

Arizona Cancer Research Platform Strategic Plan

Updated September 2003





Table of Contents

I. Proposed Strategic Vision and Focus for Cancer Research	1
II. Identified Resource Gaps and Collaborative Opportunities for Advancing the Cancer Research Platform	4
III. Proposed Structure and Organization for Cancer Platform.....	8
IV. Specific Investment Requirements For Cancer.....	10
V. Priorities.....	16
Appendix A. Inventory for Cancer Platform	18
Appendix B. Insights from Peer Analysis.....	37

I. Proposed Strategic Vision and Focus for Cancer Research

PROPOSED STRATEGIC VISION

Over the next five years, Arizona will become a recognized national leader in cancer detection, prevention and novel therapeutics development, particularly for gastrointestinal, brain and skin and brain cancers, applying leading-edge genomics, innovative imaging technologies and a robust

IDENTIFIED FOCUS AREAS FOR CANCER RESEARCH DEVELOPMENT

Cancer research offers broad opportunities for research activities, being one of the leading areas of funded medical research and a major market segment for biosciences industry. At the same time, cancer research is one of the most competitive areas of bioscience research and development with many national centers of excellence. For Arizona to position itself for a nationally recognized leadership role it must build upon its areas of strength and find competitive advantage in how it organizes its activities into a broad-based translational model. Specific areas of focus that represent the strengths of Arizona cancer research efforts include:

- **Gastrointestinal cancer prevention and treatment** with a focus on cancers of the colon, esophagus and pancreas, involving a broad set of efforts including risk assessment, screening, prevention, identification of therapeutic targets, clinical trials and supportive care activities. Distinctive features include a Specialized Program of Research Excellence (SPORE) in GI Cancer (one of only four GI SPOREs funded by National Cancer
- Institute [NCI]), several NCI-funded Program Project Grants supporting basic and translational research in colon cancer prevention, and an established network of participating gastroenterologists throughout Arizona.
- **Skin cancer prevention and treatment** with a focus on both melanoma and non-melanoma skin cancers, involving both basic and translational research activities. Distinctive features include a major NCI-funded Program Project Grant in Skin Cancer Prevention and the fact that Arizona has the highest rate of certain skin cancers within the United States of America.
- **Cancer drug discovery and development** involving activities today in target evaluation and identification, drug design, natural products drug therapies, pharmacology and toxicology and cancer immunotherapies with distinctive features including the focus of Arizona Cancer Center on novel therapeutic drug development, especially for GI and skin cancers, and the

formation of The Translational Genomics Research institute (TGEN) and presence of the International Genomics Center (IGC) in Arizona. A major emphasis for Arizona will be developing personalized medicine approaches based on genetic factors.

- **Cancer imaging**, which is an evolving field of science contributing to both basic cancer research and progress in clinical cancer management through early detection and assessment of disease progression. Distinctive features include one of five NCI-funded experimental animal imaging cores, which provides investigators in Arizona access to state-of-the-art in vivo imaging technologies based on magnetic resonance (MR), single photon emission computed tomograph (SPECT) and optical coherence tomograph (OCT) and the existence of

significant optics technology development in Arizona. Commercial development of novel imaging technologies, based on MR, SPECT, OCT or other approaches, would have significant applications in the detection and management of many cancers, including GI and skin cancers.

- **Neurooncology** is a potential strength involving early detection with brain imaging, neuro-surgery, biology of brain tumors and clinical trials. Distinctive features include the internationally recognized program in basic neurosciences at the University of Arizona and the internationally known Barrow Neurological Institute (BNI) in Phoenix, which maintains a brain tumor tissue bank. Further, this area will benefit from the strong Cancer Imaging resources available in Arizona.

POTENTIAL DELIVERABLES OF ARIZONA CANCER RESEARCH FOCUS AREAS

- **Gastrointestinal cancer.** GI cancers, including those of the colon, esophagus and pancreas, are currently the second most common cause of cancer death (behind smoking-related lung cancers), and account for nearly 20 percent of all cancer deaths, in Arizona and the USA. Screening methods, including colonoscopy for colon cancer and upper GI endoscopy for esophageal cancer are effective means of preventing many of these cancers. For those situations where screening is either not effective, or not available, treatment of precancerous lesions is a potentially effective strategy. For patients who ultimately develop colon cancer, treatment at an early stage of disease progression is associated with nearly a 90 percent five year survival rate, while treatment at an advanced stage, after this cancer has metastasized, is associated

with survival rates of less than 20 percent. Developments in understanding the genetic basis of colon cancer, along with existing effective screening and early-stage treatment technologies make colon cancer a likely candidate cancer in which this specific cancer can be either prevented or effectively treated in essentially everyone at risk for this disease by 2015 (a stated goal of the current NCI director). The likelihood of success will depend on the availability of adequate resources, as outlined in the next section. Advances in this cancer should have applications in other epithelial cancers.

- **Skin cancers.** Arizona has the highest rate of melanoma of any state in the USA, and this cancer is increasing in incidence and mortality faster than any other invasive cancer. Non-melanoma skin cancers account for 40

percent of all cancers in the USA. Prevention of both melanoma and non-melanoma skin cancers is an effective strategy for reducing mortality due to these cancers. However, recognized genetic factors render some individuals at elevated risk for these cancers and can reduce the effectiveness of strategies (e.g. sunscreens) to prevent these cancers. Application of rational strategies to prevent sunlight-induced skin cancers should dramatically reduce mortality due to both melanoma and non-melanoma skin cancers in Arizona by the year 2015. As in GI cancers, the likelihood of success will depend significantly on the availability of adequate resources, as discussed in the next section.

- **Cancer drug discovery and development.** Technologies now exist at several institutions in Arizona to apply state-of-the-art genetic, chemical and pharmacological methodologies to identify specific molecular targets for specific cancers. Clinical research programs have been established to test the efficacy of target-directed therapies, and are led by experienced translational investigators with experience in taking novel agents from pre-clinical through clinical testing to approval for clinical use by the Food and Drug Administration. Specific resources, as described in the next section, are now required to take advantage of the unique opportunity to promote collaborations between public and private sector groups in Arizona.

- **Cancer Imaging.** The science, and associated technologies, of Cancer Imaging are rapidly evolving and it is becoming more evident that this area of cancer research will have both intellectual and economic benefits to society. Arizona has certain unique resources (e.g. the Southwest Small Animal Imaging Resource), but a significant investment in basic and translational research investigators is needed to realize this potential investment. These investments are discussed in the next section.
- **Neurooncology.** Astrocytomas arise from supportive tissue in the brain (astrocytes of the neuroglia), and account for about half of all tumors of the brain and spinal cord. Glioblastomas (GBM) account for 30 percent of all primary brain tumors and 50% of all astrocytomas. GBM are especially lethal tumors, which have proved very resistant to treatment. Arizona has certain resources which have the potential to place it in a very advantageous position to make improvements in the treatment of these tumors. The basic neurosciences research group at the University of Arizona and the clinical resources at the Barrow Neurological Institute (BNI) are both internationally recognized for their basic and clinical activities. Investments in translational scientists, who will work to capitalize on new information regarding genetic information relating to normal and neoplastic regulation of cells in the brain and spinal cord to develop novel target-directed therapies, is needed.

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

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

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

- **Building the base of basic biological scientists who understand basic science of cancer and specific cancer diseases:** Arizona does not have a sufficient critical mass of basic scientists examining the fundamental biological mechanisms of cancer, particularly in the gastrointestinal cancer areas and the neuro-oncology area. While over time there is an opportunity to gain more involvement of biological scientists present in Arizona to focus on the biology of specific cancer diseases, it is crucial that additional teams of basic cancer biology scientists be recruited with existing expertise in the biological mechanisms of cancer, and who in turn can be key to bringing along other biologists from across the research institutions in Arizona to study related key issues.
- Key disciplines identified by the members of the Cancer Platform include microbiology, immunology, cell and molecular biology, and biochemistry. These teams of basic researchers need to focus on specific cancer areas to apply their expertise and gain specific knowledge of the biological mechanisms associated with particular cancers.
- **Strengthening epidemiology and biostatistics.** To ensure the proper development and analysis of population and clinical research databases for cancer prevention, GI cancer, neuro-oncology and drug development, there is a need for greater depth of epidemiologists and biostatisticians in Arizona. There is a direct return on investment by having more epidemiologists and biostatisticians through increased grant awards, because they can help structure research programs and develop and analyze pilot data leading to competitive grant awards from NIH and other funding organizations. Interestingly, this capacity may be developed as a shared statewide staffing resource through a particular center or institution to serve all of the technology platforms, as long as mechanisms to ensure accessibility for all research teams across the state regardless of institution are developed. This need is also found in the neurosciences platform.
- **Bioinformatics core:** Through use of leading edge genomic techniques and imaging analysis, complex databases are being generated across the focus areas of the cancer research platform that require sophisticated data management and programming expertise. This

expertise is not broadly available to cancer researchers, and is holding back the flow of research discoveries.


- **Broadening transgenic animal facilities:** A key tool for unlocking the mechanisms involved in cancers is working in transgenic animal models, which help in studying [the] complex genetic basis of cancers. All research teams need ready access to animal research facilities.
- **Enhancing imaging facilities,** which is a broad based need across all of the bioscience platform areas, is of importance in the cancer platform for brain imaging, improving the techniques for targeting tumors, and for enabling small animal micro-imaging. It is particularly important that the latter be co-located with animal research facilities to minimize any delays and facilitate proper handling of the animal models. In addition, developing more dedicated research time for human imaging is important, particularly for neuro-oncology.

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

- **Need for addressing how IP is handled** – Assigning ownership rights in development of new cancer drugs can become highly complex. There needs to be a more consistent, upfront understanding that can take the form of an umbrella agreement rather than handling IP situation by situation. Ultimately, there is a need to build trust across the parties involved. This will require getting high level leadership involved, including [the Arizona Board of Regents (ABOR)]. There may be a need to move towards a statewide patent policy.
- **Promoting clinical research** – Multifaceted approaches are needed to promote the participation of community

physicians and oncologists to participate in clinical trials by providing support for enrolling patients, conducting paper work and ensuring quality control. Beyond clinical trials, there is a need to promote development of physician-investigators, who can team with basic researchers, on clinical research efforts, requiring addressing release time, mentoring and grant writing skills.

- **Building the community of cancer researchers** – We need to improve the capacity for seeking out and identifying researchers with certain expertise. This includes the need to have more comprehensive and up-to-date directories of cancer researchers and ways to match them by expertise and interest. There will also be a need to go beyond just those involved in cancer research today in order to build more robust connections with basic researchers, such as by broadening those included in cancer meetings. There is an interest in moving away from more structured, competitive request for proposal process into having more flexible resources for building teams in identified areas of opportunity.
- **Developing shared use facilities** – from imaging to transgenic animal to specialized drug discovery that can tap into NIH funding sources.
- **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



need to be flexible and make protocol changes; and it will take longer to complete the work.

Tissue Banking – The quality and depth of biological/tissue samples is key to advancing cancer research, and attracting more basic research activities. More focused development of tissue banking is needed for specific cancer diseases. For the initial focus areas of GI and brain cancers, greater investment in tissue procurement, characterization and storage is needed. This issue is also a key one for neuroscience.

Within each of the focus areas other specific enhancements were identified:

Focus Areas and Enhancements

Focus Area	Enhancements
Gastrointestinal Cancer	<ul style="list-style-type: none"> • Broaden range of therapeutic applications • Expand capacity of screening, including more behavioral research • Promote collaborations on pancreatic cancer • Advance emerging activities in liver cancer • Leverage imaging capabilities more widely
Skin Cancer	<ul style="list-style-type: none"> • Invest in base of basic researchers • Continue to grow cancer prevention efforts including addressing risk factors and behavioral aspects relating to cancer prevention • Pursue linkages between basic science research and genomics
Cancer Drug Discovery and Development	<ul style="list-style-type: none"> • Strengthen pharmaceutical and toxicology capacity to translate promising chemical therapeutic agents into drugs • Advance proteomics capabilities • Increase high throughput screening capabilities against unique cells • Advance pre-clinical testing capabilities for conducting animal model studies that can validate innovative new cancer therapies • Enable Phase I clinical trials scale-up efforts • Bring ASU genotyping capabilities into clinical settings • Better link chemical genetics into TGEN activities • Advance new biological therapeutics emerging across institutions
Cancer Imaging	<ul style="list-style-type: none"> • Broaden involvement of faculty with expertise in imaging to cancer imaging efforts • Advance application of imaging for tumor targeting • Coordinate statewide efforts in image analysis/image informatics
Neuro-Oncology	<ul style="list-style-type: none"> • Missing acquisition of biological data from clinical trials activities • Form a rare disease physician research network • Upgrade research facilities in clinical settings • More pro-active approach for generating preliminary research data needed to pursue larger competitive grant opportunities • Address absence of population studies on brain cancers

III. Proposed Structure and Organization for Cancer Platform

The Arizona Cancer Center was established in 1976, successfully competed for an NCI funded cancer center support grant in 1978 and was awarded status as a comprehensive cancer center in 1986. With the opening of the Scottsdale location of the Mayo Clinic, Arizona now has two NCI-designated comprehensive cancer centers.

Over the past several years, the University of Arizona and the Arizona Cancer Center have worked to establish functional collaborative relationships throughout the state of Arizona. Examples of significant collaborations expanding the clinical cancer research base include the University of Arizona, Phoenix Campus, the Arizona Cancer Center Drug

Development Program at the Virginia G. Piper Cancer Center at Scottsdale Healthcare and the Arizona Colon Cancer Prevention Consortium.

Other institutions in Arizona have significant resources which impact cancer research. These include Arizona State University, which has established a Cancer Research Institute specializing in drug development. Northern Arizona University has partnered with the Arizona Cancer Center to win a substantial NIH award to support research on cancers relevant to Native American people. Institutions such as BNI, TGen and others have been mentioned previously.

ESTABLISHING AN “ARIZONA CANCER ALLIANCE”

In order to promote a new mode of interaction, fostering collaborations between public and private academic and private sector groups, the Cancer Research Platform committee proposes the establishment of the “Arizona Cancer Alliance.” Initial participants in this group would include:

The University of Arizona

- Arizona Cancer Center (NCI-designated Comprehensive Cancer Center), Tucson
- University of Arizona, Phoenix Campus, Phoenix

- Virginia G. Piper Cancer Center at Scottsdale Healthcare, Home of the Arizona Cancer Center, Greater Phoenix Area

Mayo Clinic Cancer Center (NCI-designated Comprehensive Cancer Center)

- Mayo Clinic Scottsdale

Arizona State University

- Arizona BioDesign Institute
- Cancer Research Center at ASU, Tempe



Northern Arizona University

Barrow Neurological Institute (BNI)

Translational Genomics Institute (TGen)

International Genomics Consortium (IGC)

The Arizona Cancer Alliance will be organized as a state-wide resource working to facilitate collaboration within and across each of the niche areas and to achieve the deliverables described above for the Arizona Cancer Research Platform.

The specific responsibilities of the Arizona Cancer Alliance will be to:

- oversee the allocation of resources across niche areas, together with matching funds for participating institutions
- support recruitment of faculty
- identify and prioritize new equipment and laboratory development
- manage the collaboration funding and hosting series of cancer collaboration meetings, seminars and annual retreat.

IV. Specific Investment Requirements For Cancer

The Cancer Research Platform committee identified an illustrative program of investments for each of the focus areas. These plans were then aggregated to provide a costing for supporting the development of the Cancer Research Platform over the next five years.

INVESTMENT PROGRAM

For each of the focus areas, a specific program of investments have been identified focusing on faculty, facilities and equipment, clinical infrastructure and enabling initiatives.

Gastrointestinal Cancer

Faculty	Facilities and Equipment	Clinical Infrastructure	Enabling Initiatives
<ul style="list-style-type: none"> Enhance the base of basic researchers in GI cancers – need integrated team including microbiologists, immunologists, biochemists, and cell biologists Augment epidemiology and biostatistics Deepen clinical researchers in radiation and surgical oncology linked with basic research activities. Form interdisciplinary teams of public health, anthropology, psychology, nursing, MD and evolutionary psychology 	<ul style="list-style-type: none"> Enhance screening infrastructure across the state for specimen collection and conducting colonoscopies Upgrade transgenic animal facilities and link with small animal imaging Genetically altered resources for knockout animals Experimental endoscopy lab New accelerators and dosimetry for radiation oncology 	<ul style="list-style-type: none"> Conduct survivorship studies examining behavioral aspects 	

Skin Cancer/Melanoma (needs to be further developed)

Faculty	Facilities and Equipment	Clinical Infrastructure	Enabling Initiatives
<ul style="list-style-type: none"> • Build base of basic scientists • Recruit epidemiologists and biostatisticians with research interests in prevention trials • Focus on recruiting genetic epidemiologists 	<ul style="list-style-type: none"> • Bioinformatics core facilities – equipment, software • Screening facilities 		

Cancer Drug Discovery and Development

Faculty	Facilities and Equipment	Clinical Infrastructure	Enabling Initiatives
<ul style="list-style-type: none"> • Leverage existing molecular biology faculty with expertise to study signal transduction, mechanisms of tumor suppressors • Enhance existing faculty in biochemistry, medicinal chemistry and proteomics focusing on anti-cancer drug discovery • Develop a research capacity in chemical genetics • Need for biostatisticians focused on translational research • Recruit vaccine immunologists • Clinical research faculty to advance innovative therapies into clinical trials 	<ul style="list-style-type: none"> • Upgrade mass spectrometry and high field NMR and offer as a core service facility • Establish high throughput robotics facility for combinatorial chemistry and screening capabilities • Center for computer aided drug design, including a statewide database to facilitate structure-based design of new anti-cancer drugs • Upgrade transgenic animal facilities and provide for imaging of small animals • Provide operational support to leverage existing assay systems for testing candidate drug therapies, with an emphasis of testing against unique cell lines. • Pre-clinical animal testing facility focusing on toxicology and pharmacokinetics testing, etc, as part of commercialization process • High end flow cytometry • Video conferencing between sites 	<ul style="list-style-type: none"> • Establish stronger linkages with academic physicians that go between lab and bedside 	<ul style="list-style-type: none"> • Provide seed funding to allow basic researchers to pursue cancer biology. • Promote interaction of medicinal, synthetic and natural product chemists with biologists investigating novel molecular targets • Leverage current physician involvement across Arizona in Western Regional Community Clinical Oncology Program • Develop a statewide intermediary mechanism that involves special population groups and is sensitive to their key issues • Work with Health Career Clubs on reservations and in communities where we find special populations, providing education and internship opportunities.

Cancer Imaging

Faculty	Facilities and Equipment	Clinical Infrastructure	Enabling Initiatives
<ul style="list-style-type: none"> • 4-5 more PIs in cancer imaging including radiopharmaceutics, optical contrast agents/molecular imaging and PET imaging 	<ul style="list-style-type: none"> • Generate a better inventory • Small animal micro-imaging with experiential model development • PET with radiotracers 	<ul style="list-style-type: none"> • Need for physician-investigators who have cancer imaging as a major focus of their research programs 	<ul style="list-style-type: none"> • Mechanism for enabling greater usage of imaging for research – i.e. scheduling, shared use facilities • Seed grants to encourage cancer researchers to partner with imagers, including supporting release time of physicians to pursue imaging research. • Use of statewide coordination effort to seize potential for funding from industrial partners, such as instrument manufacturers and pharma

Neuro-Oncology

Faculty	Facilities and Equipment	Clinical Infrastructure	Enabling Initiatives
<ul style="list-style-type: none"> • Build base of basic scientists involved in neuro-oncology – with linkages to neurobiology • Recruit epidemiologists and biostatisticians • Recruit a neuropathologist with specific expertise in neuro-oncology 	<ul style="list-style-type: none"> • Facility for brain tumor banking • Facilities that can accommodate research in the clinical setting 	<ul style="list-style-type: none"> • Create a physician research network for clinical trials 	<ul style="list-style-type: none"> • Funding to establish banking of tissue, data entry and patient follow-up • Gaining industry support for molecular studies of clinical trials materials based on ability to enroll patients in clinical trials • Development of investigator-physicians teams

COST ESTIMATES

The specific cancer investment requirements are as follows:

Recruitment of 60 to 80 faculty

- Basic scientists – 32 to 40 faculty
- Academic physician – 12 to 20 faculty

- Epidemiology – 6 to 9 (are 3 additional recruits for special populations initiative)
- Medicinal and other applied Chemistry/pharmacology – 10 to 11

Possible allocation of faculty across niche areas is as follows:

Possible Allocation of Faculty Across Niche Areas

	Basic Scientists	Academic Physician	Epidemiology	Medicinal and Other Applied Chemistry/ Pharmacology
GI Cancer	10-12	4-6	2-3	
Skin Cancer	10-12	4-6	2-3	
Drug Discovery and Development				10-11
Cancer Imaging	4-6	2-4		
Neuro-Oncology	8-10	2-4	2-3	
Total	32-40	12-20	6-9	10-11

Associated Space Needs for Faculty Recruitment

- Professor – 2000 nasf (includes office)
- Assistant Professor – 1500 nasf (includes office)
- Associate Professor – 1200 nasf (includes office)

Pool of Funds for Specialized Labs

- \$20-\$29M for enhancement of existing resources, including mass spectrophotometry, high field NMR, high throughput robotics, computer aided drug design, high end flow cytometry, high through put screening, and endoscopy laboratory. Investment pool includes funding for appropriate support staff.

Incentives/Discretionary Funding for Collaboration

- \$250,000/year to promote and facilitate collaborative research projects
- \$100,000 to \$250,000 to establish a physician’s research network for rare diseases (brain cancers) reaching across Arizona and Southwestern states

Ten Year Projections for Increases in Research Awards

- Over the period of ten years, research awards could increase by \$106M–\$160M.

Projected Investments

Position	Five Year Total	GI Cancer	Skin Cancer	Cancer Drug Discovery and Development	Cancer Imaging	Neuro-Oncology
Faculty	\$20.8–\$30.0M	\$5.5–\$7.5M	\$5.5–\$7.5M	\$3.5–\$4.1M	\$2.4–\$4.5M	\$3.8–\$6.4M
Post-Doctoral Fellows	\$1.2–\$1.8M	\$0.32–\$0.45M	\$0.32–\$0.45M	\$0.2–\$0.25M	\$0.14–\$0.27M	\$0.22–\$0.38M
Graduate Students	\$0.8–\$1.2M	\$0.21–\$0.3M	\$0.21–\$0.3M	\$0.13–\$0.16M	\$0.09–\$0.18M	\$0.15–\$0.26M
Support Staff	\$0.5–\$0.65M	\$0.13–\$0.16M	\$0.13–\$0.16M	\$0.08–\$0.09M	\$0.06–\$0.10M	\$0.09–\$0.14M
<i>Subtotal</i>	\$23.3–\$33.65M	\$6.2–\$8.4M	\$6.2–\$8.4M	\$3.9–\$4.6M	\$2.7–\$5.05M	\$4.3–\$7.2M
Recruitment Packages	\$33.6–\$40.2M	\$9.0–\$10.0M	\$9.0–\$10.0M	\$5.6–\$6.0M	\$3.9–\$6.0M	\$6.2–\$8.6M
Pooled Equip and Support	\$20–\$29M	\$5.3–\$7.25M	\$5.3–\$7.25M	\$3.3–\$4.0M	\$2.3–\$4.3M	\$3.7–\$6.2M
Funds for Collaborative Research	\$1.35–\$1.5M	\$0.33–\$0.38M	\$0.33–\$0.38M	\$0.20–\$0.21M	\$0.15–\$0.2M	\$0.23–\$0.3M
Space Renovation	\$15–\$30M	\$4.0–\$7.5M	\$4.0–\$7.5M	\$2.5–\$4.1M	\$1.75–\$4.5M	\$2.75–\$6.4M
<i>Total</i>	\$93.2–\$134.3M	\$24.8–\$33.5M	\$24.8–\$33.5M	\$15.5–\$18.9M	\$10.8–\$20.0M	\$17.2–\$28.7M

Note: Allocations among research niches has been estimated by percent (faculty recruited per niche/total faculty recruited).

Key Assumptions for Investment and Revenue Projections

Recruitment	Equipment	Space																								
<ul style="list-style-type: none"> Faculty Salaries were assumed at 100% institutional coverage. Salary levels for academic physicians were assumed at \$150,000 (professor), \$110,000 (associate), \$90,000 (assistant). Salary levels for basic research scientists were assumed at \$120,000 (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 \$1M (professor), \$0.75M (associate), \$0.375M (assistant). Set Up Package expenditures were assumed to occur over three years. 	<ul style="list-style-type: none"> Investment pool for equipment and relevant support staff was assumed at 35% of total salaries (ten years). Replacement costs/service contracts. No assumptions have been made regarding replacement of equipment or service contracts. 	<ul style="list-style-type: none"> Renovations of space was assumed at \$200/nasf Operations and Maintenance. No assumptions have been made regarding ongoing operations and maintenance costs. 																								
<ul style="list-style-type: none"> Collaborative Research Funds were assumed at \$0.25M/year Establishment of Physician's Research Network was assumed at \$100,000 to \$250,000. 																										
<ul style="list-style-type: none"> 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 border="1" data-bbox="283 1274 745 1396"> <thead> <tr> <th>Rank</th> <th>Yr1</th> <th>Yr 2</th> <th>Yr 3</th> <th>Yr4</th> <th>Yr5</th> </tr> </thead> <tbody> <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> </tbody> </table>	Rank	Yr1	Yr 2	Yr 3	Yr4	Yr5	Professor	50%	100%	100%	100%	100%	Associate	50%	75%	100%	100%	100%	Assistant	0%	25%	50%	75%	100%		
Rank	Yr1	Yr 2	Yr 3	Yr4	Yr5																					
Professor	50%	100%	100%	100%	100%																					
Associate	50%	75%	100%	100%	100%																					
Assistant	0%	25%	50%	75%	100%																					

V. Priorities

Below is an initial discussion on priorities to guide investments for the Cancer 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.

One key priority that emerged from discussions among the members of the Cancer Research Platform and that is built into the investment program is the need for a greater critical mass of cancer basic researchers, spanning basic scientists, academic physicians, epidemiologists and medicinal and applied chemists.

PRIORITIES ACROSS FOCUS AREAS

Looking across the focus areas identified, the members of the Cancer Research Platform were able to identify a three-stage level of priorities:

The lead priority brings together three focus areas organized around a primary cancer disease, gastro-intestinal cancers, where Arizona has a growing national position, supported by cancer drug discovery and development and cancer imaging.

The next priority is skin cancer where Arizona has a key interest and growing research program.

The third-level priority is neuro-oncology, where Arizona's clinical strengths offer a platform for future growth.

Appendices for Arizona Cancer Platform Strategic Action Plan

Updated August 2003



Appendix A. Inventory for Cancer Platform

I. Gastrointestinal Cancer

KEY PROGRAMS AND MAJOR RESEARCH PROJECTS

University of Arizona:

GI SPORE focused on colon, esophagus and pancreas cancer. Involved in screening activities for high risk populations including identification of genetic risk factors. Also involved in key therapeutic approaches—immunoprevention and chemoprevention.

Apoptosis PPG???

The Arizona Cancer Center's Colon Cancer Prevention Project is working to find out if polyp formation can be

reduced by taking celecoxib and/or selenium among individuals who have already had at least one adenomatous polyp removed.

Mayo Clinic:

Focused on pancreatic cancer with major multi-disciplinary approach involving gastroenterology, oncology, radiation oncology, surgery, population sciences, pathology, radiology and research. Pending SPORE award for Mayo Clinic nationally—handle 2% pancreatic cases nationally, active in Scottsdale.

Linkages to Enabling Areas:

	University of Arizona	Mayo Clinic	ASU
Therapeutic Target Identification and Development	<ul style="list-style-type: none"> • Neurological Chemoprevention • Immunoprevention 		Jacobs/Newfeld work in tumor suppressors
Cancer Prevention	<ul style="list-style-type: none"> • GI physician network involving 120 physicians 	Across Mayo handle 2% of all pancreatic cancers nationally – 83 new analytical cases in pancreatic cancer at Scottsdale in 2001	
Surveillance, Diagnosis, Imaging	<ul style="list-style-type: none"> • Identification of SNPs – genetic risk factors • Optical imaging and spectroscopy of mouse GI tissue (Barton) • Fluorescence endoscopic imaging of the pancreas (Gmitro) 		

FACULTY UNIVERSITY OF ARIZONA:

- Gene Gerner – GI carcinogenesis, cancer prevention
- David Alpert – Cancer prevention
- Emmanuel Akporiaye – Immunology of cancer
- Garth Powis, Redox mechanisms in cancer
- Tom Dragovich – GI cancer therapeutic trials
- Achyut Bhattacharyya – Markers of GI neoplasia
- Harinder Garewal – Markers of GI cancers, Barrett’s esophagus
- Evan Hersh – Cancer immunology and gene therapy
- Dan Von Hoff – Cancer clinical trials, identifying novel targets for GI cancer therapy
- Laurence Hurley – Pre-clinical development of cancer treating agents
- David Mount – Informatics
- Ray Nagle – Immunohistochemical identification of prostate and pancreatic cancers
- Mark Nelson – Molecular biology of cancer, cancer prevention
- Claire Payne – Markers of GI cancer, bile acids in GI cancers
- Jennifer Barton – Department of Biomedical Engineering
- Arthur Gmitro – Department of Radiology

Mayo Clinic

- Larry Miller
- Len Gunderson

- Sandra Gendler
- Darius Sorbi
- Adyr Moss

MAJOR RESEARCH FACILITIES AND LABS

University of Arizona:

- GI Tissue Resource Core provides SPORE investigators, engaged in translational research efforts, access to a wide variety of human specimens and GI tissues following Institutional Review Board approval of specific protocols. Includes basic histology services as well as clinical information on patients associated with tissue samples.
- The Markers Core serves as a resource for the development and optimization of established as well as new methods for measuring research endpoints in the individual projects. The Markers Core serves as a resource for assay development, analysis and quantitation of immunohistochemical procedures in support of each project.
- Clinical resources for facilitating patient research.
- Biometry core to develop and apply statistical methods for design and analysis.
- Informatics core to support sophisticated databases and internet-based tools for developing and testing hypotheses for all of the data to be generated in the SPORE.

Mayo Clinic

- Clinical databases
- Tissue repository
- Animal models – Murine tumor models facility—full floor of Johnson Research Building with full spectrum of expertise (transgenic, knock-in, knock-out, genetic and immune background)
- Histology core permitting analysis of the abnormalities of patterns of expression of foreign genes
- Immunology core providing technical assistance in tissue and cell culture, freezing, and storage

II. Skin Cancer/Melanoma

KEY PROGRAMS AND MAJOR RESEARCH PROJECTS UNIVERSITY OF ARIZONA:

Arizona Cancer Center has an active program in **Skin cancer prevention research** – Projects include testing the effectiveness of different chemopreventive methods, such as vitamins and topical agents. One study is evaluating the use of a topical ointment containing EGCG, a chemical extract from green tea, to prevent skin cancer as well as repair sun-damaged skin. In a separate study, NDGA—a chemical found in the creosotebush, a plant native to the Southern Arizona desert—also is being tested as a potential treatment for patients with severely sun-damaged skin.

TGEN:

Melanoma Research Program is a key component of the Genetic Basis of Human Disease activities at TGEN.

Involves understanding the molecular events that characterize melanocytic transformation through a combination of gene identification, genotype-phenotype correlations and functional analyses.

Mayo Institute

Melanoma Study Group is an interdisciplinary group of clinicians and scientists at the Mayo Clinic in Rochester, MN, Jacksonville, FL and Scottsdale, AZ working together with the goal of developing new and more effective therapies for malignant melanoma. Involves 12 clinical trials in 2002, of which Mayo investigators developed nine studies. Includes use of immunotherapies and vaccines.

FACULTY

University of Arizona

- David Alpert

TGEN

- Pam Pollack
- Kevin Brown

Mayo Clinic

- Mark Dahl
- David DiCaudo
- Katherine Kar-Hwee Lim
- Michael Gornet

III. Cancer Drug Discovery and Development

KEY PROGRAMS AND MAJOR RESEARCH PROJECTS

University of Arizona:

Therapeutic Development Program at Arizona Cancer Center – novel target identification and validation and the discovery and testing of new agents to interact with these targets. Interdisciplinary group organized via the Arizona Cancer Center identifying and developing agents in a variety of novel classes including targeted therapies, anti-angiogenic agents and anti-tumor pathways. Focused on Phase I and Phase II with anticipated annual accrual target of 500/year on Phase I trials within three to five years.

University of Arizona:

Medicinal and Natural Chemistry Program at UA School of Pharmacy – Broad range of research activities involved in development of novel antitumor agents from structural based approaches to bioprospecting, as well as protein targeting strategies using mass spec and identifying molecular mechanisms involved in cell death.

Arizona State University:

Rational cancer drug design projects including enzyme active site tailored anticancer drugs (Rose), design of selective antitumor agents for melanoma (Skibo), and multiplexed reactive sequencing of DNA leading to low-cost genotyping of hereditary cancer genes and rapid identification of specific mutations in tumors.

Arizona State University:

Target identification and development, including tumor suppressors, natural products and vaccine development.

- Tumor suppressors for pancreatic and colon cancer – Jacobs, Newfeld
- Natural products from desert legumes – Dennis Clark
- Vaccine development for cancer immunology – Arntzen, Jacobs

TGen:

- Family studies—focused on prostate cancer – John Carpens
- Use of DNA microarrays for gene expression profiling targeting breast, prostate, colon, lung, melanoma, sarcoma – Spyro Mousses
 - Tumor suppressors
 - Rapid clinical validation of targets
 - RNA functional validation
 - RNA screening of therapeutic inhibitors
- Molecular diagnostics and target validation—how cells carry out computation, modeling biological network

Mayo Clinic:

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

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

FACULTY

University of Arizona

Pharmacology/Toxicology

- Laurence Hurley – TDP, target identification, drug design
- Barbara Timmermann – natural products
- Elaine Jacobson
- Mike Jacobson
- Bernard Futscher
- Dan Liebler, TDP
- Brad Moore, TDP
- Charlene Ann McQueen, TDP
- William Remers, TDP
- David Segal

Pharmacology

- Robert Dorr, TDP Director
- Tom Davis, TDP

Pathology

- William Bellamy, TDP
- Margret Briehl, TDP
- Garth Powis, TDP

Medicine

- Scott Ebbinghaus, TDP
- Evan Hersh, TDP
- Alan List, TDP
- Thomas Miller, TDP
- Alison Stopeck, TDP
- Charles Taylor, TDP
- Daniel Von Hoff, TDP
- Luke Whitesell, Pediatrics, TDP

Other Fields

- Victor Hruby, Chemistry, TDP
- Eugene Mash, Chemistry, TDP
- Doug Lake, Microbiology/Immunology, TDP

Arizona State University:

- Seth Rose, Chemistry
- Edward Skibo, also part of UA TDP
- George R. Pettit, Chemistry, also part of UA TDP
- Bioengineering In Situ Gels for drug delivery

TGen:

- Carpens
- Spyro Mousset
- Bittner

Mayo:

- Riordan
- Gendler
- Miller
- Lee
- Smith
- Loftus
- Chang

MAJOR RESEARCH FACILITIES AND LABS


University of Arizona:

- DNA Microarray Core Facility
- Arizona Research Laboratory for **Protein Sequence Analysis providing services in** Protein sequencing, Amino acid analyses and Mass spectrometry
- Nuclear Magnetic Resonance Center at the College of Pharmacy
- Protein X-ray Crystallography at the College of Pharmacy

- GATC Affymetrix Core Facility providing start to finish chip service at Arizona Research Labs.
- Cancer Center Bioinformatics Core Facility
- Arizona Cancer Center Proteomics Facility provides a full mass spectrometry (MS) service facility

Arizona State University:

- Arizona Cancer Research Institute – Has an integrated set of in-house laboratory facilities for the discovery of new anticancer constituents from natural including a Cell Line Lab, a Microbiology Lab, a large-scale Extraction Lab,



Archive Lab, a Mass Spec Lab and an X-ray crystallography lab.

- NMR Facility operated by the Department of Chemistry and Biochemistry.
- Electron Microscopy Facility
- Electron Paramagnetic Resonance (EPR) Facility
- Bioresources Facilities.
- Culture Transfer/Growth Chamber/ Greenhouse facilities

TGen:

- DNA sequencing core
- Tumor Micro-array core
- High performance computing

Mayo Clinic:

- Planned cGMP lab for cell graft engineering
- Animal models – Murine tumor models facility—full floor of Johnson Research Building with full spectrum of expertise (transgenic, knock-in, knock-out, genetic and immune background)
- Histology core

IV. Cancer Imaging

KEY PROGRAMS AND MAJOR RESEARCH PROJECTS

University of Arizona:

Arizona Cancer Center has an emerging program area in cancer imaging involving use of imaging for image-directed therapy, detecting response to therapy (e.g., virtual colonoscopy), cancer screening and image directed biopsies (e.g., confocal imaging). Breadth of activities from optical image analysis to gamma ray imaging to optical coherence tomographic imaging to use of diffusion MRI and correlating response to chemotherapy to development of integrated miniaturized microscopes to molecular imaging to examine drug action and response. Key breakthroughs involve novel imaging techniques for assessing tumor vasculature, optical

endoscopy, imaging the microenvironment using novel agents for imaging.

GI SPORE is advancing the use of imaging in its development research awards including use of optical imaging and spectroscopy of mouse GI tissue and fluorescence endoscopic imaging of the pancreas.

Mayo Clinic.

Cancer Membrane Proteomics Program focused on identifying receptors, targets for immunotherapy, gene therapy and tumor imaging, as well as molecules important for drug handling. Also applying imaging to detection of **colorectal cancer**.

FACULTY

University of Arizona

- Robert Gillies – Biochemistry and Molecular Biophysics/Radiology
- Harrison Barrett – Optical Sciences/Radiology/Applied Math
- Peter Bartels – Optical Sciences/Pathology
- Jennifer Barton – Biomedical Engineering
- Molly Brewer – Optical Sciences/Pathology

- Michael Descour – Optical Sciences/Pathology
- Jean-Phillippe – Galons, Radiology
- Arthur Gmitro – Radiology
- Ron Lynch – Physiology/Pharmacology
- Seth Marder – Chemistry/Optical Sciences
- Kathy McGovern – Radiation Oncology
- Eric Outwater – Radiology

- Dennis Patton – Radiology
- Theodore Trouard – Radiology/Biomedical Engineering
- Urs Utzinger – Biomedical Engineering

Mayo Clinic (not sure all of these should be included—group from membrane proteomics)

- Riordan

- Gendler
- Miller
- Lee
- Smith
- Loftus
- Chang

MAJOR RESEARCH FACILITIES AND LABS

Equipment across Arizona:

- Clinical SPECT and MRI most places
- Clinical PET/cyclotron at Good Samaritan
- Pre-clinical SPECT, CT, MRI in Tucson

University of Arizona

- Arizona Research Lab Imaging Facilities is equipped to view the ultrastructure of cells, such as analyzing the chemical composition of cell and tissue structure.
- Arizona Research Laboratory Biological Magnetic Resonance Facility
- Radiology Research Laboratory, including a FASTSPECT, a multiple-pinhole system originally designed as a dynamic brain imager. In a high-magnification mode, the system has been used to image small animals at about 2 mm spatial resolution.
- Radiology Research Imaging Room for small animal imaging

- Micro/Nano Fabrication Facility at the Optical Sciences Center
- Nuclear Medicine Clinic
- Optical Detector Laboratory, McKale Memorial Observatory
- Infrared Detector Laboratory, Steward Observatory

At ASU

- NMR Facility operated by the Department of Chemistry and Biochemistry.
- Electron Microscopy Facility
- Electron Paramagnetic Resonance (EPR) Facility
- W.M. Keck BioImaging Laboratory

V. Neuro-oncology

KEY PROGRAMS AND MAJOR RESEARCH PROJECTS

Barrow Neurological Institute:

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

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.

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

FACULTY

Barrow Neurological Institute:

- Joan Shapiro
- William R. Shapiro
- Lynn Ashby
- Irina Beloozerova
- Anna Joy

- Ronald Lukas
- Adrienne Scheck

University of Arizona:

- B. Stea, Radiation Oncology
- J.D. Martinez, Radiation Oncology
- E. Meuillet, Molecular and Cellular Biology

- L. Whitesell, Pediatrics
- D. Mahadeyan, Hematology Oncology
- A. Hamilton, Neurosurgery

TGEN:

- Michael Berens

MAJOR RESEARCH FACILITIES AND LABS

Barrow Neurological Institute

- Brain Tumor Bank

University of Arizona

- Analytical – B. Dorr
- Experimental Mice – C. Taylor
- Molecular and Cellular Pathology – T. Grogan

More Detailed Description of Core Laboratory Facilities

UNIVERSITY OF ARIZONA

- DNA Microarray Core Facility – using two-color fluorescence hybridization to measure relative levels of gene expression in paired samples
- Arizona Research Laboratory for Protein Sequence Analysis providing services in Protein sequencing, Amino acid analyses and Mass spectrometry. Equipment includes: Applied Biosystems 477A pulsed-liquid protein sequencer; Applied Biosystems 420A/H amino acid analyzer; Beckmann 7300 amino acid analyzer; Rainin HPLC; P/ACE 2100 CZE; Michrom Magic 2002 microbore HPLC; Finnigan MAT LCQ Ion Trap Mass Spectrometer.
- Nuclear Magnetic Resonance Center – Houses a 600 MHz Bruker NMR spectrophotometer used primarily for the structural characterization of drug target interactions with DNA and protein and provides access to a 300 MHz instrument. Has supporting computer workstations and software to conduct computational calculations to analyze drug-receptor interactions and structure-based drug design strategies.

Protein X-ray Crystallography

GATC Affymetrix Core Facility, a campus-wide facility supported by the ARL Division of Biotechnology and the Institute for Biomedical Sciences and Biotechnology (IBSB). The facility, housed in Life Sciences South 211, is open to all university investigators. Our facility provides a “start-to-

finish” chip service. This includes cDNA synthesis, in vitro transcription, hybridization, staining, and scanning of the premanufactured GeneChip®. By providing the “start-to-finish” chip service, we hope to significantly reduce chip-to-chip variability and greatly enhance the quality and reproducibility of the data. In addition, software and analysis tools to analyze data are available in the Biotechnology Computing Facility (BCF) Data Analysis and Processing Lab (Biological Sciences West 240).

For high volume experiments, a local installation of the analysis tools can be made available for duration of the experiment. The BCF will provide user-support for these software packages.

Arizona Cancer Center’s Bioinformatics Core Facility is responsible for assisting research investigators with access to Internet tools and resources in cancer research and related fields. Also generates computer programs and scripts to collect large data sets, analyze them and display the results on web pages. The Bioinformatics Core Facility provides database and data warehouse environments for analysis of biological data on cancer cells and tissues.

Arizona Cancer Center Proteomics Facility provides a full mass spectrometry (MS) service facility for investigators of the SWEHSC/ACC and the University of Arizona as an aid in their proteomics research endeavours. +/- Electrospray Ionization (ESI) and Atmospheric Pressure Ionization (APCI)

on TSQ-7000 and on LCQ, preparative and analytical HPLC, UV-Vis spectroscopy, 1-D and 2-D gel electrophoresis (mini and full size gels), Matrix-assisted laser desorption time-of-flight (MALDI-TOF) mass spectrometry, a variety of proteomic procedures and protocols

Arizona Research Lab Imaging Facilities is equipped to view the ultrastructure of cells, such as analyzing the chemical composition of cell and tissue structure, optically sectioning a sample and using light imaging to isolate antigens and substrates. Focused on studying the morphology of viruses, bacteria and molecules. Key equipment includes:

Transmission electron microscopes; Scanning electron microscopes; Scanning Transmission electron microscope; Laser scanning confocal microscope; Optical microscopes; Ultramicrotomes; Vacuum evaporators; Critical point driers; Magnetron sputtering devices; Ultrarapid freezing equipment; Freeze-hydrated sample holders; Freeze-substitution chamber; Freeze-fracture equipment; Energy-dispersive X-ray spectrometers; Darkroom (from 35mm to 5" x 7" formats); Dye sublimation printer; Film recorder

Arizona Research Laboratory Biological Magnetic Resonance Facility

The BMR facility provides access to state-of-the-art MRS and MRI instrumentation for biomedical research.

- **The Bruker DRX500** is a 11.7 Tesla multinuclear spectrometer with three independent rf channels and triple axis field gradients. Ideal for high resolution spectroscopy of liquid samples and protein and peptide structure determination.
- Capabilities: 1D multinuclear spectroscopy; 2D direct and indirect detection; triple resonance ¹H, ¹³C and ¹⁵N; watergate water suppression; digital quadrature detection

DQD; automatic gradient shimming; variable temperature (223 K to 353K); on-site and remote data processing

NMR Experiments at 500 MHz done at the BMR

- Homonuclear / Heteronuclear
- Relaxation: T1, T1rho and T2 Relaxation
- Shift correlation 1D or 2D
- J-coupling Homonuclear
- Exchange spectroscopy (cross-relaxation and chemical exchange)
- **The Bruker BIOSPEC** is a 4.7 Tesla horizontal-bore, multinuclear MRI / MRS system ideal for small animal imaging and localized spectroscopy.

Capabilities: high-resolution anatomic imaging of small animals (7cm open bore); rapid imaging of physiologic functions; diffusion-weighted MRI (DWMRI); perfusion MRI (pMRI); functional MRI (fMRI); MR angiography (MRA); localized spectroscopy and chemical shift imaging (CSI); physiologic monitoring and gating; on-site expertise and assistance with experimental setup

Current Applications: Tumor growth and angiogenesis (MRA and pMRI in mice); Tumor response to chemotherapy (DWMRI and CSI in mice); Alzheimer's disease (MRI and MRS in mice); cerebral ischemia (DWMRI in rats and cell cultures); sleep apnea (MRI in rats); Blood vessel compliance in arteriosclerosis; Materials characterization.

- **The Bruker DRX400** is a 9.4 Tesla multinuclear instrument with micro imaging capabilities. The triple axis gradients enable localized spectroscopy, diffusion measurements and microimaging. The system allows ¹H, ³¹P, ¹³C, ²³Na and ¹⁹F spectroscopy of mammalian cell

utilizing bioreactor technology. This spectrometer is equipped with 5mm, 10mm and 20mm probes.

Standard Probes

- 5,10,20 and 25 mm standard probes for all nuclei

Current Applications: measurement and regulation of pH in tumors and cultured cells; tumor and tissue perfusion measurements; diffusion of water in tumors and cultured cells; metabolism of polyamines in tumors and tumor cells; regulation of phosphomonoester metabolism in cells and tumors; use of MRI and MRS to monitor response of tumors to chemotherapy; microimaging of embryos in vivo; imaging of transgenic mice.

Radiology Research Laboratory. The 13,000 square foot building in the Arizona Health Sciences Center has three laboratory rooms, a small machine shop and six offices for the use of CGRI faculty, staff and students. Equipment assigned for CGRI research includes: Rucker and Kolls 660J wafer prober; Gamma-ray mapper using Tennelec preamplifiers and amplifiers, a Canberra AccuSPEC PC-MCA and a 2-D translation stage (runs in LABVIEW); Spot imager housing, collimators and a full electronics suite for running hybrid semiconductor detector arrays; 3 NIM bins and various NIM units; Keithley 614 and 602 electrometers; Tektronix 455 oscilloscope and TD 5420 digital oscilloscope; Hewlett-Packard 8012 pulse generator; Simpson 420 function generator and power supplies; Bausch and Lomb stereoscopic microscope. Another unique resource in the Radiology Research Laboratory is FASTSPECT, a multiple-pinhole system originally designed as a dynamic brain imager. In a high-magnification mode, the system has been used to image small animals at about 2 mm spatial resolution.

Radiology Research Imaging Room. The Imaging Room houses: Complete gas anesthesia system for small animals; Animal positioning system; Spot imager; FASTSPECT II

- X-ray systems in development

Micro/Nano Fabrication Facility at the Optical Sciences Center. The 2,000 square foot facility provides full processing capability with all the necessary instruments for micro/nano fabrication. Included are: Carl Zeiss mask aligner (resolution 0.8 μm); ECR-RIE (etching system) with load-lock and 6 gas lines; Electron-beam lithography system; Edwards electron-beam metal evaporator; Rapid thermal annealing system; K&S ball bonder; Newport precision alignment packaging system;

Nuclear Medicine Clinic. The 2,000 square foot facility is located in the clinical wing of the University Medical Center/Arizona Health Sciences Center. Equipment available for CGRI use includes: Picker Prism-2000 dual-headed SPECT camera; Toshiba 90B SPECT/whole-body scanners; ADAC mobile camera; Capintec thyroid probe and well counter system; Complete radiopharmacy laboratory and radiotracers, e.g., $^{99\text{m}}\text{Tc}$, ^{67}Ga , ^{201}Tl , ^{131}I and ^{133}Xe are routinely available for our research.

Optical Detector Laboratory, McKale Memorial Observatory. The 2,000 square foot facility is located on the second floor of the basketball arena at the University of Arizona. Equipment available for CGRI research includes: Complete suite of driver electronics and data acquisition; Test electronics for the 48 x 48 detector arrays; Dewar set-up and temperature controlled cold finger;

Infrared Detector Laboratory, Steward Observatory. Equipment available for CGRI research includes: Visible and infrared solid-state, high-speed cameras; Class 1,000 clean

room with full photolithographic capability; Photoresist spinner; Oriel ultraviolet flood illuminator, ovens and wet chemical benches. Semiconductor processing capability

includes: Lindberg oxidation furnace; Disco DAD-320 dicing saw; Electronics assembly in class 1,000 and 10,000 clean rooms.

AT ARIZONA STATE UNIVERSITY:

- AZ Cancer Research Institute – Has an integrated set of in-house laboratory facilities for the discovery of new anticancer constituents from natural sources involving a progressive series of refinement and isolation steps, from the crude extracts of the plant or animal, to a final pure compound. Once pure, an important prerequisite for subsequent drug development is the determination of the chemical structure and accurate biological activity of the new anticancer agent. These in-house facilities include a Cell Line Lab, a Microbiology Lab, a large-scale Extraction Lab, Archive Lab, a Mass Spec Lab and a X-ray crystallography lab.
- Chemistry department at ASU supports an NMR Facility is comprised of two shared-use instrumentation laboratories operated by the Department of Chemistry and Biochemistry. The research-oriented NMR laboratory is located in room C-2 of the Bateman Physical Science building and houses three Varian superconducting fourier-transform NMR spectrometers, an Inova 500, an Inova 400 and a Gemini-300. Seven high-performance UNIX-based graphics workstations (SUN and Silicon Graphics) are available for instrument control and data analysis. The workstations are equipped with a wide variety of NMR analysis, molecular modeling and distance geometry software. A variety of plotters, tape drives and disk devices are available for spectral output and storage. A Mattson FT-IR spectrometer is also available for routine IR analysis.
- **Electron Microscopy Facility** – Although the Life Sciences Electron Microscopy Facility is shared among the three Life Science Departments, it is administered by Dr. Roberson of our Department. The facility includes two electron microscopes: (1) a Philips CM-12S scanning-transmission electron microscope with an EDAX 9800Plus energy dispersive X-ray analysis system and secondary electron detector) and a slow scan CCD direct digital imaging system, which is "on line" for image sharing and transfer, and (2) a Philips EM201 transmission electron microscope. A grant to buy a new scanning electron microscope is currently being reviewed. The facility is equipped with several ultramicrotomes, cryofixation instrumentation (including a Balzers high pressure freezer), and extensive preparatory equipment for a variety of applications, such as those involving freeze fracture techniques and gold plating. Photographic development is also routinely done within the facility.
- **Electron Paramagnetic Resonance (EPR) Facility** – The primary mission of the EPR facility is to determine structural details of proteins which contain paramagnetic centers. It is operated in conjunction with the Center for the Study of Early Events in Photosynthesis and administered by Dr. LoBrutto of our Department. It is

used to characterize a wide variety of biochemical systems (e.g. providing information on an atomic scale in free radicals and in the vicinity of certain paramagnetic metal ions) at temperatures down to 4.2°K. Major equipment includes a Bruker 300E continuous wave EPR/ENDOR spectrometer and an electron spin echo spectrometer. Measurements at S-band (2-4 GHz), X-band (9-10 GHz) and Q-band (35 GHz) are available, as well as advanced techniques for resolving couplings of magnetic nuclei to paramagnetic centers. A massive upgrade of the facility added such capabilities as pulsed ENDOR, 35 Ghz continuous-wave ENDOR, and Fourier Transform EPR.

- **Bioresources Facilities** – Support laboratories have been established that encompass: (1) DNA sequencing and synthesis (DNA Sequencing Lab), (2) inorganic and organic environmental analyses, (3) protein analysis, (4) immunobiology, (5) image analysis and (6) fermentation/cell culture. These facilities offers molecular biologists DNA and peptide synthesis (Cruachem PS 250 and Millipore 9050), DNA sequencing (ABI 377), protein sequencing (Porton 2090) and amino acid (Hewlett-Packard AminoQuant) analysis. In addition HPLC (Beckman 125) and capillary electrophoresis (Beckman P/ACE model 2050) systems are available for purification of macromolecules. Molecular weight determinations of proteins can be made by a Vestec matrix-assisted laser desorption time of flight mass spectrometry (MALDI-TOF MS). The environmental analysis laboratory includes two atomic absorption spectrophotometers (one with and one without a graphite furnace detector), a Bran and Luebbe autoanalyzer, a dissolved organic carbon analyzer, a CHN

S/O analyzer and a gas chromatograph-mass spectrometer. The fermentation/cell culture facility includes two walk-in growth chambers for plant propagation, smaller incubators for bacterial and algal growth, two superspeed centrifuges for cell harvesting and sterile transfer facilities.

- **W.M. Keck BioImaging Laboratory** – This lab is a multi-user facility that engages in biological and physical imaging using several light-microscope workstations. The systems housed in the laboratory include a ratio imaging/morphometric inverted light microscope system designed by Inovision, an upright scanning (single) laser confocal microscope designed by Molecular Dynamics, a scanning (four) laser confocal microscope designed by Leica and a Strom PhosphorImaging system designed by Molecular Dynamics. In addition to structural and molecular imaging, the laboratory supports the GCG database server that is used by over 50 researchers to analyze DNA information collected by researchers from all over the world. A molecular modeling facility with MSI software allows creation and analysis of molecular structure and interactions.
- **Culture Transfer/ Growth Chamber/ Greenhouse facilities** – The Department has a wide variety of facilities for maintaining organisms of various sizes. Culture transfer hoods, autoclaves, cold rooms and environmentally controlled growth chambers are available on each floor of the Life Science center. Altogether there are 17 growth chambers and these are maintained under a variety of experimental condidtions. Four glass greenhouses are maintained on campus and four greenhouses (three glass and one fiberglass) are maintained on the 43 acre ASU Horticultural Resources

Center located 3 miles from campus. On campus the 3500 sq. ft. greenhouse on top of the Life Science Center includes several climate-controlled modules.

- **Herbaria** – The Department maintains major research collections of vascular plants, lichens and fossils. The Vascular Plant Herbarium has over 200,000 specimens with an emphasis on the American Southwest, although substantial collections from throughout the Americas are included. The collections are particularly rich in the Cactaceae, Compositae and Myrtaceae. The Lichen Herbarium has well over 85,000 specimens. Although the emphasis is on the western U.S. and Mexico, representation is world-wide in scope. Collections are particularly rich in the Lecanoraceae and Parmeliaceae. The Plant Fossil Collections include over 5,000 megafossil specimens of worldwide representation, as well as fossil and extant palynomorph samples and extant wood and other anatomical specimens. Special emphasis in the collections is on the American West, including permineralized and petrified Tertiary materials.
- **The Desert Botanical Garden** – The garden, a privately run organization with an emphasis on the Sonoran Desert and ethnobotany of the Southwest, is situated on 60 hectares of Papago Park about two miles north of the University. It displays approximately 3500 desert plants

from around the world and employs a staff of 50, include several professional botanists with interests in the ecology and systematics of Sonoran Desert plants and communities. It also has a vascular plant herbarium with approximately 33,000 specimens and maintains a botanical and horticultural library. The Department interacts with the Garden in a number of ways and some of the professional staff are adjunct members of the Department.

- **Other Departmental equipment** – Facilities of individual laboratories are too numerous to enumerate comprehensively. However, the following list will give the reader some feel for the range of our capabilities: anaerobic chambers, walk-in cold rooms, electroporator, a "gene gun", ultracentrifuges with rotors, protein transblotters, spectrofluorometers, various spectrophotometers, PCR (polymerase chain reaction) machines, digital camera, liquid scintillation counters, various gas chromatographs (trace N and S gases), liquid chromatographs, UV visible scanning spectroradiometer, fiber optic microsensors for in vivo radiation measurements, CO₂ exchange systems, air pollutant analyzers, ion chromatograph, and various research microscopes (UV, fluorescence, phase, bright field).

TGEN

- DNA sequencing core
- Tumor Micro-array core
- High performance computing

MAYO CLINIC

- Planned cGMP lab for cell graft engineering
- Animal models – Murine tumor models facility – full floor of Johnson Research Building with full spectrum of expertise (transgenic, knock-in, knock-out, genetic and immune background)
- Histology core

Appendix B. Insights from Peer Analysis

The Platform committee members identified leading peer institutions across the focus areas, informed by an analysis of NIH awards conducted by Battelle. Detailed surveys were undertaken to gain the perspectives of these leading national programs. Below we present insights learned regarding cutting edge issues for each of the focus areas from the 10 peer institutions that responded. While not a scientific survey, these responses are on track with the enhancements set out by the Platform committee members.

Peer Institution Insights

Focus Areas	Peer Institution Insights into Cutting Edge Issues	Peer Institution Responding
Cancer Drug Discovery and Development	<ul style="list-style-type: none"> • Individualization of cancer therapy, detection and prevention. • Defining new molecular targets by gaining a deeper understanding of the molecular machinery of various cancers • Developing ways and means to sort through the huge volumes of targets. • Validate new molecular targets in develop pre-clinical animal models that can validate new therapeutic agents. • Better use of Phase I and II trials to see if new therapeutics are effective. • Exploring new forms of therapy – vaccines, antibodies, small molecules 	MD Anderson Duke University
Cancer Prevention	<ul style="list-style-type: none"> • Application of molecular epidemiology to identify genetics related to increased risk • Drug discovery for chemoprevention, including molecular targeting, pharmacogenomics and genomics • Tailor interventions via the screening of drugs • Improved techniques for behavior modification • Cancer programs able to tackle both disease treatment and disease prevention and intervention. • Advancing risk-based management using drug therapy and surgical therapy as preventative tools 	Johns Hopkins University MD Anderson

Focus Areas	Peer Institution Insights into Cutting Edge Issues	Peer Institution Responding
Gastrointestinal Cancer	<ul style="list-style-type: none"> • Development of novel biological targets and agents • Development of markers to identify which patient's tumor will respond to which biological or cytotoxic agents (pharmacogenomics) • The identification of new methods for the early diagnosis of GI cancer • Innovative strategies for prevention • More detailed understanding of the molecular signaling pathways as well as understanding of mechanisms of tumor suppressor genes • Having better models of colon cancer with a robust metastatic model being very desirable 	UCLA Vanderbilt
Neuro-Oncology	<ul style="list-style-type: none"> • Molecular neuro-oncology, especially molecular characterization of tumors. • Development of imaging strategies for early responses • Immunotherapy and gene therapy • Genomic analysis to provide a better understanding of the abnormalities that lead to or contribute to brain tumors • Small molecule targeting • Novel approaches for developing drug/therapy delivery systems 	University of Pittsburgh Duke University
Cancer Imaging	<ul style="list-style-type: none"> • Use of imaging to individualize patient therapy • Development of image enhancement agents for targeting specific cancer tumors, whether they be contrast agents for MR or optical techniques, or are nuclear labeled probes • Big issue of deciding which competing technologies are the best to use in specific situations and/or how to use competing techniques in complementary combinations 	Washington University