

**NEUROSCIENCE AT THE UNIVERSITY OF ARIZONA:
RECOMMENDATIONS FOR THE ARIZONA HEALTH SCIENCES CENTER**

**Final Strategic Planning Report of AHSC Neuroscience Advisory Council (NAC)
March 28, 2014**

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EXECUTIVE SUMMARY

The long-range vision for neuroscience research at the University of Arizona (UA) is to deepen our fundamental understanding of brain function in health and disease and to apply that knowledge to improve patient health and medical care. UA's strength in neuroscience, distributed across many colleges and well represented in BIO5 and other Institutes, is a ready springboard for strategic investment in a set of research teams focused in areas of critical need. Bringing UA's diverse neuroscience entities together under the umbrella of a **Center for Innovation in Brain Science** will provide a hub for directly linking fundamental discoveries to solutions for important clinical problems, as well as for training the next generation of biomedical investigators. Strengthening basic, translational and clinical research areas under this umbrella will require investments in faculty, facilities, and administrative infrastructure. Taking into consideration the full spectrum of neuroscience work being conducted across UA campuses and the state of Arizona, the Neuroscience Advisory Council respectfully submits the following recommendations for strategic investments by UA's Arizona Health Sciences Center.

Opportunities

Most urgent:

- Create a university-wide **Center for Innovation in Brain Science** and hire a well-established, highly visible, inclusive, and collaborative clinician-scientist as its Director.
- Establish a **clinical research facility** for patient enrollment, referral and routine cognitive assessment and biospecimen collection, one that can provide the infrastructure for conducting and leading multi-center clinical trials.
- Provide **strong administrative and research staff support for clinical research studies**, specifically experienced support personnel for patient recruitment and retention, as well as biostatistical support for experimental design and data analysis.
- Promote synergy between clinical and basic neuroscience research through guaranteed **protected time for clinician-scientists** to conduct research, and **targeted hires** of basic scientists to fill critical gaps in areas linked to clinical needs.

Over the next three years:

We recommend the hiring of new basic science and clinical faculty to round out existing collaborative teams in the following areas for which there are critical needs and likely sources of extramural funding:

- **Cognitive aging in health and disease**
- **Chronic pain and traumatic brain injury**
- **Stroke and aphasia**
- **Integrative systems neuroscience**

In addition, we recommend hiring in a less-well-established area:

- **Normal and abnormal development of the brain and cognition**, to meet the needs of Arizona families, complement the four stronger areas, and facilitate large-scale research on brain health across the lifespan.

To support innovative, cutting-edge neuroscience research, now and into the future, we urgently need:

- **Imaging facilities** that include state-of-the-art instrumentation for microscopy and whole-brain imaging in animal models and human subjects, and high-level technical support staff.
- Support for flexible **bioinformatics/biostatistics** consultation, through a shared core facility.
- Expanded **specialized facilities for research animals**, notably genetic models, to conduct experiments using complex technologies that cannot be applied to humans.

Expected return on investment over 5 years: increased federal and non-federal funding of research and training grants, increased private philanthropic donations, novel discoveries leading to peer-reviewed publications and valuable intellectual property, improved teaching of the next generation of scientists and physicians, increased national rankings, and better clinical care for citizens of Arizona and beyond.

NEUROSCIENCE ADVISORY COUNCIL REPORT

NEUROSCIENCE STRENGTHS, CHALLENGES, AND OPPORTUNITIES

The global burden of brain disorders can be appreciated in statistics collected by the World Health Organization that indicate that there are more than 1 billion people with 1000 different neurological disorders worldwide. These problems range from conditions such as Alzheimer's disease, Parkinson's disease, stroke, epilepsy, and headache, to serious psychiatric disorders. Every year, at least 1.7 million cases of traumatic brain injury (TBI) occur, either as an isolated injury or along with other injuries, and are estimated to cost ~\$77 billion annually. TBI also contributes to about a third of all injury-related deaths in the U.S. Additionally, in the U.S. alone, more than 795,000 people have a stroke each year; stroke is the fourth leading cause of death and costs an estimated \$36.5 billion. Thirty-six million Americans incur the pain of migraine headaches, at an estimated annual cost of \$30 billion in lost productivity; and one in 88 children is affected by an autism spectrum disorder. Beyond treating neurological disorders such as these, it is critical to understand how to optimize brain function in individuals as they age, so that people who are living longer can maintain their independence and quality of life.

The state of Arizona has an aging population, with the greatest percentage gains from 2000 to 2010 in the ages between 55 and 64 years old. In many counties in Arizona, 20 percent or more of the population is 65 or older. In addition Arizona has a number of military bases and retirees served by the Veterans Affairs Health Care System. These demographics lead to a high percentage of individuals who have neurological disorders such as Alzheimer's disease, Parkinson's disease, TBI, pain, stroke, aphasia, and psychiatric disorders. The University of Arizona is poised to have a significant impact on brain health, based on existing research strengths that include neurological aging and age-related degenerative diseases, gene/environment interactions, chronic pain, TBI, stroke, and brain imaging. Current neuroscience strengths are complemented by world-class research in optics and biomedical engineering. With focused investments, these neuroscience areas can go from being strong to unparalleled. UA should emerge in the next three years as a premier destination recognized nationally and internationally for collaborative basic and clinical translational research in neuroscience.

Strengths. Review of the research currently conducted at UA revealed multiple areas of neuroscience excellence. We have faculty with national and international reputations who are successful in obtaining federal research funding, have excellent publication records, and demonstrate abilities to develop collaborative groups for growth and training. Focused examination revealed especially strong faculty groups with expertise in the following areas:

- 1) Cognitive aging in health and disease
- 2) Chronic pain and traumatic brain injury
- 3) Stroke and aphasia
- 4) Integrative neuroscience

An additional area was identified as less mature but complementary to existing strengths and of strategic importance for Arizona:

- 5) Brain development in health and disease.

Challenges. Broadly, the shrinking federal budget for research and the reduction in support from the State of Arizona create serious pressures on biomedical research. In addition, the tendency of universities to focus on purely individual accomplishment as the basis for promotion and tenure can hinder collaboration.

More locally, while UA's neuroscience community has multiple formal and informal seminar series and numerous ongoing collaborative projects, we need a more comprehensive way to bring the full breadth of the community together – from fundamental researchers to clinical practitioners – to maximize the impact of our neuroscience research. There exist "silos" of work that do not currently interact, and thus do not share in big data collection, training, and larger funding opportunities. Those silos are exacerbated by a

lack of core infrastructure, lack of communication, and a shortage of basic- and clinician-scientist teams to propel research efforts towards improved patient outcomes.

Opportunities. Focusing UA’s and AHSC’s limited resources on building teams with expertise in key areas and on rewarding collaborative efforts to obtain external funding would help to overcome these challenges. A university-wide **Center for Innovation in Brain Science**, including shared technical and clinical facilities and administrative support, would create a more interactive community environment in which to conduct neuroscience research. These teams would:

- collaborate together to write successful individual and large federal grants
- perform cutting-edge research on normal brain function, brain disorders and diseases
- design and execute clinical trials
- work with pharmaceutical companies on SBIR/STTR grants
- create novel intellectual property
- generate new start-up companies
- grow research training programs for graduate education and mentoring programs for junior faculty
- expand outreach programs for the local community and State of Arizona on brain awareness
- generate philanthropic support for **Center** operations as well as for retention of key faculty, for instance by creating endowed chairs.

CONCISE VISION STATEMENT

UA will become one of the foremost centers for brain science in the country. Building on our collaborative spirit, we envision strategic team-building to take advantage of funding opportunities that address critical needs in the state of Arizona and beyond. To attain maximum synergy, teams will be developed in cognitive aging in health and disease, pain and traumatic brain injury, stroke and aphasia, and integrative neuroscience; in addition, a new focus will be placed on brain development in health and disease, to meet community needs and complement the other areas of focus.

SPECIFIC RECOMMENDATIONS FOR NEAR-TERM INVESTMENTS

Faculty:

The need for new faculty, including basic scientists, clinician-scientists, and clinician/scientist teams, arose in every discussion. A pervading theme is that team hires are more effective than independent hires, to ensure support and success in research efforts. Areas in which we can have special impact in our communities and across the state, while having potential to achieve national recognition, include clinician and basic science hires in the following areas:

	clinician scientists	basic scientists
• aging in health and disease	Alzheimer’s disease	cognition/imaging
• chronic pain and TBI	pain	behavior/electrophys or molecular
• stroke and aphasia	neurointensive care	language/imaging
• integrative neuroscience	mind/body interactions	primate model/genetics/computation
• development in health and disease	pediatric neurology	animal models/molecular/genetics/ drug development

Team hires will rapidly enhance success by offering new faculty support and development from existing productive faculty. These faculty leaders will aid new hires in writing manuscripts and grants, mentor them for training awards, help in collaborative efforts, aid in technical design, share equipment, introduce and support them in the context of the national and international science community, and in management of time.

Facilities:

Research facilities needed to achieve excellence in key areas include:

- space dedicated to clinical research – populated with experienced research support personnel,

including personnel to perform routine patient assessments, sample collection and preliminary data analysis

- state-of-the-art imaging facilities – including both microscopy and whole-brain imaging technologies and expertise, for animal and human work
- robust bioinformatics/biostatistics expertise
- “genetic” animal models for studies in health and disease

Infrastructure:

Improved and expanded infrastructure in support of neuroscience research:

- Strong administrative support for clinical research – including large-scale patient referral and leadership’s support for clinical research activities
- Stronger partnership with UAHN to better support current and new research collaborations
- Develop guidelines for storage of human subject records that distinguish between clinical and research data
- Creating an environment that fosters research including protection of research time for clinician-researchers
- Easier access to UA collaborators, perhaps via a web-based system that enables neuroscience researchers to find others with similar or complementary interests
- Improved processing of research contract agreements
- Engaging with Tech Launch Arizona to capitalize innovative research
- Education/training support for the full research workforce pipeline
- Seed funding for interdisciplinary research projects targeting large extramural funding opportunities (e.g., CTSA), and strategic funding to bridge gaps in research continuity

Major Enabling Vision for UA Neuroscience

As outlined above, the committee identified the need for the creation of an overarching **University of Arizona Center for Innovation in Brain Science** set firmly on three legs: excellence in fundamental and translational neuroscience research, clinical neuroscience research (including clinical trials), and evidence-based clinical care. This Center will provide a focal point for integrating brain science research across University of Arizona colleges, institutes and campuses, and a bridge with other institutions with significant neuroscience presence across the state. Critical to the success of this plan will be to recruit a dynamic director for the Center, one who will guide and facilitate teams of collaborative scientists to reach the potential that exists for significant scientific discoveries in the five critical areas identified in our review.

Foremost in this plan is the **training of a diverse workforce**, including a new cadre of clinician-scientists, woven through all three fundamental areas; this would include expansion of the existing Arizona Clinical and Translational Research Graduate Certificate Program currently administered by the College of Public Health. Strategic investments in **new faculty**, critical cutting-edge **research facilities**, and specific **administrative infrastructure** for the Health Sciences will be required for this Center to become *the* “go-to” center for neuroscience research and for clinical care of key neurological disorders.

Why is this effort so important? Why now?

The Arizona Health Sciences Center has a golden opportunity to build on neuroscience strengths that are broadly distributed across the university and its campuses, both in the Health Sciences colleges and in other institutes and colleges across the campus, to create unparalleled excellence in several key areas.

To achieve our goal of alleviating the suffering and lost productivity caused by brain dysfunction, we propose a coordinated effort to support teams of scientists coming together to focus on several significant neuroscience research problems. There exists great strength and promise at the University of Arizona to uncover, for example, critical mechanisms that may promote resistance to disease or facilitate recovery from injury, and to appreciate how these processes may differ across gender, ethnicity, and other variables critical to the citizens of our state and beyond. We have faculty at the university who are currently developing interventions to improve quality of life, protect against injury and disease, mitigate

developmental disabilities, and enhance memory. These advances can and must be translated directly into clinical care – and this will be facilitated by the implementation of the strategic investments outlined in our report. Other advances, such as gene-based diagnostics, therapeutics and wearable monitors of physiological processes, will be developed commercially, while working with our business community partners in these endeavors. The promise of such clinical and commercial applications provides opportunities to work with federal agencies that fund research and also with private industry and disease-oriented foundations, while embracing our own intellectual property and growth.

Despite limited growth of the NIH budget, NIH still is the largest source of support for neuroscience research. UA will be more competitive for NIH funding if recommendations made by the Neuroscience Advisory Committee are adopted. President Obama has created a special funding opportunity, the BRAIN Initiative, which initially is set to invest \$100 million and should double neuroscience funding in 2015. The Initiative, involving NIH and other federal agencies, is focused on developing *“integrated cellular, anatomical, and physiological data sets of unprecedented scope, rendered intelligible through theoretical and behavioral analyses... [The NIH will] focus on circuits and technology development, the emphasis on tight interdisciplinary interaction between experimentalists and theorists, and between tool-makers and tool-users, and the importance of integrating animal models with human neuroscience”* (C. Bargmann and W.T. Newsome in Neuroscience Quarterly winter 2014 edition). At the UA, we already have harnessed our distributed neuroscience strengths to produce several U01 proposals that cut across investigators housed in BIO5 and the Colleges of Medicine, Science, and Optical Sciences. By deploying special resources into the areas that hold high promise for garnering competitive grant awards from the federal agencies, such as those illustrated by the current BRAIN Initiative, UA will increase its success in garnering awards in the form of R01 grants, Center Grants, Program Project Grants, U-type cooperative agreements, larger consortium-style grants, and training grants.

As we compete more successfully for federal grants, both large and small, we also will attract increased funding from industry, private agencies/foundations, and philanthropic sources. This increased research activity will in turn generate more intellectual property and potential start-up companies, in collaboration with Tech Launch Arizona. These efforts will improve the neurological and mental health of people in our community, State of Arizona and worldwide, while developing a pipeline of well trained and educated pool of faculty, clinicians, students, and staff for ongoing research and clinical care.

With strategically targeted investments that start in 2014, AHSC can help to bring UA neuroscience to the national forefront in five strategic areas. In this way, we believe that the UA will be able to develop and support an unparalleled flow of creative new ideas from the neuroscience research lab to the clinical setting.

APPENDIX

PROCESS FOLLOWED BY NEUROSCIENCE ADVISORY COUNCIL

1. The Neuroscience Advisory Council (NAC), with co-chairs Drs. Carol Barnes (Psychology), Leslie Tolbert (Neuroscience), and Todd Vanderah (Pharmacology), was appointed in November 2013 and had its first meeting on Dec. 18, 2013. At that meeting Senior Vice President for Health Sciences Skip Garcia gave NAC its charge to make recommendations for the strategic deployment of AHSC resources to achieve national distinction in areas of neuroscience where UA has strength and high potential for leadership. Particular requests were that the Council consider performing a SWOT analysis and make recommendations for where resources could be invested most effectively to build on specific strengths and opportunities, with a proposed timeline for maximum return on those investments. The following areas were mentioned by Dr. Garcia as possibilities to consider for investment:

- Recruitment of thought leaders and faculty members with specific expertise
- Enhancement of faculty training opportunities (e.g., seek more K-funded physician-scientists, T-32 training grants)
- Development of pilot funding for interdisciplinary collaboration
- Allocation of funding to hire pre- and post-award administrative support as well as development staff to increase philanthropic support and community outreach.

All NAC members were asked to submit information to the group about their own broad areas of interest and knowledge and needs that they would immediately identify as critical or of especially high promise.

2. NAC's co-chairs reviewed the input received from NAC members and compared it with the conclusions of a 2009 SWOT analysis of neuroscience done for the BIO5 Institute. As a basis for further NAC discussion, they developed a chart that listed fundamental research areas, translational/clinical research areas, and research methods/approaches under the categories of "major expertise," "significant presence," "emerging presence," "at risk," and "weaknesses/gaps."

On Jan. 13, 2014, NAC met to vet and refine the elements of the chart. The revised chart (provided below) then formed the basis for the development of six thematic subcommittees to delve into specific areas for potential neuroscience focus. The six themes were:

- Systems neuroscience – including sensory, cognitive, motor, and affect/emotion neuroscience
- Development and aging – including normal development and aging, as well as Alzheimer's, Parkinson's, other neurodegenerative diseases and stem cell approaches
- Movement disorders – including robotics applications
- Pain – including cancer pain, diabetic neuropathy, migraine, arthritis pain
- Traumatic brain injury – including basic pharmacology, acute and long-term care
- Stroke and other vascular-related areas – including aphasia, blood-brain barrier, inflammation, and infection

Members of NAC volunteered to serve on as many of the subcommittees as they wished, to help drive a robust and interdisciplinary discussion of relevant issues. Each subcommittee also was free to invite other people who could provide important insights to join in the discussions (e.g., other faculty members not invited to the original committee, including more investigators from Phoenix, and members of other Advisory Councils). The charge to the subcommittees was to address in their thematic areas of attention:

- What particular areas are ripe for specific focus, either to meet a crying need or to put UA at the cutting edge?

- What could be done in these areas that would enhance the collaborative research potential, clinical/translational research efforts, and research training potential?
- What infrastructure would be needed, if any?
- What strategic hires would significantly impact our ability to acquire large collaborative grants, as well as individual grants, such as such as R01s?
- What federal and other sources will be the prime targets for future funding?

All subcommittees also were asked to consider broader, cross-cutting elements:

- Physician-scientists – how can we attract, support, and retain them?
- Animal models
 - How to build on UA’s invertebrate-model expertise
 - What genetic models beyond flies and mice are needed
- Imaging methods and bioinformatics to analyze and store images
 - MRI and fMRI, PET, DTI
 - Confocal and multi-photon microscopy
 - Electron microscopy for 3-D reconstruction
 - Development of new imaging technologies
- How to maximize diversity in the pipeline (including garnering more training grants, NIH Minority Supplements, collaborative grants)

3. Each subcommittee had several free-standing meetings, and each submitted a report for discussion by the full NAC at its next meetings, on Feb. 3 and Feb. 17, 2014. At the Feb. 17 meeting, Sangita Pawar from the College of Medicine-Tucson Research Office and Rakhi Gibbons from Tech Launch Arizona gave short presentations on new initiatives in their offices that should provide helpful support to neuroscience researchers.

4. On March 10, 2014, the NAC met to discuss a short-list of five themes and specific targeted investments in basic-science and clinician-scientist faculty, core research facilities, and administrative infrastructure that emerged from the subcommittee reports. The group suggested some additions and changes, which were then incorporated into a first draft of the Council’s final report.

5. On March 21, 2014, the NAC met to review and discuss a draft report developed by the co-chairs. Several suggestions were made for change, and were incorporated to generate the final white paper.

SWOT ANALYSIS

Please see next page for a summary of the SWOT analysis done as the basis for the NAC recommendations.

SWOT ANALYSIS

	FUNDAMENTAL RESEARCH AREAS	TRANSLATIONAL/ CLINICAL RESEARCH AREAS	RESEARCH METHODS/APPROACHES
Major Expertise	Cognitive neuroscience Systems neuroscience: normal aging pain learning and memory olfaction	Alzheimer's Disease/other dementias Parkinson's/other neurodegenerative disease Pain/analgesics/anesthetics Blood-brain barrier/drug delivery Stroke Speech & language Aphasias/stroke rehab Brain tumors (esp. children)	Imaging (confocal, multiphoton, MRI, PET, DTI) Single-unit and ensemble recordings Behavioral/cognitive assessment Evidence-based clinical practice Neuropharm/pharmacokinetics Clinical trials Clinical epidemiology Invertebrate model systems Interdisciplinary collaboration
Significant Presence	Cellular neuroscience of n & glia Molecular neuroscience Developmental neuroscience	Parkinson's/other movement disorders Epilepsy Down Syndrome & Other Neuro-Developmental Disorders Trauma, including TBI Ophthalmology Neurologic emergencies Inflammatory processes	Medicinal chemistry Molecular genetics Evolutionary bio Multi-center clinical trials Drug development Vertebrate Model Systems
Emerging Presence	Stem cell biology Epigenetics Microbiome/microbiology Molecular neuroscience Computational neuroscience Robotics Neuroimmunology	ALS Depression, anxiety disorders Migraine/neuropathic pain Autism Stress Sleep effects on memory Emotion/affect and disorders	Genetic models of disease Mathematical modeling Medical nanotechnology Biostatistics
At Risk	Mammalian neurosci (systems, molec., genetic) Human neuroanatomy Motor control Vision		High-end electron microscopy/3D reconst'n Synaptic physiology
Weaknesses/Gaps		Pediatric neurology Neurobiology Diabetes Comprehensive Translational Pain Clinic, including Patient Referral System Emergencies associated with aging	Bioinformatics Pharmacogenomics Small Animal PET Shared high-end instrumentation Optogenetics Brain-machine interface Clinical genetics

SUBCOMMITTEE REPORTS

Reports of five of the six subcommittees formed by the Neuroscience Advisory Council to inform its development of recommendations follow. The sixth subcommittee, on movement and movement disorders, discussed ideas that were brought to the full NAC, but did not provide a written report. Members of that subcommittee were:

Katalin Gothard (Physiology)
Andy Fuglevand (Physiology)
Chuck Higgins (Neuroscience)
Scott Sherman (Neurology)

Neuroscience Advisory Council Pain Subcommittee

Subcommittee members:

Todd Vanderah (Pharmacology)	C. Kent Kwoh (Medicine)
Frank Porreca (Pharmacology)	Zhao Chen (Epidemiology and Biostatistics)
Tom Davis (Pharmacology)	Wayne Jacobsen (Anesthesiology)
Victor Hruby (Chemistry and Biochemistry)	Ole Thienhaus (Psychiatry)
Kurt Denninghoff (Emergency Medicine)	

a) What particular areas are ripe for investment, either to fill a crying need or to propel the UA to the cutting edge?

Current strengths in Pain Research at the UofA:

- Critical mass in basic scientists in pain research (11 - 15 faculty)
Nationally and Internationally recognized
- Currently there are a total of 15 NIH grants on pain, 3 related to pain
8 in review or new submissions – in 2014
- Currently faculty in pain research collaborate with approx. 15 pharmaceutical companies
- 2013 Publications in Pain research – Approximately 58 peer reviewed manuscripts
10 reviews/chapters
- Six faculty act as Editors of Pain- and/or Headache-Peer Reviewed Journals
- Six faculty act as Reviewers on NIH grants/ One on VA/DOD grants
- Track record of training physician scientist/junior professors/post doctoral fellows/ graduate students in achieving funding (K-awards, R21/R01/STTR/SBIR/T-awards)
- Excellent collaboration between chemistry, pharmacology, physiology, Cancer Center
- Currently have two pain fellows at South campus; New pain Faculty member (MD/PHD) starts in July 2014 – an additional MD/PHD pain faculty is being recruited

The need for Pain Research:

- 100 million Americans are currently suffering from chronic pain (Institutes of Medicine of the National Academies of Science) (this is more than diabetes, cardiovascular events and cancer put together), 1.5 billion people world wide suffer from chronic pain

- Majority of chronic pain patients are still using old drugs (NSAIDs, reuptake blockers, opioids - desperate need for novel therapies)
prescribed opioids are now the leading drug of abuse
- 1.2 to 1.5 million people in Arizona live with pain from Arthritis
- 1.0 million people in Arizona suffer from chronic back and neck pain
- Pain is the number one reason people miss work (headache, back pain, arthritis)
- Arthritis and Back Pain are the two top reasons individuals go on disability
- Cancer pain (only two to three labs in the US that have grants in this area)
- Chemotherapeutic, Geriatric and Diabetic Pain (growing populations)
- Migraine is the most prevalent neurological disorder in the world; 2 faculty have preclinical R01 grants on headache pain.

b) What could be done in these areas that would enhance the collaborative research potential, clinical/translational research efforts, and research training potential?

Collaborative Research Potential:

- Pain research could build strong research collaborations with Anesthesiology, Cancer Center, Neurology, Arthritis Center, Ageing Center, Radiology, Medicine, Emergency Department, Psychiatry, Pharmacy, Public Health, Nursing
- Expand our collaborations/partnerships with pharma, biotech, bioengineering companies, TGen, BNI, Mayo Clinic
- Novel molecular targets for the attenuation in pain are being discovered in house with IP for drug development by in house chemistry, pharma, and biotech companies
- Drug abuse due to narcotics can reach across multiple disciplines from developing non-addictive narcotics, to understanding the neurobiology/neurochemistry of narcotic addiction to collecting data on populations using narcotics for pain.

Clinical/Translational Research and Training:

- Take novel compounds (developed by our chemistry faculty and pharma) into clinical trials in cancer pain, neuropathic pain, headache, arthritis, chemotherapeutic/diabetic pain, etc.
- Develop a “Pain Institute” that integrates clinical and basic science research as well as training
- Develop Clinical Research Projects in the use of current methods and medications for pain (i.e., neuroimaging of the CNS in both humans and animals in pain to determine cortical control/connectivity of pain)
- Mentoring of physician scientists – (submit K-award & T-award applications) – create an invited speaker list that includes young faculty and success in research careers

c) What infrastructure would be needed, if any?

- A comprehensive pain clinic that would allow clinical trials and research testing in pain patients;
- Streamline clinical trials for pain research
- Imaging needed to identify areas of CNS and chronic pain (Animal and Human imaging);
- Imaging needed to determine how drugs may affect the CNS
- Core facilities for measurements of biochemical markers (HPLC, NMR, Mass Spec, Elisa, etc.)
- Core facilities for novel drug development/toxicology/pharmacogenetics
- Core facilities for advanced behavioral testing
- Core facilities for human bio-specimens

- Bioinformatics (human gene analysis in pain populations – correlations in animal studies)

d) What strategic hires would significantly impact our ability to acquire large collaborative grants as well as individual grants, such as R01s?

- Clinician scientists interested in pain research (Anesthesiology, Neurology, Medicine, Cancer Pain, etc.)
- Clinical faculty with experience and interest in radiological imaging of pain patients
- Clinician scientists in areas of arthritis, headache and cancer pain research
- Chemist with drug discovery experience
- Toxicologist with drug development experience
- Pharmacologist with drug development experience
- Continue to established courses and programs to educate (i.e., BME 466 “Clinical Research”, PHCL 553 “Pain Research”, PHCL 595B “Ethics, Grant and Manuscript Writing”)

e) What federal and other sources will be the prime targets for funding?

Remember to keep in mind the cross-cutting issues listed at the bottom of the document describing the six themes.

Funding sources:

- Large NIH U-grants in drug development
- PPG grants that would allow for novel molecular targets that may be linked to chronic pain
- CDMR and DOD grants for novel non-addictive drugs for chronic pain
- Individual R01s in a multitude of areas of chronic pain
- Individual K-award grants for training in pain research
- Training grants for postdoctoral fellows and graduate students
- Pharmaceutical and biotech company in testing compounds from bench to bedside
- Philanthropy from those who suffer from chronic pain (endowed chairs-faculty retention)

Cross-cutting with other themes:

- Aging – multiple areas include impact of pain on cognitive function and impulsivity, arthritis, back pain, MS, trigeminal neuralgia, shingles, etc.
- TBI – brain injury and pain, headache, psychological pain
- Sensory Systems – Identification of novel molecular targets on sensory fibers, further identification of unique fiber innervation, further identification of spinal cord neuro-damage
- Stroke – Pain after stroke and/or CV events is a unique area that has very little research, drug delivery to the brain,
- Center of Integrative Medicine – alternative methods of pain relief along with measurable biomarkers (i.e., endogenous opioids, cannabinoids, dopamine and norepinephrine)
- Patient-centered Outcomes Research institute (PCORI) – (i.e., sleep and pain)
- Precision Health – identifying targets in chronic pain that may be due to genetics/epigenetics and developing personalized treatment regimens.
- Population Health and Health Outcomes – Identifying whether individuals in Arizona are receiving adequate pain treatment, % of individuals that may become addicted to narcotics

- Health Disparities – Identify whether there is equity in pain management and whether certain populations are more likely to suffer from chronic pain and/or whether there are populations that are more likely to become addicted to narcotics
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Neuroscience Advisory Council Traumatic Brain Injury Subcommittee

Subcommittee members:

Kurt Denninghoff - Chair (Emergency Medicine)
Pélagie Beeson (Speech, Language and Hearing Sciences)
Jonathan Lifshitz (Child Health)
Uwe Stolz (Emergency Medicine)
Bentley Bobrow (Emergency Medicine)
G. Alex Hishaw (Neurology)
Dan Spaite (Emergency Medicine)

Randall Friese (Surgery)
David Adelson (Child Health)
Frank Porreca (Pharmacology)
C. Kent Kwoh (Medicine)
Joseph Dagher (Electrical and Computer Engineering)
Gene Alexander (Psychology)
Katalin Gothard (Physiology)

I. What particular areas are ripe for focus, either to meet a crying need or to put the University of Arizona at the cutting edge?

A. Traumatic brain injury (TBI) is a crying need

It is difficult to overstate the impact of Traumatic Brain Injury (TBI) on American society. Approximately 1.4 million victims of TBI are seen in emergency departments each year in the U.S. and of those 50,000 die and 235,000 are hospitalized. It is the leading cause of death and disability in children. Even following mild TBI, ten to fifteen percent are left with a permanent disability. The Centers for Disease Control (CDC) estimates that at least 5.3 million Americans or approximately two percent of the U.S. population have a long-term need for help to perform activities of daily living as a result of a TBI. Direct medical expenditures and indirect costs of TBI totaled an estimated \$60 billion in the U.S. in 2000.

B. TBI is an area ripe for focus

In Arizona and at the University our current strengths in TBI research are:

1. We have nationally and internationally recognized clinical scientists and faculty specializing in adult and pediatric TBI research, of those faculty there are a total five NIH grants explicitly studying TBI and thirteen publications related to TBI which three are in review or new submissions in 2014.
2. Currently TBI focused research Faculty lead the country in enrollment in the largest clinical trial ever funded by the NINDS that includes researchers from Maricopa Hospital, Phoenix Children's Hospital, the State of Arizona Department of Public Health, the University of Arizona College of Medicine in Phoenix, the University of Arizona College of Medicine in Tucson and the University of Arizona College of Public Health.

3. Excellent clinical trials partnership between the University and multiple Maricopa county hospitals and the University of New Mexico.
4. A regional clinical trials network was established in Phoenix to provide on-call coordinator support for hospitals who are participating in clinical trials with the University and a national leading innovative collaborative support system, that captures a hundred percent patient screening for acute care trials including TBI, was developed at the University of Arizona Healthcare Network campuses to provide 24:7 in-house enrollment for clinical trials in the emergency departments.
5. Our consortium participants completed the appropriate Institutional Review Board and compliance training, including participants in Phoenix, Tucson and Albuquerque that have multiple exception from informed consent trials.
6. Starting in 2013, we are joined forces with the Department of Biomedical Engineering at the University to actively train undergraduate students in clinical trials ethics, design and enrollment. The 2014 spring semester had fifteen students enrolled.

II. What could be done in these areas that would enhance the collaborative research potential, clinical/translational research efforts, and research training potential?

A. Collaborative Research Potential

Our database of patients in Arizona with TBI, generated by the NINDS funded EPIC and EPIC Jr. trials, could be used in multiple ways to expand our collaborations/partnerships with pharmacy, biotechnology, bioengineering companies, and researchers evaluating pain and “minor” TBI.

B. Clinical/Translational Research and Training

1. Deploy novel compounds and therapies, developed by basic scientists from across the collaborative network, the NIH, the DOD and pharmacy, in clinical trials testing their use in TBI areas of acute care, post headache and language a speech recovery, post seizures, and etc.
2. Develop **The Arizona Institute for Innovative TBI Management** that offers clinical and basic science research training.

III. What infrastructure would be needed, if any?

Needed infrastructure would include: 1) Imaging needed to identify areas of CNS and TBI that can identify the type and severity of TBI in order to facilitate therapeutic decisions during the acute, subacute and chronic phase of care, 2) imaging needed to determine how drugs may affect the CNS, 3) core facilities for measurements of TBI serum markers (e.g.:HPLC, NMR, Mass Spec, Elisa), 4) core facilities for novel drug development/toxicology/pharmacogenetics, and 5) core facilities for advanced behavioral testing and treatment.

IV. What strategic hires would significantly impact our ability to acquire large collaborative grants as well as individual grants, such as R01s?

New hires would significantly impact areas of basic science faculty in TBI research, clinical faculty in TBI radiological imaging, chemist with TBI drug development experience, pharmacologist with TBI drug development experience, and epidemiologist(s) with TBI experience.

- V. **What federal and other sources will be the prime targets for funding?**
Remember to keep in mind the cross-cutting issues listed at the bottom of the document describing the six themes.

A. Potential Funding sources

- PPG grants that would facilitate the collaboration between basic scientists studying TBI in animal models, developing new therapies and testing them in our clinical trials laboratory
- NINDS and DOD grants for novel new therapeutics in TBI
- Large NIH U-grants in drug development
- Individual R01s in a multitude of areas of TBI including pain, recovery of function, acute treatment
- K12/08/23 and T32 grants with a focus on the treatment of TBI
- Pharmaceutical and biotech company support for testing compounds (actively underway now but easily expandable with additional support)
- Philanthropy from those whose family suffer from the effects of TBI (endowed chairs-faculty retention)

B. Cross-cutting with other themes/subcommittees

- **Aging:** TBI across the continuum of life including Alzheimer's and other degenerative diseases of the brain
- **Pain:** Brain injury and pain, headache, psychological pain
- **Stroke:** Rehabilitation, language recovery, return to work, long term care

Neuroscience Advisory Council
Aging/Development Subcommittee: Brain Health across the Lifespan

27 March 2014

Subcommittee members:

Carol Barnes (Psychology)

Leslie Tolbert (Neuroscience)

Lynn Nadel (Psychology)

Linda Restifo (Neurology)

Lalitha Madhavan (Neurology)

Katalin Gothard (Physiology)

Brad Story (Speech, Language and Hearing Sciences)

Naomi Rance (Pathology)

Terry Monks (Pharmacology and Toxicology)

Geoff Ahern (Neurology)

Eric Reiman (Psychiatry)

Meeting summary:

The subcommittee met on Wednesday, January 29, 2014, in the Evelyn F. McKnight Brain Institute conference room, LSN 352. Discussion focused on two main topics: (i) the established, well-coordinated statewide efforts in cognitive aging and age-related neurodegenerative diseases (e.g., Alzheimer's, Parkinson's, ALS); and (ii) the fragmented areas of cognitive development and developmental brain disorders (intellectual disabilities, including Down syndrome; autism spectrum disorders, ASD; and

schizophrenia). There was strong agreement on overarching goals:

Vision: an integrated effort that marries research and medical care to optimize brain health across the lifespan.

Mission: to maximize human potential by

- creating new knowledge about brain development and aging
- translating that knowledge into outstanding diagnostics and therapeutics for brain diseases

There are great strengths and successes in a number of domains of aging research conducted at UA and across the state. These include both animal and human work on normal aging, and an Institute (Evelyn F. McKnight Institute) devoted to discovering ways to optimize successful aging trajectories. The Center on Aging is synergistic with this theme, as their emphasis is on understanding and ameliorating frailty. Work in Alzheimer's disease is also extremely strong at UA campuses and across the state. Some of the state-wide programs for early disease detection, prevention trials, and tracking and obtaining brains of AD and normal individuals are essentially unsurpassed in the country. There are specific areas, however, in which we are vulnerable, and strategic investment would have enormous benefit. In Tucson, in particular, we struggle to enroll living participants for experiments to feed into the state wide Alzheimer's Consortium projects, into the Federal Alzheimer's Disease Core Center efforts and for individually-funded research by investigators at this institution. Several factors contribute to these constraints, including inadequate dedicated space and staffing for clinical neuropsychology assessments, and too few clinician scientists to handle needed increases in patient recruitment. Both of these factors hamper the ability to conduct comprehensive longitudinal research, which includes testing cognition, biomarkers in blood and CSF, and brain imaging, as well as for conducting large scale clinical trials. The BIO5 Institute is in negotiations to fill one of their CTSI positions with a promising young M.D. whose research expertise is in animal models of Alzheimer's disease, and who is very interested in developing the necessary memory clinics, and other parts of infrastructure needed to strengthen our AD patient pipeline. It is critical that we are successful in this recruitment, and can expand beyond this single young investigator to build AD research here in Tucson. Another place that we will become vulnerable in the next few years concerns an imminent retirement of a well-known cognitive aging scientist (Glisky), who has been key to development of sensitive cognitive test batteries that can detect changes in normal aging as well as in brain damage, AD and other neurodegenerative disease populations. It is critical not to lose that expertise that is so central to developing large grants, or for clinical trials.

Research and clinical care in developmental neuroscience areas are also ripe for focused investment. Existing UA funding (based largely in Pediatrics) includes multiple surveillance grants from CDC for ASD, fetal alcohol syndrome, and developmental disabilities, as well as a large training grant from HSRA on neurodevelopmental disorders. Additionally, UA has applied to join the Fragile X Clinical and Research Consortium. The case for strengthening the area of normal and abnormal development can be found in a number of areas.

Key points:

- With the incidence of ASD higher in Arizona than the US average, and higher yet among Hispanic children, the state has an urgent need for greater focus on brain development.
- There is great potential to partner with SARRC, the Phoenix-based Southwest Autism Research & Resource Center, and Phoenix Children's Hospital, which is now UA-affiliated.

- **Neural plasticity** is already the focus of diverse basic research programs at UA using animal models or human subjects. Enhancement of brain function by tapping into plasticity mechanisms is the underlying premise of existing translational research programs involving faculty in Psychology, Neurology, and Speech Language and Hearing Sciences in Tucson. These range from drug discovery to teaching motor control for speech production.
- A research program based in the Arizona Research Laboratories uses cutting-edge genomic sequencing technology to find mutations that cause intractable epilepsy and other neurodevelopmental disorders.
- Diamond Children’s Hospital provides new opportunities to expand these programs.
- On the other hand, recent and imminent faculty losses, e.g., in Child and Adolescent Psychiatry and Pediatrics, threaten both clinical care and research activities.

Critical investments needed:

- **Urgent infrastructure needs:**
 - Dedicated clinical research space (neither existing space nor CATS is adequate)
 - A Center for interdisciplinary translational research and clinical care
 - ideally ‘under one roof’
 - planning should begin immediately, as ‘new buildings’ are being discussed
 - Expanded brain imaging capabilities
- **Intellectual capital and research resources:**
 - Expand Clinical Neuropsychology Core facility
 - Recruit physician-scientists with expertise in Alzheimer’s disease, child neurology, and child psychiatry; genetics or imaging approaches would be particularly helpful
 - Recruit scientists with expertise in imaging and biomarkers
 - Fill imminent vacancies in cognitive aging and pediatric clinical genetics
 - Recruit scientist with stem cell biology expertise, especially patient-specific iPSCs

Return on investment anticipated:

- NIH grants (R01s, PPGs, T32s in the near term; P50 Center grant longer term, then P30)
- Expanded development (i.e., fundraising) is critical for our success, with ongoing opportunities to solicit/collect donations of all sizes from families and philanthropies

Connectivity with other Neuroscience areas:

- Traumatic brain injury (see the TBI subcommittee concept paper)
- Stroke (maximizing recovery of function)

Connectivity with other designated AHSC priority areas:

- Precision Health (molecular genetic diagnostics)
- Health Disparities (e.g., ASD incidence, AD delayed diagnosis)
- Population/Outcomes (surveillance)

Connectivity with Arizona statewide priorities:

- large populations of children and older adults with many unmet needs

One final comment concerns the consensus of the committee that while there is an imbalance of current strengths in the areas of aging and development, a case for a strong conceptual and scientific link between these areas can clearly be made. In Alzheimer’s disease, for example, it is evident that we will require earlier and earlier detection for truly effective preventions to be developed, and there are some who believe that the best way to modify either disease or normal cognition in late life is to begin interventions in childhood. With coordinated effort the UA can be in a position to make serious contributions to the science of **lifespan brain health**, which needs to take into account the full range of early development through late life.

Neuroscience Advisory Council Systems/Integrative Neuroscience Subcommittee

Subcommittee members:

Kati Gothard (Physiology)	Alan Nighorn (Neuroscience)
Victor Hruby (Chemistry and Biochemistry)	Mary Peterson (Psychology)
Anita Koshy (Neurology)	Ole Thienhaus (Psychiatry)
Richard Lane (Psychiatry)	Leslie Tolbert (Neuroscience)
Joe Miller (Ophthalmology and Vision Science)	

Notes based on meetings on Jan. 21 and Feb. 12, 2014 and ensuing email discussions

Broadly speaking, Systems/Integrative Neuroscience is concerned with the neural basis for sensory, cognitive, and motor processes as the foundation for behavior. In other words, this part of neuroscience strives to reveal how molecules and cells are organized into neural circuitry that produces higher mental functions (such as language, memory, and mood) and complex behaviors, both normal and impaired – and to understand the neural impacts of system-wide insults to the brain. The importance of this field is growing as the massive amounts of information being generated about individual genes, molecules, and cells now has to be connected to their roles in the neural circuits that produce thought or behavior.

We define UA’s strengths in Systems/Integrative Neuroscience as including strong groups studying aspects of sensory, cognitive, and motor neuroscience, as well as groups that study interactions between mind and body. Levels of analysis range from the biochemistry and electrophysiology of cells and circuits to functional imaging of the working brain to outcomes such as behavior and affect. Significantly, at the UA, the faculty in these areas span the five AHSC colleges and the Colleges of Science, Engineering, and Optical Science.

A robust subcommittee discussion on Feb. 12 helped us to flesh out ideas from our meeting of Jan. 21 for building the strength of Systems Neuroscience research at the UA.

We discussed several items in some detail:

- Ole Thienhaus, chair of the Department of Psychiatry, described strategic initiatives in his department, all focused on mind-body medicine. A cluster of recent and planned hires complements the strength in the psychology and neurobiology of emotion and the brain’s influence

on peripheral physiology represented by long-standing faculty member Richard Lane. Recent hires include Chuck Raison, who has a background in neuro-immunology and –endocrinology and focuses on peripheral autonomic influences on brain function, and Karen Weihs, whose focus is on the relationship between mental health and disease progression, especially in relation to cancer. A new senior neuropsychologist will arrive from Harvard soon and will add a more junior physician-scientist to his group. Dr. Thienhaus sees physician-scientists as essential to the department’s future. He also mentioned that neuroimaging technology is key to much of the department’s work, and said he would ask Dr. Lane to provide details regarding imaging strengths and needs. Since the meeting Dr. Lane has shared some valuable information, which is included below

- Mary Peterson pointed out that researchers in her department (Psychology), including social and clinical psychologists, interact with faculty in Psychiatry through a cross-college group of 20 investigators, called MESH – “Mechanisms of Emotion, Social Relationships, and Health.” A new faculty member in the College of Nursing, Thaddeus Pace, also participates in this program.
- Joe Miller brought up the importance of having a strong foundation for clinical research. He is working with Iman Hakim, Dean of Public Health, to provide a description of what would be needed for UA to be able to routinely host multi-center clinical trials.

As a result of our conversation and subsequent email conversations, we have revised the document that grew out of our Jan. 21 discussions.

Major recommendations for improving neuroscience research (in Systems and more broadly):

1. **Hire faculty who are able to integrate the many strengths of the main campus with clinical programs in AHSC.** Targeted hiring in key areas in Neurology and Psychiatry would be especially important for increasing UA-wide research strength in neuroscience. In general, researchers who work on issues of fundamental importance in mammalian systems will bridge between the basic research using invertebrates in the Department of Neuroscience, research with humans in cognitive neuroscience, and the clinical work in the Health Sciences Center. One example of the kind of person who might be sought for a faculty position is Jude Mitchell (Salk Institute, currently working with marmosets, a small primate species that has the potential to become a new “genetic” model), who would make research connections across many departments (Ophthalmology, Physiology, Neuroscience, Psychology) and would want to be a member of the Neuroscience Graduate Interdisciplinary Program (GIDP), thereby integrating the AHSC colleges with the School of Mind, Brain, and Behavior.
2. Create themed groups of faculty statewide, with the UA as the hub. A strong suggestion is that we **create a Center for Innovation in Brain Science** at the UA. This sort of center should include depth in Phoenix as well as in Tucson – depth that builds complementary (and minimally duplicative) basic, translational, and clinical research strengths in carefully selected strategic areas in the two metropolitan areas. This plan will build on the distributed strengths in neuroscience in many UA colleges (beyond the AHSC) and will take advantage of the huge clinical opportunities in Phoenix, give us broad visibility, and attract Phoenix-based private donors. Donors are interested in supporting the elimination of human disease; clinicians can help potential donors to understand that one important way to accomplish that goal is by enhancing UA’s ability to attract and retain basic research faculty, in addition to more clinically oriented faculty, in health sciences areas.
3. **Create a culture of research that includes a serious focus on clinical, as well as basic, research.** It is essential all clinicians at UAHN recognize the pillars of academic medicine as educating and research (excellent clinical care is a given), and that every member views his/her clinical work from

this standpoint. In particular, clinically active AHSC faculty who are expected to conduct research (outcome studies, multi-center trials, small cohort studies) must be able to collaborate with basic scientists and be guaranteed adequate relief from clinical duties. It must be understood that some of the clinical revenues in clinical departments will flow back into departments to support research. To increase physician/physician-scientist productivity, unnecessary paperwork should be eliminated and more paperwork should be handled by staff. In addition, a robust infrastructure must be developed to support enrollment of subjects, generation of consent from virtually all patients for the use of depersonalized information, management and analysis of large data sets, etc. The existence of such an infrastructure will be important for reinforcing the central idea that as a major academic medical center, we focus on clinical, translational, and basic research that improves human health.

4. **Enhance core facilities** to be shared by the neuroscience community. For instance, imaging core facilities for specific state-of-the-art light and electron microscopy applications and whole-brain imaging could put us at the forefront of research in key fields represented by our Systems Neuroscience faculty. Such facilities, which require both advanced equipment and dedicated technical expertise, will draw researchers from the Colleges of Optical Sciences and Engineering into collaboration with neuroscientists and enhance interactions among faculty -- both those already here and new faculty. Ideas for group grant proposals are likely to arise out of these interactions. One particular technology that would be very helpful to the MESH research program mentioned above is a state-of-the-art 64-channel EEG system and an 8-channel peripheral physiological recording system including electrocardiography (ECG), electro-myography (EMG), respiration, skin conductance, and movement. The EEG system would significantly advance MRI-based research on the emotional consequences of sleep deprivation, enabling characterization of sleep stages in the scanner (possible only via EEG), and would advance collaborative cross-campus research on brain systems (EEG and fMRI) and brain-body interactions (EEG, fMRI, ECG and respiration) in depression. Vagal tone (ECG and respiration) measurement in conjunction with brain imaging is a centerpiece of the MESH research agenda, and EMG and skin conductance provide objective measures of emotional valence and arousal during imaging. This new set of capabilities would create new extramural funding opportunities and enhance many grant applications that already are in the planning stages.
 5. **Introduce mechanisms to facilitate collaborations between researchers with joint interests across the UA.** Potential methods include (1) Providing funds for themed workshops that include faculty on main campus, AHSC, and CoM-Phoenix, (2) Creating a website where it is easy to identify faculty interests and expertise across the UA, (3) Creating a fund for seed grants for pilot data to increase the competitiveness of grant proposals arising from new collaborations.
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Neuroscience Advisory Council

Stroke Subcommittee

Subcommittee members:

Leslie Ritter - Chair (Nursing)	Travis Dumont (Surgery)
Pélagie Beeson (Speech, Language and Hearing Sciences)	Chelsea Kidwell (Neurology)
Bruce Coull (Neurology)	Anita Koshy (Neurology)
Tom Davis (Pharmacology)	Diego Martin (Medical Imaging)
Kristian Doyle (Immunobiology)	Ted Trouard (Biomedical Engineering)
Kurt Denninghoff (Emergency Medicine)	Stephen Wilson (Speech, Language and Hearing Sciences)
Kendra Drake (Neurology)	

Process: The Stroke Subcommittee members met on Jan 23, 2014 to conduct its own SWOT analysis and to discuss responses to the charge of the subcommittee. Additional subcommittee members were identified: Kristian Doyle, Kendra Drake, Travis Dumont, Ted Trouard. A second meeting was held Jan 30, 2014 to finalize consensus on the committee report from the participating members.

Report of the Stroke Subcommittee

A. Areas that are ripe for focus, either to meet a crying need or to put UA at the cutting edge:

Stroke is our nation's 4th leading cause of death and a major cause of adult disability. With our aging population, all causes of stroke and transient ischemic attack (TIA) are projected to increase exponentially in the next decades, making foundational and translational stroke research a necessary focus. Neuroscience priorities of the nation (President Obama's BRAIN Initiative) and major granting agencies (NIH Brain Research through Advancing Innovative Neurotechnologies (**BRAIN**) Initiative) emphasize the need for large scale clinical trials and rapid bench to bedside translational research using innovative technologies. Our existing and emerging strengths in three distinct areas related to stroke, along with the support of additional infrastructure, will meet these needs and position the UA at the cutting edge of stroke research.

1. Clinical stroke research

- Faculty in the Dept. of Neurology have a long history of participating in large, multicenter NIH funded acute stroke clinical trials.
- Recruitment into many of these clinical stroke trials was significantly enhanced through an Emergency Dept. multi-year NIH funded grant.
- Currently, faculty in the Depts. of Neurology and Neurosurgery lead three multicenter NIH funded stroke trials (P50, P60) focusing on acute stroke interventions and stroke prevention. Senior and junior faculty clinician researchers in Neurology and Neurosurgery serve as PI and/or Core Directors on these trials; several clinical trial applications are currently under review.
- In addition the strength in clinical trials, junior and senior faculty in the Dept. of Speech, Language, and Hearing Sciences conduct clinical stroke research in the area of stroke recovery (aphasia); junior faculty RO1 application recently (Feb 2014) received a (likely) fundable score and a senior faculty is currently supported by multi-year NIH RO1 funding. These projects include interdisciplinary efforts that include faculty in the Departments of Neurology and Medical Imaging.

- Clinical stroke research efforts are strengthened by the existing strong clinical (UAMC) milieu, including a Joint Commission certified stroke center and Dept. of Neurology resident training program in stroke.

2. Stroke Imaging

- There is a crying need for state-of-the-art imaging in foundational, translational and clinical stroke research. Imaging is central to the work of at five stroke researchers at the UA.
- Senior faculty stroke clinical trialist in the Dept. of Neurology and junior faculty collaborator in Dept. Radiology represent a significant strength in acute ischemic stroke, transient ischemic attack (TIA), and hemorrhagic stroke imaging.
- Two clinical researchers in Speech and Language provide expertise in post- stroke aphasia imaging.
- Opportunities for the development of novel pre-clinical testing of new imaging modalities for stroke exists with faculty in Bioengineering, who have expertise in developing novel brain imaging in human pathologies.
- Significant opportunities exist for developing a comprehensive stroke imaging program that would include translational/basic stroke imaging. With the investment of sophisticated imaging modalities, basic science researchers (Nursing, Neurology, and Immunology) with expertise in the immunobiology of stroke could both translate findings to the bedside and explore new avenues of research brought forward by stroke clinician researchers.

3. Immunobiology of stroke

- Three junior faculty (NIH funded K08, K99/00) (Neurology, Immunology, Nursing) and one senior faculty (Nursing, Neurology) have expertise in the study of acute and chronic immunobiology of ischemic stroke.
- Collectively, areas of research include the effects of acute microvascular inflammation and the interplay of systemic and resident brain cell inflammatory brain cells in acute stroke, and the effects of immune cell activation on cognition and function during chronic recovery from stroke.
- Animal models in use include mice and rat models of ischemic stroke, and genetic mouse models of inflammation, diabetic rat models, and *Toxoplasma gondii* brain injury model to understand immune responses to stroke.
- Methodological expertise includes in *in-vivo* microscopy of the cerebral microcirculation, *in-vitro* brain slice interrogation, intracellular calcium signaling recordings, state-of the art immunohistochemistry, and flow cytometry.
- Senior faculty in the College of Pharmacy (NIH RO1 funding in the study of blood brain barrier) also has expertise in manufacturing and trialing a compound for stroke-related brain edema, representing a clinical trial opportunity at the UA.

B. Areas that would enhance the collaborative research potential, clinical/translational research efforts, and research training potential:

- A stroke clinical trial emphasis would a) enhance existing internal research collaborations among UA clinical (e.g., Neuroradiology, Neurosurgery, Emergency Services) and academic units (e.g., Speech and Language, Bioengineering, Pharmacology, Public Health, Nursing, Aging) b) strengthen existing and forge new external collaborations with local, state, regional and national stroke researchers c) provide opportunities for research training in clinical trials (residents, junior and senior faculty).

- Expanding stroke database capacity beyond the existing database (Get With The Guidelines) would significantly enhance existing collaborations with local, state, regional and national stroke researchers.
- Partnering with UAHN/UAMC on initiatives to expand clinical neuroscience capacity (e.g., neurointensivist clinician researcher, dedicated neurointensive care unit, Comprehensive Stroke Center status) would enhance current collaborative research and training potential in stroke.

C. Infrastructure needed:

- Increase imaging capacity (e.g., animal and clinical PET, SPECT)
- Increase clinical imaging capabilities: Bi-plane suite
- Seed monies to support pilot studies in foundational (basic science), pre-clinical/translational and clinical trial stroke research (50K/yr X 2 yrs, 3/year)
- Resource sharing with UAHN to enhance clinical neuroscience capacity
- Develop guidelines for storage of human subjects records that appropriately distinguish between clinical and research stroke data
- Develop a Comprehensive Neuroscience Institute in which stroke would reside as a center of excellence. Such infrastructure would attract world class clinician researchers and research partners that will enhance current areas of research excellence (stroke clinical trials, clinical research, basic science research) and provide support for areas of growth (e.g., -omics, nanotechnologies for therapeutic drug delivery, brain/technology interfaces for stroke recovery).

D. Strategic hires that would significantly impact our ability to acquire large collaborative grants and individual grants

- Neuroscientist in area of stroke-cognition-imaging
- Medical Imaging Neuro-Interventionalist with interest in stroke
- Neurointensivist clinician researcher with interest in stroke
- Clinician researcher with interest in immunobiology of stroke
- Biostatistician with expertise in stroke trials
- Leadership hires to support a Comprehensive Neuroscience Institute that includes a stroke center of excellence

E. What federal and other sources will be the prime targets for funding?

The following funding sources are

- Clinical trial (P series): targeted for 2014 (Dept Neurology)
- Center Grants, Training Grants (T32, P20): opportunity
- Individual Development Grant (K series): targeted for 2014 (College of Nursing faculty)
- Individual grants (R series); in review (Speech and Language, Neurology); planned for 2014 (senior faculty in Neurology/Nursing)
- Foundation (eg, AHA/ASA): opportunity in 2014
- State: AzDHS: opportunity
- Industry, Pharma: opportunity
- Philanthropy: continue Neurology/Nursing faculty partnership with Sarver Heart Center and College of Medicine Office of Development to reach those who have experienced stroke

F. Cross-cutting issues among the six Neuroscience themes

- **Stroke-TBI:** Imaging, cognition, recovery/long term outcomes, patient tracking (databases) Cognitive testing, Biochemistry/pharmacology, Acute and long-term care
- **Stroke-Aging:** cognition, acute injury and long term recovery
- **Stroke-Systems neuroscience** – sensory, cognitive, motor, affect/emotion, immunology
- **Stroke-Pain-TBI-Aging-Systems Neuroscience:** University of Arizona Comprehensive Neuroscience Institute with each of these represented as Centers of Excellence

G. Cross-cutting issues with other Council theme based areas of excellence

- **Stroke-Disparities:** current strength in Dept. of Neurology includes imaging expertise in stroke disparities and transitions of care for stroke/TIA; opportunities in disparities research includes collaborations with existing expertise in Colleges of Nursing and Public Health)
- **Stroke—Population Health and Health Outcomes:** opportunities with College of Public Health