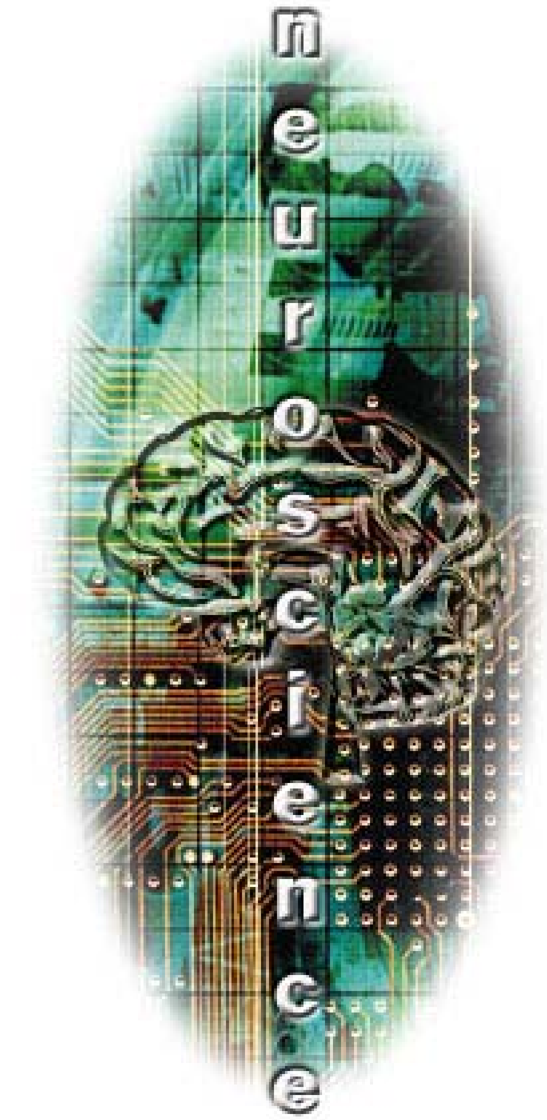
Arizona Neurosciences Research Platform Strategic Plan

Updated September 2003



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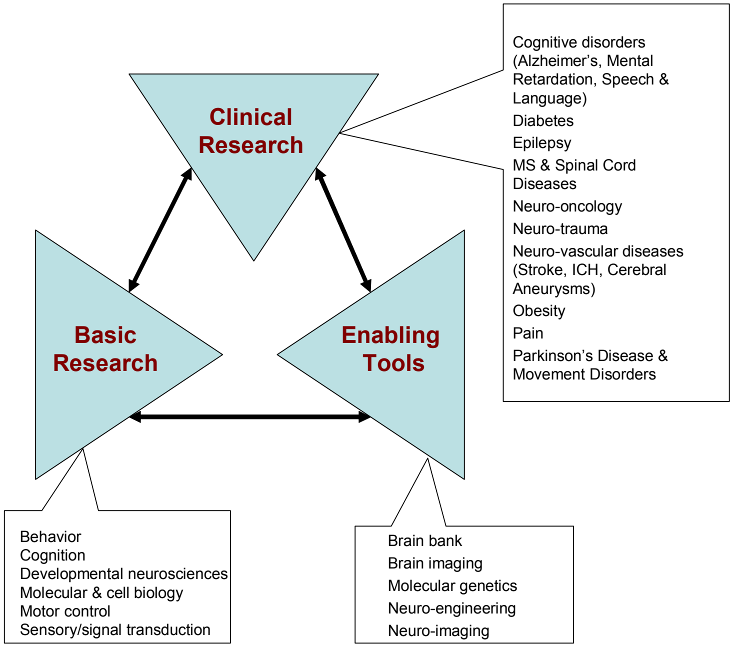
I. Proposed Strategic Vision and Focus for Neuroscience Platform

Proposed Strategic Vision

Over the next five years, Arizona will gain national recognition as a leader in neurosciences research spanning the broad collection of clinical researchers, basic scientists and key enabling technologies found in Arizona through the formation of a unique statewide, multi-institutional Arizona Neurosciences Consortium that addresses key resource needs, promotes collaboration and leveraging of research resources, builds areas of research excellence and reaches out to broaden the base of neuroscience research community in Arizona.

Identified Focus Areas for Neuroscience Research Development

Neuroscience research offers broad opportunities for basic, disease-related and enabling technology research activities, being one of the most complex areas of science as well as a leading area of funded research and a major market segment for the biosciences industry. The demands of establishing a leading research program requires going from the molecular level to the systems to the cognitive levels in understanding the mechanisms of the brain, sensory systems and specific diseases and their treatment, diagnosis and prevention.



Toward the goal of bringing Arizona to leadership in the prevention, diagnosis, and treatment of neurological and degenerative disorders, the committee felt that a broadly based initiative should capitalize on the strengths of Arizona's base of more than 200 neuroscience researchers, spawning new levels of interaction and research excellence with a special focus on developing increased ties between basic and clinical investigators. Already key multi-consortium efforts are underway in the neurosciences, including the Alzheimer's

Disease Consortium and the emerging Parkinson's Disease Consortium, which positions Arizona as a leading center for understanding, tracking, treatment and prevention of neurological aging and the disorders to which they are related. It is expected that this statewide, multi-institutional collaboration approach will be critical for other areas of effort in the neurosciences in Arizona. Other promising themes of focus include computational neuroscience ranging from molecular genetic to neural-systems applications, multiple sclerosis and spinal cord disorders, neuro-oncology, and neurological correlates of diabetes. An important component of each of these foci will be the fostering of a range of activities from basic research to bedside treatment.

The diagram sets out the key areas of research focus found in Arizona relating to the neurosciences.

II. Identified Resource Gaps and Collaborative Opportunities for Advancing the Neuroscience Research Platform

Based on the guidance of the Neuroscience Platform committee, resource gaps and collaborative opportunities were identified as areas for enhancement to enable Arizona to position its neuroscience research activities for national excellence. Below we examine a number of these key enhancements.

Across the neuroscience platform a number of key resource gaps were identified:

- **Lack of transgenic animal facilities.** There is a strong need for additional animal models – mice, rats, rabbits, drosphila – and better links with translational models. Accessibility throughout the state of animal facilities is a need, with each institution needing some capacity to support transgenic animals to enable research. This cannot be done equably or practically at a single designated site (even a state-wide center), and the demand is sufficiently great to warrant a facility at each institution.
- **Need for neuro-imaging dedicated to research** -- Existing imaging facilities are at capacity and some gaps emerging such as micro-PET in Phoenix area. There is a need to provide a shared staffing capacity to assist with programming and image analysis. It is particularly important to address the need for dedicated time for human research, which often gets squeezed out by clinical demands. Also, there is a need for separate facilities between human research and animal research, even beyond small animals, because of cross-species virus contamination.
- **Upgrading the bioinformatics infrastructure.** A service-oriented core facility needs to be established to address the full set of integrated needs from data base development, hardware, software. Of critical importance is having the key personnel in-place to make this happen from designing databases to building applications, etc. A major issue is the lack of data analysis capabilities for micro-array analyses being generated. There is also a need to address data sharing infrastructure, especially given hospital system fire-walls.
- **Development of stem cell and other cell-based therapies.** The use of stem cell and other cell based therapies is gaining greater importance are for translational research into neurologically related diseases, such as Parkinson's. Arizona is behind other states in this area, and needs to address the production of clinical grade cellular materials.
- **Expanding brain banking** to support other neuro-diseases beyond Alzheimer's and Parkinson's diseases, such as MS and mental illness. Tissue banks need to be supported and tissue made uniform, in terms of consent/privacy rules and collection and storing. Arizona does well in brain banking for older persons, but does not

have well characterized brain tissues for younger people. A particular need in Arizona is to expand brain banking to Tucson, perhaps doing so in a coordinated fashion to ensure consistency and standardization with Sun Health's leading brain bank program.

- **Expand epidemiology and biostatistics capacity** to analyze risk factors as a service-oriented core. Arizona is not strong in this area, but needs to be in order to be competitive for national center grant initiatives.
- **Engagement and commitment of physician researchers** Clinicians can become overloaded and difficult to ensure their commitment to ongoing research activities. It was observed that many may secure initial grant funding, but fail to complete the work needed to ensure grant renewals. A major gap in Arizona is the lack of presence of physicians able to write grants. In addition, the lack of physician release-time and weak links with PhD researchers seen as major hurdles to advancing neurosciences research in the state.

At the same time, a range of key collaborative opportunities were identified across the neuroscience research platform:

- **Apply molecular, cell and systems** expertise to support translational research involving innovative enabling technologies. Neurogenomics, neuro-imaging and neuro-oncology depend on cell and molecular biology in all phases of research: 1) formulating the right experimental questions, 2) interpreting the data, 3) functional validation, 4) biologic relevance. Arizona's leading depth in these enabling technologies needs to be strongly linked with the presence of more basic biological research.
- **Working in partnership with specialized populations** -- For Native Americans it is important to create something state wide that allows for a more predictable and proactive approach, without having to recreate the partnering process. Also true for geriatric population, Hispanics, and African Americans. It is very important that researchers understand that they cannot just walk onto a reservation and do research. It takes two to three years of ground work in order to write a proposal, and researchers need to be flexible in approaching the design of research protocols.
- **Need for addressing how IP, IRB and HIPAA is handled** – There is much confusion, inconsistency and bottlenecks faced by researchers that need to be addressed in navigating the maze of regulations underpinning collaborative activities. A key opportunity for Arizona to address this issue is putting in place across institutions more blanket/umbrella agreements that can enable organizations to work together in a predictable fashion.
- **Bridging geographic divide**. There is a need to find creative ways to bridge distances of neuroscience researchers, especially across Tucson and the Phoenix region. Ideas of video conferencing, data blitzes, web sites.

III. Proposed Structure and Organization for Arizona Neurosciences Research Platform

For Arizona to take the next step forward in advancing the neurosciences research platform, there is a major need to improve the development of shared resources and better formalize the mechanisms for collaboration.

The Neuroscience Platform Committee has proposed a statewide institute without walls that can facilitate and promote neuroscience research excellence and collaboration.

Some of the key elements for the Consortium would include:

- Having statewide resources for the neurosciences platform be allocated through the consortium rather than going directly to individual institutions;
- Seek to use resources allocated through the Consortium as incentives to encourage additional investments by individual institutions, which can in turn be utilized in a more shared approach on a project-by-project basis;
- Develop mechanisms for recruitment of leading researchers to advance overall platform;
- Be a neutral place and facilitator for addressing IP, IRB and HIPAA issues;
- Focus on being a convenor and match-maker to broaden specific research collaborations and facilitate the growth of the neuroscience research community through:
    - Hosting of seminars, workshops, and researcher expertise databases;
    - Using a limited amount of resources as seed and glue funding to bring groups together for pilot activities.
    - Focusing on upgrading the capacity of Arizona researchers to develop and write competitive grants.
- Pursue development of a limited number of centralized services, such as bioinformatics core support, epidemiology core support, etc.;
- Complement but not replace more focused collaborative efforts found in Arizona in the neurosciences area, such as the Alzheimer's Research Center, the Parkinson's Research Center and the newly forming Institute of Mental Health, enabling access to unique core facilities developed and providing a forum for broader outreach to the neuroscience research community.
- Establish a business model on participation and sustaining the consortium, including involvement of industry partners and sharing of core expenses.

It is suggested that the Arizona Neurosciences Consortium build on existing statewide models, such as the Arizona Alzheimer's Research Center, in developing its governance and day-to-day collaborative processes. This involves having articles of incorporation and by-laws for the organization and management of the Consortium as a joint effort of institutions in Arizona and access to high level decision-makers at each institution to serve as members of the Board of Directors.

IV. Specific Investment Requirements For Neuroscience Research Platform

The Neuroscience Research Platform identified a number of key investments apart from the shared resource infrastructure investments needed to support each of the research platforms, such as animal facilities, imaging facilities, bioinformatics, collaboration information technologies, etc. These specific investment needs for the Neuroscience Research Platform are presented below, followed by cost estimates.

Investment Program

Specific program of investments have been identified focusing on faculty, facilities and equipment, clinical infrastructure and enabling initiatives.

Enhancement Investments

Opportunities and Gaps	Investment Needed to Address Enhancement			
	Faculty	Facilities and Equipment and Resources	Clinical Infrastructure	Enabling Initiatives
Gap: Development of stem cell and other cell-based therapies	Laboratory manager and technician team Stem cell/immunology biologists	Need a cell culture facility that would be Good Laboratory Practice Compliant and Good Tissue Culture Compliant. Requires physical space dedicated to projects including work with animal models.		

Opportunities and Gaps	Investment Needed to Address Enhancement			
	Faculty	**Facilities and Equipment and Resources**	**Clinical Infrastructure**	**Enabling Initiatives**
Gap: Expanding brain banking to support other neuro-diseases beyond Alzheimer's and Parkinson's diseases, such as MS and mental illness.	Add new teams of 1 PhD and 4-5 technicians to expand brain bank capacity at: • Sun Health • BNI Tucson (new capacity) Add three neuropathologists to handle antemortem clinical assessments, commensurate with brain bank expansion. – one at Sun Health, BNI and Tucson -- with key specializations in neuro-oncology, Alzheimer's and Parkinson's.	More space at SHRI and BNI, as well as storage for bodies. Opportunities not only for normal aging but to secure brains in younger individuals • 4,000 to 7,000 sq ft of new space, plus 10 ultra-low freezers at SHRI and BNI. Adding a brain bank at UA would probably require at least 4,000 square feet of new space, and ultra-low freezers.		Excellent opportunity for industry investment, especially if extended beyond brain to the entire body in the most user-friendly and ethical way.
Gap: Engagement and commitment of physician researchers, and broader collaborations with basic neuroscience reseachers	We need a critical mass of academic neurologists and psychiatrists at each of the major institutions Address clinical release time for physicians. Possible need for endowment to pay for academic time of clinicians as BNI does.		Secure funding for Fellowship positions to provide both teaching opportunities but also manpower for assisting with clinical load and research projects.	Separate funding opportunities should exist to specifically support clinicians engaged in research via seed grants. Clinicians engaged part time in research competing against "professional PhD scientists" who do research full time lose in the current competitive structure. National issue, not just local. Notice in our own discussions, the word "clinical" did not arise, and the gauge of success is entirely research based. You never asked, who are the best doctors.

Opportunities and Gaps	Investment Needed to Address Enhancement			
	Faculty	**Facilities and Equipment and Resources**	**Clinical Infrastructure**	**Enabling Initiatives**
Opportunity: Apply molecular, cell and systems expertise to support translational research	Recruit approximately 8 "star" research teams to Arizona as the backbone for the neuroscience platform focusing on: • Glial cell biology • Stem cell biology • Immunology • Neurology (emphasis on clinical research) (Expect average start-up package will run $5 million per star team) This "star group" will bolster what is otherwise a cadre of well-qualified but non-star researchers found in Arizona.	Aside from major investments in new major players, equipment grants to existing faculty to substantially upgrade to the latest, most sophisticated techniques would be extremely helpful.	not applicable	There needs to be increased incentives among existing cell and molecular faculty to seek neurogenomics and neuroimaging collaborations.

COST ESTIMATES

The specific Neuroscience investment requirements are as follows:

- Recruitment of 32 faculty: 8 star teams in (basic science) glia cell biology, stem cell biology, immunology; clinical science (neurology and psychiatry)
  - Basic scientists – 20 faculty
  - Academic physician – 12 faculty
- Associated Space Needs for Faculty Recruitment
  - Professor – 2000 nasf (includes office)
  - Assistant Professor – 1500 nasf (includes office)
  - Associate Professor – 1200 nasf (includes office)
- Funds for Specialized Labs
  - Stem Cell: equipment plus staff -- $2.1M
  - Brain Bank Facility: staff -- $7.8M
- Incentives/Discretionary Funding for Collaboration
  - $250,000/year to promote and facilitate collaborative research projects
- Space
  - 47,950 nasf/general laboratory and office

- 1,000 nasf stem cell facility
- 4,000 nasf brain bank facility

- Ten Year Projections for Increases in Research Awards
  - Over the period of ten years, research awards could increase by $77M.

Projected Investments

Position	Five Year Total
Faculty	$13.9M
Post-Doctoral Fellows	$1.2M
Graduate Students	$0.74M
Support Staff	$0.74M
Subtotal	$16.6M
Recruitment Packages	$24.0M
Specialized Labs	$8.8M
Funds for Collaborative Research	$1.25M
Space Renovation	$11.4M
Total	$62.05M

Key Assumptions for Investment and Revenue Projections

<table>
<tr><th>Recruitment</th><th>Equipment</th><th>Space</th></tr>
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Faculty Salaries were assumed at 100% institutional coverage.
Star Team composition was assumed to be 1 professor, 1 associate and 2 assistants.
Star Team recruitment was assumed at 3 clinical teams and 5 basic science teams.
Salary levels for academic physicians were assumed at $200,000 (professor), $135,000 (associate), $110,000 (assistant).
Salary levels for basic research scientists were assumed at $150,000 (professor), $90,000 (associate), $75,000 (assistant).
Salary levels for post-doctoral fellows were assumed at $40,000.
Salary levels for graduate students were assumed at $20,000.
Benefits were assumed at 32%.
Set up packages were assumed at $3.5M/team of 4 scientists.
Set up package expenditures were assumed to occur over three years.

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Equipment for stem cell facility was assumed at $1,000.000.
Replacement costs/service contracts. No assumptions have been made regarding replacement of equipment or service contracts.

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Renovations of space was assumed at $200/nasf for general laboratory, $350/nasf for stem cell laboratory and brain bank.
Operations and Maintenance. No assumptions have been made regarding ongoing operations and maintenance costs.

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Collaborative Research Funds were assumed at $0.25M/year.

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Research Award Expectations (Direct Only) were assumed at: $750,000/yr (professor), $400,000/yr (associate), $200,000/yr (assistant).
Phase In Schedule for funding was assumed at:

<table>
<tr><th>Rank</th><th>Yr1</th><th>Yr 2</th><th>Yr 3</th><th>Yr4</th><th>Yr5</th></tr>
<tr><td>Professor</td><td>50%</td><td>100%</td><td>100%</td><td>100%</td><td>100%</td></tr>
<tr><td>Associate</td><td>50%</td><td>75%</td><td>100%</td><td>100%</td><td>100%</td></tr>
<tr><td>Assistant</td><td>0%</td><td>25%</td><td>50%</td><td>75%</td><td>100%</td></tr>
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V. Priorities

Below is an initial discussion on priorities to guide investments for the Neurosciences Research Platform:

Setting priorities within a platform area is not an easy task. It requires balancing the opportunities to accomplish key initiatives today, with ensuring long-term capacities are established.

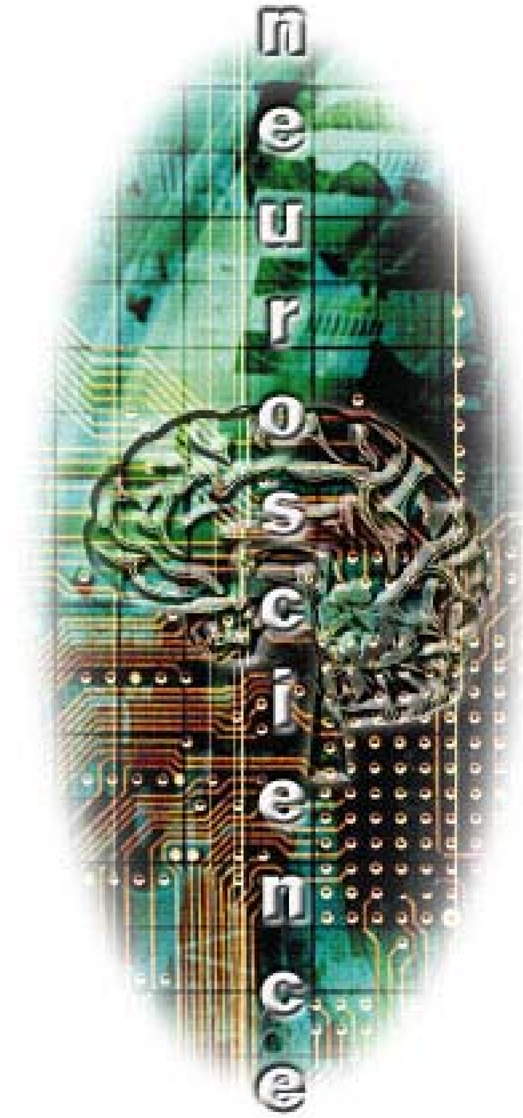
Perhaps most important for the Neurosciences Research Platform is establishing a more collaborative environment in Arizona that can link researchers and facilitate greater participation in all dimensions of translational research. These types of multi-institutional collaborative initiatives are already advancing key areas of neurosciences research, including the areas of Alzheimer's Disease and Parkinson's Disease.

For the Neurosciences Research Platform, the breadth and depth of the activity ongoing makes the task of identifying specific priorities especially difficult. Much of what has been identified to move neurosciences research forward involves basic infrastructure needed by other Platforms, such as epidemiology, imaging facilities and animal facilities.

Nevertheless, the key specific investment activities for the Neurosciences Research Platform establish an important focus – with key investments in cell and glial biology basic researchers key for neuro-degenerative diseases and brain cancers as well as in bringing more academic physicians to Arizona to advance translational research.

These specific investments will provide Arizona the opportunity to emphasize high payoff areas involving neurologic disorders and stem cells, which will capitalize on existing strengths in brain imaging, cognitive neuroscience, systems neuroscience, neurogenomics, cell and molecular neurobiology and the presence of a world-class brain bank.

Appendices for Arizona Neuroscience Strategic Platform



Appendix A. Inventory for Neuroscience Research Platform

I. Key Programs and Major Research Projects

DISEASE NICHE: ALZHEIMER'S DISEASE

Arizona Alzheimer's Research Center (AARC) is a statewide research laboratory without walls, established in 1998, which seeks to capitalize on the state's complementary resources in brain imaging, computer science, the basic and behavioral neurosciences and clinical and neuropathological research. Key aims are to advance the understanding, early detection, treatment and prevention of Alzheimer's Disease (AD); develop a leading brain imaging center in the world; maximize research productivity; and provide a model of multi-disciplinary, multi-institutional collaboration. AARC has received between $1 million to $2 million annually from the state, and another $1 million from the participating institutions.

In 2001, Arizona was awarded a National Institute of Aging-funded Alzheimer's Disease Core Center, building on the success of the AARC, with the major theme of early detection and prevention of AD. Sun Health Research Institute serves as the applicant organization on behalf of the Arizona consortium, including eight other Arizona institutions.

Key accomplishments on Alzheimer's Disease through the efforts of the AARC and ADCC include: pioneering contributions in the early detection and tracking of AD related to APOE, a common Alzheimer's disease susceptibility gene; discovery and characterization of potentially important AD risk factors and molecular mechanisms relating to neuroinflammation, cholesterol and cerebrovascular disease; deepening understanding of cognitive operations involved in aspects of memory, language, emotion and consciousness and the extent to which they are affected by AD and normal aging; and developed innovative brain image acquisition and analysis methods in humans and animals as well as advances in experimental models of AD in lab animals and development of neuronal cell cultures.

Major research efforts of the participating institutions relating to Alzheimer's are summarized below:

- ***Arizona State University*** focusing on advancing the acquisition and analysis of structural and functional brain images utilizing positron emission tomography (PET) and functional magnetic resonance imaging (fMRI).

- ***Barrow Neurological Institute*** focusing on effective ways to detect changes in brain functioning in normal development and neuropathological conditions.
- ***Good Samaritan Regional Medical Center*** focusing on using brain imaging techniques to help identify treatments to prevent AD via slowing down the progression of brain changes in persons at genetic risk.
- ***Harrington Arthritis Research Center*** is focusing on elucidating the role of energy metabolism in AD to investigate the role of dysfunctional energy production in the pathophysiology of the disease by using functional brain imaging to bridge the gap between studies of AD in humans and lab animals.
- ***Mayo Clinic Scottsdale's*** main area of emphasis is determining the correlation between genetic risk for AD (APOE genotype) and the effect of normal aging on certain measures of cognitive function, brain volume and brain metabolism.
- ***Northern Arizona University*** is developing an AD outreach and education for Navajo Nation.
- ***Sun Health Research Institute*** is focusing on fundamental understandings of the neuropathogenic mechanism that underlies AD to advance development of early detection markers and early treatment approaches, particularly inflammation and the cerebrovascular interface. The Institute has developed new techniques for preparing highly purified, viable microglia and astrocyte cultures from rapid autopsies of AD and non-AD patients, and is extending to neuronal cultures.
- ***University of Arizona*** has active group of researchers involved in understanding AD and aging, including how changes in the hippocampus are a major factor in age-related memory impairment and a neuropharmacological study of the role of inflammation in AD. The University of Arizona Cognition and Neuroimaging Laboratories is advancing use of neuro-imaging for studying normal brain functioning and disorders of the central nervous systems.

DISEASE NICHE: PARKINSON'S DISEASE

Arizona Parkinson's Disease Center, supported by the Arizona Disease Control Research Commission, involves four institutions: Sun Health Research Institute, Mayo Clinic Scottsdale, Barrow Neurologic Institute and Arizona State University. Over the past four years, research collaborations have focused on clinical, neuropathologic and basic science projects related to mechanisms of loss of clinical response to anti-parkinsonian drugs, hippocampal sclerosis as a cause of clinical parkinsonism, inflammatory responses in Parkinson's Disease (PD), proteasome inhibition, expression of brain derived neurotrophic factors, and clinical progression of PD.

Sun Health Research Institute has an active PD research effort through the Christopher Center investigating why PD patients lose responsiveness to medications; if certain antiparkinsonian medications might slow down the progression of the illness; and what symptoms will allow us to diagnose PD at the very earliest inception of the illness.

Mayo Clinic Scottsdale involved in genetic studies of PD, electrophysiologic studies PD, cinicopathologic/neurochemical correlations and maintaining clinical core for Arizona Parkinson's Disease Center.

University of Arizona has a multidisciplinary movement disorder clinic that is active in clinical trials and is engaged in multiple research projects such as employing tissue culture model systems for the selective control of basal ganglia pathways, development of cell-based therapies for PD and use of kinematics and physical therapy for PD.

DISEASE NICHE: NEURO-ONCOLOGY

Barrow Neurological Institute: Active Clinical Trials efforts with 105 studies underway, largely based on radiation therapy protocols.

Barrow Neurological Institute: Basic research activities include a major effort on primary brain tumors (glioma, primary CNS and lymphoma) involving drug resistant studies, cell invasion studies, and identification of prognostic markers for diagnosis and progression.

University of Arizona: Wide range of research projects across faculty from radiation oncology, molecular and cellular biology, pediatrics, hematology oncology and neurosurgery. Among the projects are development of signal transduction inhibitors and radiosensitizers, use of advanced MRI techniques for brain imaging and use of gene therapy for glioblastoma.

TGen Ongoing projects for characterizing invasive glioma cells by expression profiling and identifying applicable existing therapeutic modalities by matching molecular profiles.

Mayo Clinic: Cancer membrane proteomics program focusing on receptors, targets for immunotherapy, gene therapy and molecules important for drug handling.

Mayo Clinic: Immunotherapy program focused on cellular immunology working in animal models, preclinical studies and planned clinical trials.

DISEASE NICHE: EPILEPSY

University of Arizona is home to the Arizona Comprehensive Epilepsy Program involving clinical evaluation, treatment, invasive monitoring, and epilepsy surgery. Research efforts include pathophysiology of temporal lobe epilepsy, and genetic modulation of ion channels.

Mayo Clinic Scottsdale has a team focused on epilepsy including a six bed epilepsy monitoring unit.

Barrow Neurological Institute participates in ongoing clinical research studies including how quickly patients recover from seizures, the patterns of seizure spread electrically through the brain and the development of anticonvulsant medications.

DISEASE NICHE: NEURO-MUSCULAR DISORDERS

University of Arizona broad range of clinical care, clinical research and translational research activities in neuromuscular diseases including a general neuromuscular clinic, ALS research and clinical center supported and children's clinic for rehabilitative services. Translational research efforts include projects involving development of neural progenitors, role of MuSK in NM disease, inclusion body myositis and ion channel research.

Mayo Clinic Scottsdale involved in genetic studies, electrophysiologic studies of myoclonus and golfer's dystonia, and cincopathologic and neurochemical correlations of movement disorders.

Northern Arizona University has ongoing research efforts into neural and muscular mechanisms for movements with high velocities and accelerations, leading to new molecular and mathematical modeling of muscle spring properties.

TOOL NICHE: BRAIN IMAGING

Banner Health-Good Samaritan Medical Center has a wide range of brain imaging projects underway involving use of PET and MRI including:

- Longitudinal study of APOE for Alzheimer's Disease
- Identification of drugs to treat and prevent AD
- Brain mapping studies
- Tracer-kinetic modeling and image analysis
- Extending brain imaging findings to animals and the post-mortem human brain

Arizona State University has a number of faculty through its computational biosciences efforts involved in algorithm development for the effective utilization of imaging modalities involving both PET and MRI. In addition, through

TOOL NICHE: BRAIN BANKS

The Brain Donation Program, or "Brain Bank," at Sun Health Research Institute in Sun City, AZ has been providing brain tissue to researchers for more than 15 years. Over this time period, brain tissue from more than 750 individuals, including those with Alzheimer's disease, Parkinson's disease and stroke, has been collected, stored and disbursed to more than 200 researchers around the world. Locally, the Brain Bank serves the National Institutes of Health-funded Arizona Alzheimer's Core Center and the state-funded Parkinson's Disease Research Center, both of which are coalitions including the University of Arizona, Arizona State University, Barrow Neurological Institute, Mayo Clinic Scottsdale and Banner Health. Particular strengths of the Brain Donation Program include a short postmortem delay (median 2.6 hours) and a large number of normal control donors. The latter are very important in order to provide a comparison with diseased individuals and in order to study normal brain aging. All donors who have consented to brain donation are being followed with annual tests of motor and mental function during life, in order to better understand the relationship between living brain function and post-mortem brain chemistry. Scientific study of this brain tissue will lead to an increased understanding of the molecular causes of neurological disease and will generate new ideas for treatment. The continued availability of well-characterized brain tissue will be a major factor in allowing us to continue to expand neuroscience research in Arizona.

TOOL NICHE: NEURO-PHARMACOLOGY

University of Arizona has research teams addressing pain research from a broad range of perspectives from central and peripheral mechanisms to drug abuse and stimulants to molecular receptor studies to blood-brain barrier.

Pain res and neural basis of pain and pharmacology of neuropathic pain.

Banner Health-Good Samaritan Medical Center is involved in medical toxicology providing occupational and environmental toxicology services, paramedical training for medical aspects of exposure to hazardous materials and research related to toxicopharmacology of CNS drugs and neurotransmitters.

TOOL NICHE: NEURAL ENGINEERING

One key area of neural engineering found in Arizona is the rehabilitation of motor function through emerging neural interfaces and brain control technologies, involving interfacing the central nervous system to artificial devices that replace either lost senses, missing limbs or paralyzed limbs.

- At ASU, includes developing new biocompatible materials for neural interface and surface modification, multi-functional biosensors for neuroprosthetics, brain machine interface for motor function rehabilitation after stroke and spinal cord injury, and neuro and electro-physiological investigation to discover neural structures and information transfers for movement control and regulation.
- At University of Arizona, includes development of neuroprosthetics, interface of biomechanics, robotics and prosthetics with neurophysiology of multi-jointed movements, neural control of breathing and electrophysiological properties of spinal motoneurons and interneurons.
- At Barrow Neurological Institute includes how nervous system controls limb movements, determining which neurons process information related to locomotion and posture maintainence, self-assembling scaffolds for nerve regeneration, novel spinal fixation systems.
- At Banner Health (Good Sam), in collaboration with ASU, includes effects of epidural spinal cord stimulation on brain activity for walking, implanted neuroprotheses for standing after SCI and spasticity of the arm in patients with stroke.
- Another key area of activity includes neuromorphic engineering applying the signal processing structures found in the brain and physical attributes of animals to design new computers and robots. Involves development at both ASU and University of Arizona of VLSI chips for compact, low power vision sensors and robotic control systems.

TOOL NICHE: NEUROGENOMICS

The Translational Genomics Research Institute is adopting genomics technology to the understanding of human brain function and dysfunction through its neurogenomics program. Key targets of opportunity for TGEN's neurogenomic program are to further the understanding, diagnosis, and treatment of Parkinson's and Alzheimer's disease, Multiple sclerosis, Epilepsy, and brain tumors. Mental illness is a target theme for genomics and genetics studies in TGen; strategies by which to gain insight into schizophrenia are being implemented. Future developments in the Neurogenomics Program will attend to the areas of neurotrauma (spinal cord injury), neurodevelopmental disorders (a wide spectrum of learning disabilities and behavioral disorders), and some configuration of brain stem cell research. Specific technologies to be used include DNA scanning for linkage analysis and SNP scanning, RNA scanning for expression profiling and soon-to-be-in-place proteome scanning using mass spec. Specific biological systems to be elucidated are signal transduction pathways and synaptic signaling.

BASIC RESEARCH NICHE: DEVELOPMENTAL

University of Arizona has a range of activities underway in developmental neuroscience.

- Cellular, molecular and behavioral studies of the development of sensory systems.
- Anatomical, physiological and molecular aspects of synapse development, with special focus on neuromuscular synapses in vertebrates and invertebrates.

A specialized program of excellence at University of Arizona is its insect neurobiology efforts involving:

- Insects as models for studying the organization, function, development and plasticity of neural systems.
- Advancing understanding, and ultimately control, of agriculturally and medically harmful insects.
- Insects as bio-sensors.

BASIC RESEARCH NICHE: BEHAVIORAL NEUROSCIENCES

University of Arizona is involved in emotional processing and mood disorders including how amygdale function in emotional processing of macaque monkeys, neuroimaging of emotional states in nomal subjects, combined pharmacotherapy and psychotherapy.

Mayo Clinic Scottsdale is looking into the normal and pathological development of aging. Largely focused on Alzheimer's Disease.

Phoenix Branch of the NIDDK is investigating the role of the human brain in the pathophysiology of obesity applying neuroimaging, cell biology and neurogenomics. Key applications to address include diabetes and cardiovascular diseases.

ASU is investigating neurotransmitter systems and neural circuitry involved in drug seeking behavior, mechanisms underlying enhanced fear conditioning after chronic stress, and presynaptic dopaminergic mechanisms of behavior modulation in its psychology department.

ASU has range of research activities involved in behavioral neuroendocrinology examining mechanisms of hormone action, vertebrate reproduction and physiological adaptations to extreme environments in its biology department.

BASIC RESEARCH NICHE: SENSORY/SIGNAL TRANSDUCTION

Northern Arizona University has research projects ongoing in chemosensory control of avian respiration that examines the CO2 signal transduction in intrapulmonary chemoreceptors, and in developing biomimetic neural network models for visual target recognition.

BASIC RESEARCH NICHE: COGNITIVE, LEARNING AND MEMORY

University of Arizona has a wide range of activities ongoing in Cognition and Neural Systems including:

- Neuroimaging analyses of cognitive functions.
- Biological organization and computational operations of systems that underlie associative memory.
- Biological underpinnings of memory disorders associated with developmental abnormalities (e.g. Down syndrome), normal aging and Alzheimer's Disease
- Biology of seizures.

- Processing of sensory information in visual, auditory, olfactory systems of both vertebrate and invertebrate models.

BASIC RESEARCH NICHE: MOTOR CONTROL

Interdisciplinary training program in the neurobiology of motor control involving 22 faculty members from across University of Arizona, Arizona State University and Barrow Neurological Institute. The approaches cover a wide range of areas, experimental paradigms, and research techniques. Areas of study include supraspinal- and spinal-control mechanisms, peripheral-neuromuscular mechanisms, and the control of a variety of movements and muscle-control systems including: eye movements, speech, breathing; the arm (forelimb) and hand, the leg (hindlimb), and, complex skilled movements involving several combinations of muscle systems. University of Arizona has specific research activities in motor control, including:

- Vertebrate and invertebrate model systems for analysis of the development and function of motor systems.
- Human and non-human models for study of motor control and diseases of motor systems.

ASU Motor Control Laboratory focus is to understand how the central nervous system controls and regulates movement in healthy individuals and in those with neurological impairments. Special emphasis include motor deficits attributed to basal ganglia dysfunction and upper extremity coordination, particularly finger and hand posture, in reaching and prehensile movements. Research includes: multi-joint coordination mechanisms; visuo-motor adaptation; handwriting control; and force control. We study how the macro and microstructure of movement is altered by transient or permanent changes in the human brain due to aging, disease (Parkinson's), or nicotine as compared to the young, healthy population. We also use human experimentation to investigate movement invariance's, which point out the underlying mechanisms responsible for specific patterns of adaptation and movement. Investigations aimed at determining the computational processes of motor organization, the time-varying influence of sensory, and visual stimuli are the major foci of the laboratory.

The ASU Motor Development and Learning Lab is currently investigating the learning and development of bimanual coordination. Timing and coordination in perceptual-motor skills are measured in normal developing children, individuals with Down syndrome, and adults to investigate cerebral asymmetries, specificity of learning, individual differences, and dynamic patterns.

BASIC RESEARCH NICHE: SPEECH, LANGUAGE AND HEARING SCIENCES

University of Arizona's research activities include:

- Language and speech behavior in normally-developing, normally-aging, and neurologically-impaired populations.
- Cochlear responses to sound through the study of otoacoustic emissions and non-invasive electrophysiological measures.

Arizona State University has a broad range of research activities across its nine faculty members such as:

- Psychoacoustics in normal and impaired auditory systems.
- Childhood language development and disorders.
- Speech perception involved with cochlear implants
- Neural processing of speech and other complex sounds
- Language, particularly semantic processing, and memory impairments underlying communication disorders in normal aging, Alzheimer's disease and Parkinson's disease.

II. Faculty

III. Key Core Facilities:

Alzheimer's Disease Core Center provides key support, including: database management program under the Administrative Core, including development and management of a central database; clinical core provides standardized procedures for subject enrollment, and data acquisition of relative types of subjects; and neuropathology core conducts autopsies and establishes neurohistopathological diagnoses leveraging the Sun Health Research Institute brain donation program.

University of Arizona Cognition and Neuroimaging Laboratories provides access to functional magnetic resonance imaging (MRI), morphometric analysis of structural MRI and new neuroimaging techniques including diffusion and perfusion of MRI. Two new MRI magnets installed recently—a 1.5 Tesla and a 3 Tesla.

The Center for Insect Science is home to the National Drosophila Species Stock Center, the major source of diverse species of living Drosophila flies used by scientists around the world. The Center currently stocks 1,500 cultures of 300 Drosophila species. Separate cultures of individual species come from Australia, South America, China, North America and Europe.

The Brain Donation Program, or "Brain Bank," at Sun Health Research Institute in Sun City, AZ has been providing brain tissue to researchers for more than 15 years. Over this time period, brain tissue from more than 750 individuals, including those with Alzheimer's disease, Parkinson's disease and stroke, has been collected, stored and disbursed to more than 200 researchers around the world. Locally, the Brain Bank serves the National Institutes of Health-funded Arizona Alzheimer's Core Center and the state-funded Parkinson's Disease Research Center, both of which are coalitions including the University of Arizona, Arizona State University, Barrow Neurological Institute, Mayo Clinic Scottsdale and Banner Health. Particular strengths of the Brain Donation Program include a short postmortem delay (median 2.6 hours) and a large number of normal control donors. The latter are very important in order to provide a comparison with diseased individuals and in order to study normal brain aging. All donors who have consented to brain donation are being followed with annual tests of motor and mental function during life, in order to better understand the relationship between living brain function and post-mortem brain chemistry. Scientific study of this brain tissue will lead to an increased understanding of the molecular causes of neurological disease and will generate new ideas for treatment. The continued availability of well-characterized brain tissue will be a major factor in allowing us to continue to expand neuroscience research in Arizona.

Banner Health-Good Samaritan Medical Center Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI) Centers. The PET center houses a CTI Radioisotope Delivery System (RDS112), a self-shielded, fully automated, negative ion cyclotron that delivers 11MeV protons; fully automated chemistry processing units for the synthesis of O-water and F-FDG; the equipment to test these and other tracers for radioactivity, purity, sterility and apyrogenicity, equipment and facilities to support the implementation of other radiotracers; and a pneumatic tube system to rapidly transport radiotracers to the PET imaging area. The PET imaging area houses a Siemens 951/31 ECAT scanner which acquires data in the stationary or dynamic mode and permits the reconstruction of images consisting of 31 horizontal slices with a resolution as high as 5.0-7.1mm full-width at half-maximum (FWHM) in the transverse and axial directions, a distance of 3.34mm between slices and a 10.4cm axial field-of-view; and a Siemens ECAT EXACT HR+ scanner which acquires data in the 2D or 3D, stationary or dynamic modes and permits the reconstruction of images consisting of 63 horizontal slices with a resolution of 4.6-6.0mm FWHM in the transverse direction and 4.2-5.1mm FWHM in the axial direction, a distance of 2.46mm between slices, and a 15.5cm axial field of view; computer equipment and ancillary medical equipment needed to safely acquire the PET data.

The MRI Center houses a 1.5 Tesla General Electric LX System and a 1.5 Tesla General Electric Signa Infinity with EXCITE, both of which offer echo planar technology for fMRI as well as state-of-art hardware and software packages.

Appendix B. Peer Analysis

In looking at peer activities we consider first key lessons in forming collaborative centers, drawn from benchmarking Battelle has undertaken across a range of bioscience areas that includes neurosciences, and then insights from surveys of leading peer institutions identified by the Platform Committee members and informed by an analysis of NIH awards conducted by Battelle.

Key Lessons in Forming Collaborative Centers

These lessons were drawn from an analysis of eleven center activities found across the nation including:

- M.D. Anderson Cancer Center (University of Texas);
- Nanobiotechnology Center (Cornell University et al.);
- Center for Behavioral Neuroscience (Emory University);
- Georgia Tech-Emory Center for Engineering of Living Tissue;
- Whitaker Institute of Biomedical Engineering and Department of Bioengineering (University of California at San Diego);
- California Institute for Bioengineering, Biotechnology and Quantitative Biomolecular Research (University of California at San Francisco);
- Keck Center, Sloan Center, and Neuroscience Program (UCSF);
- New Jersey Center for Biomaterials (Rutgers, University of Medicine and Dentistry of New Jersey, and New Jersey Institute of Technology);
- Structural biology program at the Center for Advanced Biotechnology and Medicine (UMDNJ and Rutgers);
- McDonnell Centers and Neurology Department (Washington University, St. Louis);
- University of Washington Engineered Biomaterials and Department of Bioengineering).

Center Development Lessons and Explanations

Key "Center Development" Lessons	Explanation
Start Yesterday – it takes a long time to succeed.	• Many centers have taken a decade to get where they are -- and still see themselves as at the beginning stages. • Patience is required, because it takes time to build the interpersonal relationships and trust required for progress.
Have a consistent message in recruitment and promotion of faculty.	• It's all about encouraging productive people -- particularly those who want research partnerships across disciplines. • When filling open Departmental chairmanships, think about the candidates' commitment to collaboration goals.
Collaborations cannot be commanded top-down, but needs ongoing support at the highest institutional levels.	• Only faculty communities of interest can define a research agenda to which they are committed, and which will prove attractive of federal and industrial support. • However, only top leaders can keep an initiative together by raising/authorizing funding for its core costs and keeping it from being hamstrung by traditional bureaucracies.
Create mechanisms to add value to intellectual property through research that is not fundable through peer review.	• Example of MD Anderson, where the center director has used an unrestricted donation to create an in-house funding pool that will move discoveries closer to the stage where they can be licensed at fuller value
Understand the interaction between researchers in clinical and basic-science departments.	• Physician-scientists can be a "guiding light" on translational research and need involvement in Center labs. • They are the easiest to involve in collaborations with engineering faculty. • If there is no common lab space, scientists in clinical departments will seek space in diverse basic-science departments, dissipating synergies. • On the other hand, researchers in basic science departments will do translational research only if the Chairman/promotional system is sympathetic
Have a clear rationale on what is "center" business and what is "departmental."	• when particular funding streams are involved that stress multiple faculty labs working on a single project (e.g., NSF); • when projects cross departments, schools, institutions; • when a basically common approach is desired at different physical scales or in different model systems; or • when more than one company is in a research partnership.

Key "Center Development" Lessons	Explanation
Core expenses (both administrative and community-building) cannot be fully recovered directly from grants.	• Options: • ad hoc agreements with participating departments on "taxation"; • direct, budgeted central support for core functions/salaries, financed by indirect cost recovery; and • specialized endowments/fund raising led or at least authorized by top university leaders.
Empower and use graduate students and postdoctoral students.	• Postdocs particularly can be shared across labs, used as a vehicle for cross-disciplinary instruction/knowledge sharing. • Grad students are a critical vehicle for technology transfer to participating industrial partners.

NEUROSCIENCE PEERS

Surveys were undertaken to gain the perspectives of these leading national programs. Responses were received from:

- Washington University
- UCLA
- University of Pittsburgh
- Oregon Health Sciences University
- University of California, Irvine

Below we present insights learned regarding cutting edge issues. While not a scientific survey, these responses suggest the breadth of neurosciences required for success is broad as Arizona's Neuroscience Platform Committee has identified, but there is a strong sense from peers on the need to focus on excellence rather than being spread too thin.

Neuroscience Peer Institution Insights into Cutting Edge Issues

Focus Areas	Peer Institution Insights into Cutting Edge Issues
Cutting Edge Issues	• Understanding the molecular and cellular determinants of brain development including cell fate determination and functional connectivity. • Taking advantage of the human genome to understand the nervous system, and interface between genetics and neuropsychiatric and degenerative disorders. • Develop novel treatment approaches to promote repair and recovery in the damaged nervous system, and ability to generate neural cells. • Translating advances in disease-based neuroscience into clinical treatments • There's a revolution in both ends of neurosciences. The molecular biological tools give us new options that will have enormous impact over the next 5 years. At the other end, development of functional imaging tools allows us to do integrative work. It's the marriage of these two that will lead to major new insights in systems and cognition. • The major overarching opportunity is the re-integration of data: observations from neuro-imaging, genetics, etc., that can be coupled to better understand genotype and phenotype relationships. Now we have the capability to re-integrate. • Cognitive function, the neurobiology of learning and memory must be the key issue to any inquiry because why would you care about an entity without cognitive function
Characteristics of Top Programs Nationally	• Pick areas of excellence. Can't be all things to all people. Pick things that interest you and do them well. By focusing you can compete and capture all or nearly all the funding in an area, but if you're only moderately good at many things you will compete against really good groups and not get much at all. • Don't organize around a technology. Can't say you're going to specialize in electrophysiology…the brain doesn't have electrodes! • To recruit successfully need to look at creating labs on the NIH [intramural] model of the 60s and 70s where they recruited junior people for 5-7 years without teaching or grant-writing responsibility. No one really does that any longer, not even at NIH, and almost nowhere in academia. Whitehead Institute comes closest, but MIT tried raising money for other similar ventures and failed. • Excellent leadership – a great director who is a respected leader – combined with intellectual leadership. It all comes down to people, people, people. • Ability to merge basic and clinical areas by joint appointments and really active collaborations • Location also matters. Needs to be a place people want to come to live, family friendliness, etc. People no longer crowd to just the best programs unless they also want to live there. They want a place with a bright future, good schools, nice weather. • Having multiple different funding sources, like a state program and/or foundation support, offers a competitive advantage. Protects against NIH funding temporarily dropping off and having seed money for pilot projects that could provide could be very helpful for recruiting young faculty and generating future grants.