animals showed abnormal EEG activity, which was not observed in controls. We also reported that tumor-bearing animals treated with sulfasalazine showed a reduced in the frequency of epileptic events and decreased peritumoral neuronal hyperexcitability. The second part of Dr. Campbell's work was to assess the effect of gliomas on cortical excitability at the network level. She determined that the peritumoral region of tumor-bearing slices demonstrate spontaneous epileptiform activity which was not observed in controls. This work is In Press in *Epilepsia*, with Dr. Campbell as first author.

**Dr. Campbell is finishing her postdoctoral training in 2012.**

**4. George Dobbins, Ph.D.                      09/14/2009-08/31/2011                      Co-Mentors: David Curiel, M.D.  
and Yancey Gillespie, Ph.D.**

A novel dual targeting conditionally replicating adenovirus was generated that demonstrates improved oncolysis in a range of glioma lines assayed compared to a similar virus currently in clinical trials. A similar second virus was generated that contained a fluorescent modality that aided in tracking the spread of oncolysis, and has potential in cancer staging, surgical removal and monitoring. Currently, work is being carried out on arming the virus for improved cancer immunotherapy, using GBM animal models. Two manuscripts are under review on this work (*Molecular Cell* and *Molecular Therapy*). Dr. Dobbins successfully competed for an ACS Postdoctoral Fellowship on this work, entitled "Tumor-specific Targeted Oncolytic Virotherapy", 07/01/2012-06/30/2014.

**Dr. Dobbins is continuing his postdoctoral training with Dr. Gillespie at UAB.**

**5. James Cody, Ph.D.                      12/1/2008-11/30/2011                      Mentor: Jackie Parker, Ph.D.**

The metastasis of breast cancer to the brain and central nervous system is a serious complication of late-stage breast cancer that affects thousands of individuals each year. Aggressive tumors such as those of metastatic breast cancer can rarely be controlled by a single treatment strategy. Therefore, we propose a strategy that acts on the tumor in several different ways. Immunotherapy is an anticancer strategy in which the patient's own immune system is stimulated to attack the tumor. We hypothesize that immunotherapy of breast cancer brain metastases might be improved by combining this strategy with oncolytic virotherapy. We have previously developed an oncolytic herpes simplex virus designated M002, which carries a gene for the cytokine IL-12. We propose to use M002 to provoke an anti-tumor immune response that will eliminate breast cancer brain metastases. We have developed two immunocompetent intracranial murine models of breast cancer brain metastasis, and demonstrated that M002 extends the survival of mice bearing intracranial tumors more effectively than a non-IL-12 HSV. We have also developed a subline of human brain metastatic breast cancer cells which are enhanced for growth in the brain *in vivo*. Finally, we have utilized *in vivo* passaging to derive a subline of murine mammary carcinoma cells which exhibits enhanced "brain seeking" over parental cells, when this line is implanted in the mammary fat pad. These cells are modified to enable non-invasive imaging, allowing the development of metastases to be monitored over time. We expect these models to be of significant value in the future, both in terms of the biology of breast cancer brain metastases and as platforms for the evaluation of M002 and other cytokine-expressing HSVs. Seven publications arose from this work (3 as first-author), and another first-author manuscript is in preparation (2012). This work has been presented at AACR (2009) and American Society of Gene Therapy (2009).

**Dr. Cody is continuing his postdoctoral training with Dr. Doug Hurst at UAB in the area of metastasis of breast cancer to the brain.**

**6. Yun-Jun Lai, Ph.D.                      07/01/2009-06/30/2010                      Mentor: Fang-Tsyr Lin, M.D., Ph.D.**

Dr. Lai's research is focused on molecular mechanisms that are involved in cancer progression, especially in glioblastoma. The molecules studied include focal adhesion molecules such as TRIP6 (thyroid receptor interacting protein 6), LPP (lipoma preferred partner) and paxillin, and small GTPases that regulate the cytoskeleton such as Rho and Rac. Through these studies, we aim to determine the mechanisms of cancer progression, identify new therapeutic targets, and design small molecules for use in cancer therapy. This work resulted in 1 first-author publication in *Molecular Cell Biology* (2010), and a co-author manuscript currently under review. Dr. Lai has an on-going collaboration with Dr. Benveniste to investigate the role of Rac proteins in GBM migration, and is establishing a Zebrafish GBM model at her institution in Taiwan.

**Dr. Lai received less than two years of support because she accepted a faculty position in 2010; Assistant Professor, Department of Life Sciences, National Taiwan Normal University, Taipei, Taiwan.**

**7. Braden McFarland, Ph.D.                      07/01/2011-present                      Mentor: Etty (Tika) Benveniste, Ph.D.**

Dr. McFarland's work has been focused in the area of preclinical testing for GBM, evaluating the potential anti-tumor effects of AZD1480 (AstraZeneca), a novel JAK1/2 inhibitor. AZD1480 effectively blocked constitutive and stimulus-induced JAK1, JAK2 and STAT-3 phosphorylation in both human and mouse glioma cell lines, and AZD1480 treatment led to a decrease in cell proliferation and induction of apoptosis. AZD1480 inhibited both constitutive and stimulus-induced phosphorylation of STAT-3 in GBM xenograft tumor cells *in vitro*. Furthermore, AZD1480 suppressed STAT-3 activation in the glioma-initiating cell population in GBM tumors. *In vivo*, AZD1480 inhibited the growth of subcutaneous tumors and increased survival of mice with intracranial tumors by inhibiting STAT-3 activity, indicating that pharmacologic inhibition of the JAK/STAT-3 pathway by AZD1480 should be considered for the treatment of patients with GBM tumors. This work led to a first author publication in *Molecular Cancer Therapeutics* (2011), and oral platform presentations at the SNO annual meetings (2010, 2011). This work has led to an interest in evaluating AZD1480 in a Phase I clinical trial for recurrent GBM, in conjunction with Dr. Burt Nabors.

This work has been extended to understand cellular communication and signaling in GBM, particularly the aberrant signaling between the NF- $\kappa$ B and JAK/STAT-3 pathways. The NF- $\kappa$ B and the JAK/STAT-3 pathways are two important signaling pathways that have been implicated in glioma progression. Interestingly, both NF- $\kappa$ B and STAT-3 have recently been described as key players in the mesenchymal subtype of GBM, the more malignant of the subtypes. The findings demonstrate that NF- $\kappa$ B and STAT-3 participate in a vicious cycle of crosstalk, which ultimately ensures that mesenchymal GBMs survive, proliferate, and resist therapeutic efforts. This work has led to the preparation of two manuscripts that will be submitted for review within the next few months. In addition, the American Brain Tumor Association will fund a Basic Research Fellowship on this topic (2012).

**Dr. McFarland was a trainee on this training grant for only one year since she obtained independent funding from the ABTA (07/01/2012-06/30/2014).**

**8. Jason Warram, Ph.D.                      09/01/2011-present                      Mentor: Kurt Zinn, D.V.M., Ph.D.**

In collaboration with Dr. Steve Carroll, NOD.Cg-*Prkdc*<sup>scid</sup> *Il2rg*<sup>tm1Wjl</sup>/SzJ mice were used to generate human xenograft models of malignant peripheral nerve sheath tumors (MPNST). Imaging using FDG-PET/CT and bioluminescent imaging (BLI) was performed bi-monthly following implantation. The objective of this work is to track tumor development from these human MPNST cell lines in addition to evaluate the ability of FDG-PET/CT imaging to detect tumor presence with correlating BLI. Preliminary imaging analysis showed positive development of tumors after tail vein injection of human ST88-14 and STS-26T MPNST cell lines. FDG-PET/CT imaging was shown to be a powerful, non-invasive modality for the detection of tumor development after a tail vein injection of these cells. Necropsy of collected tissues will soon be performed to validate established tumor development. In addition to imaging xenograft models of MPNST, transgenic animal models are also being imaged. The objective of this work is to determine the sensitivity of FDG-PET/CT for spontaneous tumor development detection in addition to correlate FDG-PET/CT imaging with BLI. This work has resulted in a co-author publication (2012), and a co-author manuscript under review (2012).

**In summary, the accomplishments of our Postdoctoral Trainees are as follows:** 1) two have obtained faculty positions at academic universities (Bauer and Lai) and one has obtained a permanent position as a Core Facility Director (Buckingham); and 2) 6/8 have at least one first-author publication, 7/8 have at least one co-author publication, and 3/8 have first-author and co-author manuscripts under review or in preparation.

For the 3 trainees currently supported by the training grant, their plans are as described below. Dr. S. Campbell, an URM female, will finish her fellowship with Dr. Sontheimer by the end of 2012. She has a strong interest in developmental disabilities, and plans on working for a "not-for-profit" organization such as Cure Autism Now or The Rett Syndrome Foundation. She is exploring these opportunities at the present time. Dr. B. McFarland will transition off this training grant when the funding of her ABTA Postdoctoral Fellowship starts (anticipated date of 07/01/2012). Her plans are to pursue a career in academic research, and to start the interview process for a tenure-earning Assistant Professor position in 2013. Dr. J. Warram was appointed on 09/01/2011, and we plan to support him through the NCE period until 06/30/2013. Our goal for Dr. Warram is for him to submit applications to the ABTA, ACS and NIH for an individual postdoctoral fellowship in late 2012/early 2013.

Two past trainees, Drs. J. Cody and George Dobbins, are completing their postdoctoral fellowships at UAB, and plan to obtain academic faculty positions. Dr. Dobbins will start his job search in 2013. He is committed to the field of oncolytic virotherapy in cancer, with a focus on GBMs. Dr. Cody's plans are to submit a NIH K99/ROO grant application, as well as transition award applications to ACS and Susan B. Komen within the next year, submit several first-author publications in this same time frame, and then start interviewing for an academic position in translational cancer biology in 2013-2014. His research focus will be on breast cancer metastasis to the brain.

100% of the trainees have remained, or are currently in, positions related to biomedical research, teaching, training and scientific public policy.

#### **Predoctoral Trainees:**

**1. Angel Alvarez, Ph.D.                      01/01/2011-05/06/2011                      Mentor: Markus Bredel, M.D., Ph.D.**

The thesis project for A. Alvarez involved investigating the role of tumor suppressor genes  $\text{I}\kappa\text{B}\alpha$  and TNFAIP3 in NF- $\kappa$ B signaling on neural stem cell proliferation, survival and differentiation, and the establishment of patient-derived glioma stem cell lines to examine the role of cancer stem cells in tumorigenesis. Furthermore, a high-content screening system to identify novel compounds targeting cancer stem cells is being developed. This work resulted in 1 first-author publication (2011), 2 co-author publications (2010, 2011), and 4 manuscripts in preparation (2012). Furthermore, part of this work was presented at the Keystone Symposia on Stem Cells, Cancer and Metastasis (March 2011).

**Dr. Alvarez was supported by the T32 as a predoctoral trainee for a short period of time as it was determined that he had met the necessary qualifications for defense of his thesis.**

**2. Joshua Anderson, Ph.D.                      07/01/2007-12/31/2008                      Mentor: Candace Gladson, M.D.**

The thesis work of Dr. Anderson focused on the role of the extracellular matrix (ECM) in promoting angiogenesis in GBM. The emphasis was on brain microvascular endothelial cells, and the involvement of the Thrombospondin type 1 repeat peptide (ABT510) in promoting apoptosis of brain endothelial cells. This ultimately had a beneficial effect in inhibiting GBM growth *in vivo*. This work led to 2 first-author publications in 2007 and 2008.

**Dr. Anderson is currently a postdoctoral fellow in the lab of Dr. Chris Willey.**

**3. Brandi Baker, Ph.D.                      07/01/2007-06/30/2009                      Mentor: Etty (Tika) Benveniste, Ph.D.**

Brandi Baker investigated the role of immune mediators on the functionality of normal astrocytes and microglia, and how this may lead to malignant transformation. Specifically, she investigated the role of Suppressor Of Cytokine Signaling (SOCS3), a negative regulator of the JAK/STAT pathway, and a putative tumor suppressor, in astrocytes. These studies led to the understanding of how SOCS3 expression is regulated in astrocytes, how SOCS3 suppresses STAT3 activation in astrocytes, and how its loss in GBM may contribute to aberrant STAT3 activation and GBM progression. This work was presented at the FASEB Summer Research Conference: Neural-Immune Interactions, Carefree, AZ., 2008, and resulted in 3 first-author publications and 3 co-author publications.

**Dr. Baker is currently a first-year medical student at UAB.**

**4. David Gaston                      01/01/2011-present                      Co-Mentors: Rich Whitley, M.D.,  
and Kevin Cassady, M.D.**

David's thesis project is to investigate methods to increase the efficacy of oncolytic herpes simplex type-1 virotherapy for malignant glioma through stimulation of innate immune effectors. These strategies are being tested in a variety of mouse models of GBMs. These include implantation of human xenografts in scid mice, and syngeneic GBM models. This work has thus far resulted in a first-author publication (2011), and a co-author manuscript under review (2012).

**Mr. Gaston has passed his qualifying exam, and is currently a 4th year graduate student in the UAB MSTP.**

**5. George Twitty                      07/01/2009-12/31/2010                      Mentor: Etty (Tika) Benveniste, Ph.D.**

Mr. Twitty's work involved understanding the potential cross-talk between the NF- $\kappa$ B and JAK/STAT-3 pathways, two important signaling pathways that have been implicated in glioma progression, and are critical in

promoting the mesenchymal subtype of GBM. The cytokine TNF induces the activation of STAT-3 in human GBM cells. TNF is a potent activator of NF- $\kappa$ B, but has never been shown to activate STAT-3. Moreover, the ability of TNF to activate STAT-3 is dependent on NF- $\kappa$ B, cytokine expression, and the involvement of JAK kinases. This work led to the publication of 1 co-author manuscript (2011), and another co-author manuscript is in preparation (2012).

**Mr. Twitty left the training program in December, 2010, when upon discussion with his thesis committee and mentor, it was decided that he did not have the necessary determination to obtain the Ph.D. degree.**

#### **6. Crystal Wheeler**

**01/01/2009-12/31/2010**

**Co-Mentors: Peter King, M.D.  
and Burt Nabors, M.D.**

Crystal's research focus is to understand how the RNA binding protein HuR has regulatory effects in neurological diseases. Specifically, how HuR regulates Jagged-1 expression/function in recurrent GBM has been evaluated, and how HuR regulates myeloid derived suppressor cells in GBM is also being investigated. The role of HuR in two models of neurodegenerative diseases is also being studied: one for Multiple Sclerosis, and the other for ALS. This work has resulted in 1 first-author publication (2012), 2 co-author publications (2009, 2011), and was presented at the American Academy of Neurology (2010).

**Ms. Wheeler will defend her Ph.D. work in June 2012, and do a short postdoctorate in the labs of Drs. King/Nabors to finish up the last of her work.**

**In summary, the accomplishments of our Predoctoral Trainees are as follows:** 1) of the 6 predoctoral trainees, 5/6 have published at least one first-author publication, 6/6 have published at least one co-authored publication, and 1/6 has several first-author manuscripts in preparation; and 2) 5/6 predoctoral trainees are currently training or have continued in biomedical research, teaching and/or training. G. Twitty is the 1 trainee that left the training program.

Mr. Gaston, currently supported by the training grant, is pursuing his thesis work in the laboratories of Drs. R. Whitley and K. Cassady. Of the past trainees, Drs. Alvarez (URM) and Anderson are postdoctoral fellows continuing in the field of brain tumor biology, Dr. Baker is attending medical school, and Dr. Wheeler (URM female) will be applying to NIH IRACDA programs at UC San Diego, Univ. of Pennsylvania, and Tufts to continue research and teaching to students from groups under-represented in the biomedical sciences.

#### **6E. Distribution of Training Grant Positions**

The T32 Executive Committee has made an effort to keep all of the training positions filled (**TABLE 11**) and to distribute the trainee positions among the mentors associated with the training grant. Over the five-year funding period, there have been 16-18 mentors and 14 trainees. Of the 16-18 mentors, 12 have had 1 trainee funded by the T32, 1 mentor has had 2 trainees, and 1 mentor has had 3 trainees (some of these are co-mentors). Every effort will be made in the next funding period to continue to distribute the positions in an equitable manner, with a focus on supporting trainees in the laboratories of junior investigators.