

Seizing the
Translational
Research
Opportunity
in Arizona



Report to the Arizona
Biomedical Research
Commission and the
Flinn Foundation

Battelle
The Business of Innovation



**FOR: ARIZONA BIOMEDICAL
RESEARCH COMMISSION
AND FLINN FOUNDATION**


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A NATIONAL DILEMMA, AN OPPORTUNITY FOR ARIZONA

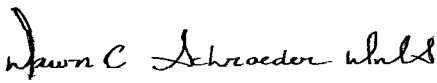
Since early 2005, leaders from Arizona's universities, nonprofit research institutes, academic health centers, and medical centers, as well as several community representatives, have been meeting to guide the development of a statewide, collaborative approach to build an effective translational research model in Arizona—something no other state has done.

Specific focus is placed on resolving issues that often hold back collaborative efforts in translational research and in taking advantage of opportunities with significant potential for advancing translational research. This includes streamlining Institutional Review Board (IRB) processes, harmonizing business practices, and advancing collaborations with special population groups.

This Arizona translational research imperative grew out of efforts to implement *Arizona's Bioscience Roadmap*. Without a strong translational research capacity to accelerate and develop the state's basic research knowledge, Arizona's ability to commercialize discoveries and advance benefits to patients would be at risk. The Arizona Biomedical Research Commission and Flinn Foundation have joined forces with Battelle to help position Arizona as a leading bioscience center.

Translational research is the conduit through which Arizona's basic biomedical research will be transformed into a high quality, improved healthcare system, allowing the state to fully realize the economic and healthcare potential of its investments. As the recent *Meds and Eds* report points out, "...in the 21st century, there is a strong rationale for treating health as an economic opportunity. As companies realize the treasure trove hiding in the life sciences, a great deal of research and development money will flow into biology, creating all sorts of revolutionary products and well-paying jobs." In order to maximize such benefits from its biology research, Arizona must address gaps in translational research.

Respectfully Submitted,



Dawn Schroeder, D.D.S., M.A.
Executive Director
Arizona Biomedical Research Commission



John W. Murphy
President and CEO
Flinn Foundation



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SUMMARY OF RECOMMENDATIONS FOR FASHIONING A SUSTAINABLE ARIZONA TRANSLATIONAL SYSTEM FOR BIOMEDICAL RESEARCH

Near-Term Recommended Activities

- Creation of an **Institutional Review Board (IRB) Networking Forum** to raise awareness of issues, foster collaborations and create a sense of community and trust.
- Institution of **Technical Policy Development Retreats** that focus on specific policy and supporting document needs of IRBs.
- Formation of an **Arizona Clinical Research Consortium** to facilitate collaborations of community physicians and clinical research leaders to increase clinical trials activities in the state.
- Advancement of **guidelines** on approaches to complex business practices that can pose barriers to collaboration in biomedical research, such as indemnification, intellectual property, cost sharing, and credentialing.
- Development of a **community-based participatory research guide** for advancing collaborations with Native American and Hispanic/Latino population groups.
- Establishment of an **Arizona Community Institutional Review Board** to provide IRB support for independent research sites that lack in-house IRBs and studies that span multiple research sites.

Possible Longer-Term Initiatives

- Development of specialty capabilities for **clinical research advisory services** in target disease areas.
- Development and implementation of a **web-based information tool** for basic and clinical researchers.
- Development of an innovative, **statewide clinical scholars program** in Arizona in target disease areas.
- Creation of a **network of site managers** to facilitate communication among investigators and assist in the identification of early stage discovery projects.

Formation of an Arizona Translational Resource Network (AZTransNet)

The formation of an Arizona Translational Resource Network (AZTransNet) will facilitate the policy, infrastructure, and cultural changes necessary to build a statewide capacity for collaboration, one that encompasses Arizona's near- and long-term translational research goals and integrates "best practice" lessons from translational leaders into the specific context of the state.

Industry, universities, non-profit research institutes, hospitals, medical centers, and private practice physicians will all be brought to the table under this statewide coordinating mechanism.

AZTransNet will have a fact-based understanding of the gaps in the current translational research system in terms of infrastructure and policy and foster interaction between the specific groups that can fill those gaps.

The Arizona Translational Resource Network (AzTransNet)

- **Purpose:** AzTransNet will be a facilitating and *coordinating organization* and *honest broker* with the goal of advancing translational and clinical research activities in Arizona.
- **Role:** AzTransNet will advance the activities set out in the Arizona Translational Research Pathway.
- **Participation:** AzTransNet will seek to work with all biomedical research institutions in Arizona engaged in translational and clinical research across universities, non-profit research organizations, and hospitals and medical centers, as well as interact with private physician practices and private industry. The directions and policies of AzTransNet will be set by participating organizations.
- **Funding:** AzTransNet will seek grants from foundations and government, and may fund specific efforts with support from member and participating institutions.

SHAPING THE NEW MODEL OF TRANSLATIONAL RESEARCH

The nation is on the cusp of a revolution in the way that bioscience research is being conducted, one that will change how basic research discoveries are translated into real-world solutions to biomedical problems. This climate of change in the biosciences presents Arizona with both a challenge and an opportunity to further its bioscience goals.

In the near term, Arizona's goal is to realize tangible economic growth and health benefits from the state's existing bioscience research base. In the long term, it is the elevation of Arizona's bioscience research to national standing, a reality that will attract industry and talent for relocation to the state and set up a cycle that will ultimately pay economic and health dividends far into the future. Strategies to reach these goals, formalized in *Arizona's Bioscience Roadmap*, have largely focused on needed policy and investments to facilitate basic bioscience research. However, **it has become clear that the state must also focus on its translational research in order to enhance its *Roadmap* strategies for bioscience success.**

VALUE OF TRANSLATIONAL RESEARCH

While basic research yields invaluable knowledge of how biological systems work, it is translational research that converts this basic research knowledge into such real-world technologies as drugs, vaccines, and diagnostic devices. The production, distribution, and marketing of these technologies drive the creation of new jobs, attract related industry to the area, and bring cutting-edge technologies to the state's patient population.

Such direct economic and health benefits are incentive for Arizona to tear down barriers in its current system that may hamper efficient translational research. There is also a national imperative for change in translational research now that offers Arizona the opportunity to springboard into prominence with a statewide example for the nation to model.

While basic research yields invaluable knowledge of how biological systems work, it is translational research that converts this basic research knowledge into such real-world technologies as drugs, vaccines, and diagnostic devices.

Federal agencies have called for a "reengineering [of] the clinical research enterprise" in response to a national translational research system that is broken. Recent years have seen a watershed of basic research discoveries, but the practical applications stemming from those discoveries have largely failed to materialize in the marketplace and the clinic. According to the Food and Drug Administration, "[the year] 2000 marked the start of the slowdown in new drug and biological submissions to regulatory agencies worldwide... This means fewer new products can be approved and made available to patients."

Failure of the current translational research system to keep pace with basic research discoveries has also prompted a shift in priority for the National Institutes of Health (NIH), one that is reflected in the types of

research projects that it is willing to fund. NIH funding is the most widely recognized benchmark for standing in the world of bioscience research. The number of NIH grant awards held by researchers at institutions in the state, as well as the amount of overall funding awarded, speaks to the quality of research being produced. As such, it is vital that Arizona position itself to successfully compete for this federal funding by addressing flaws in its translational research system and supporting research projects that are more translational in nature.

Arizona has a number of advantages that may allow it to leapfrog the competition in setting this new translational



“Federal agencies have called for a ‘reengineering [of] the clinical research enterprise’ in response to a national translational research system that is broken... this offers Arizona the opportunity to springboard into prominence with a statewide example for the nation to model.”

model. Arizona is unique in its statewide commitment of resources to furthering its bioscience goals, and thus those in translational research. This is in sharp contrast to the approach that a number of research institutions and centers have chosen to take in revamping the translational research system at the single-institution level or in small clusters of institutions. Such a piecemeal approach may lack the scope necessary to set a national standard in

translational research. Arizona’s relative newness to the playing field may also give it an advantage. While Arizona has not had a chance to establish a long-standing tradition of basic research and clinical excellence, the state is not entrenched in an outdated system and is better able to tear down barriers and adapt its approach.

Arizona has recognized that it must play to these strengths in order to seize this rare opportunity to grab the national spotlight. A broad-based group of leaders from Arizona’s universities, non-profit research institutes, academic health centers, and medical centers, along with community representatives, has been brought together under a broad umbrella initiative to fashion a new translational research system in the state, one worthy of national acclaim.

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TRANSLATIONAL RESEARCH: WHAT IS IT AND WHAT LESSONS HAVE WE LEARNED?

What is the key to fashioning a model of translational research that can set a national standard? An understanding of the nature of translational research itself precludes a single simple answer to this question.

Each practical solution to a biomedical problem—drug, vaccine, diagnostic device—begins with knowledge gleaned from basic research. Translational research ultimately converts these basic research “bench” discoveries into products that can be used at the clinic “bedside” as part of health care treatment and prevention. While there is no set path from “bench” to “bedside,” there are some commonalities: initial solution design based on evaluation of basic research data, early-stage development of that design, testing in a simplified system (preclinical trial), human testing (clinical trial), risk evaluation, and final approval for patient use. The translational process is also bidirectional—with the results at each step being fed back to those working on earlier steps, allowing necessary modifications to be made before solutions are funneled back into the pipeline toward a successful clinical application.

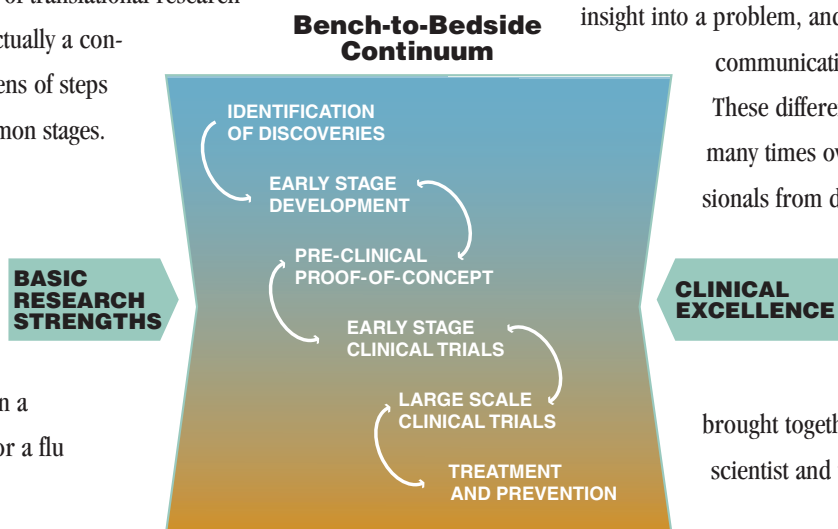
Closer inspection of translational research shows that it is actually a continuum, with dozens of steps between the common stages. These stages are also only common in the broadest sense—what is encompassed in a preclinical trial for a flu

vaccine may be very different from what is involved in a trial for a new cancer drug. The actual steps in the development of a particular product, as well as the particular players involved, can vary widely with the nature of the product itself.

NO ONE-SIZE-FITS-ALL SOLUTION TO ADVANCING TRANSLATIONAL RESEARCH

Bottlenecks often occur due to the complex nature of the translational research process. The individuals and institutions involved in translating basic research into products are many and varied—chemists, molecular biologists, medical technologists, marketing analysts, clinicians, policymakers, federal granting agencies, and review boards, to name only a few. The disparate training, culture, and rules governing this array of professionals and agencies act as a barrier to the effective communication that is vital for successful translational research. Even within a single discipline such as chemistry, there are subspecialties—synthetic chemistry, analytical chemistry, biochemistry—each with a slightly different approach,

insight into a problem, and language of communication from the others. These differences are magnified many times over when professionals from disciplines that have traditionally occupied very separate venues are brought together, such as the scientist and the policymaker.



It is the dynamic interaction between these individuals and groups that will ultimately dictate the success of a translational research system. Only through a multidisciplinary approach and a spirit of collaboration can efficient translation occur. The process of translation starts when a solution design is sparked in the imagination of one of these translators after an evaluation of basic research knowledge. In order to identify such an opportunity, that particular translator must understand the underpinnings of the basic science as well as the pressing need that it can ultimately answer in the clinic. The necessary perspective to see these connections often requires training in, or at least a basic knowledge of, many different disciplines.

Each step in the translation of this initial design involves a trial of some kind and, often, an adaptation in approach based on the results of this trial. When there is a snag at a single step—a new cancer drug works in an isolated tissue sample but fails when tested in a whole organism, for example—it is a free flow of information and a willingness to entertain ideas from different disciplines that most effectively resolves the block and moves the translation forward as efficiently as possible. In the example noted, it would likely be the job of the synthetic chemist to adapt the failed cancer drug. However, it may be the insight of the cell biologist, immunologist, clinician, or a synthesis of all three that illuminates the necessary modification that will fix the problem.

LESSONS FOR TRANSLATIONAL RESEARCH SUCCESS

In fashioning a new model of translational research, then,

there are some clear general guidelines. A multidisciplinary approach must be encouraged and rewarded—both in terms of changing the current mindset and in the training of future translational researchers. Barriers to effective communication must be torn down between disciplines, institutions, and departments.

Leaders from six institutions noted for excellence in various aspects of translational research¹ agree on some high priority

areas that will require application of these guidelines:

- **Contact between**

- physician and scientist must be facilitated.**

Translational research, according to the NIH, encompasses “studies at the interface of the bench and bedside. . .requiring close interaction between clinical and bench scientists.” This close interaction is critical for connecting unmet medical needs with new basic research discoveries and sparking initial solution designs. It is also critical for informing basic research of fundamental questions about the biology that may be hinted at in clinical observations. However, the gap between the physician and the basic scientist in terms of culture and training is one of the widest. One solution to bridge this gap has been the advent of the physician researcher. The physician researcher has both the medical and basic research training necessary to work

A multidisciplinary approach must be encouraged and rewarded....Barriers to effective communication must be torn down.

¹Partner’s Healthcare: Laboratory for Drug Discovery and Neurodegeneration; Partner’s Healthcare: Center for Integration of Medicine and Innovative Technologies; Partner’s Healthcare: MGH Clinical Research Program; Drexel University: Philadelphia Super Site; M.D. Anderson Cancer Center; Duke Clinical Research Institute

within both areas. However, recent years have seen a decline in the number of physician researchers. Economic pressures, time constraint issues, and lack of career development opportunities have resulted in a loss of mid-career physician scientists. Lack of training opportunities for new physician scientists has also caused a drop in the number of prospective students willing to pursue it as a career choice. The proper economic, career-development, and training incentives must be put in place to ensure a continued stream of physician researchers to the playing field of translational research.

- **Funding mechanisms that allow for collaborative research and tangible incentives that reward it will be required.** Traditionally, basic science researchers have had little incentive to pursue large-scale collaborative projects, both from a funding and a career development standpoint. Generally, a researcher's performance is measured in terms of the number of publications in top journals that have resulted from his/her work and the amount of funding that has been awarded to support that work. Collaborative projects, by their nature, yield publications and require grants that credit many different researchers. This makes it difficult for the current departmental/institutional metrics, as well as the peer evaluation system, to accurately parse out the credit and reward due to single researchers in those collaborations. The current metrics must be retooled to reflect a more fluid definition of research success, one that takes into account cultural and professional differences among investigators.

Rewards for collaborative work will have to come in a variety of different forms. Along with salary and career

development incentives, seed funding and intellectual property support are likely going to be required.

Projects in early stages of development are generally not mature enough to net federal funding and can put a serious strain on laboratory resources. Seed funding must be available to address this financial gap, supporting projects during proof of concept and early development stages until there is strong enough evidence of project feasibility for it to compete for federal dollars.

It is critical that researchers and institutions are vested in the fruits of their labor with intellectual property (IP) rights. While assigning IP rights to collaborative work will be complex and time consuming, early attention to these issues can prevent snags and a sense of disenfranchisement in later stages of a project.

- **There is need for an improved interface between academia and industry.** This issue is both cultural and operational. The nature of the academic research itself, along with time constraints imposed on the academic researcher, means that it is not always possible for efforts to be focused completely on one project. As a result, output from an academic institution on a particular project might be slower than from an industry counterpart possessing greater monetary and labor resources to shift to it. Some compromise in expectations between academia and industry must be struck. More applied research groups may have to accept slower timelines and scheduling constraints, while basic research groups may have to become less insular in approach in order to speed progress. Putting in place some organizational support mechanisms for academicians—both clinical and basic science—will also help to resolve regulatory, intellectual property, and financing issues in a more timely fashion.

- **Initial focus in a disease area or stage of translational research characterizes successful translational research initiatives.** This initial effort can frame a system with broad portability to other areas and stages of translational research.

There is no overarching solution to creating a successful, model translational research system. Context always

Key Success Factors for Translational Research

- Facilitating contact between physician and scientist.
- Requiring funding mechanisms that create collaborative research with tangible incentives.
- Improving the interface between academia and industry.
- Focusing on an initial disease area or stage of translational research.
- Necessitating clinical excellence as a driver of translational research.

plays a role in how the components of a system work together. Similar organizations can have somewhat different roles in different systems, and while

different systems may share the same components, the relative strength of these components may vary. The six leading institutes referenced previously are prime examples of this—all are leaders in a specific aspect or stage of translational research. M.D. Anderson Cancer Center, one of these leading institutions, excels at discovery identification and early and late stage clinical trials, while the Center for Integration of Medicine and Innovative Technologies (CIMIT) of Partner's Healthcare has strength in early stage development and preclinical trials. Leading initiatives in translational research tend to reflect this specific focus—either by

disease area, type of health care intervention, or stage of translational research.

- **Clinical excellence is often a driver of translational research.** Keen observations by clinicians can drive the development of innovative therapies, which in turn acts as a draw for patient interest. Moreover, clinical excellence is often a magnet for attracting collaborations with industry or biomedical researchers seeking partners to advance new drugs or devices.



THE ARIZONA CONTEXT: GAPS AND STRENGTHS AFFECTING TRANSLATIONAL RESEARCH SUCCESS

In order for Arizona to create a sustainable, successful translational research system, these “best practice” lessons and general guidelines must be viewed and implemented in terms of the specific context of the state. Arizona has a number of strengths that it can build upon, but it also has several weak areas that it will have to address. It is only within this Arizona context that the feasibility of a particular model translational research system can be assessed and a specific plan of action formed to reach it.

ARIZONA GAPS IN TRANSLATIONAL RESEARCH

Similar to Arizona’s biomedical research position, the state’s base of hospitals and medical centers is growing and emerging in clinical excellence.

Clinical excellence is a critical driver for translational research. Arizona is creating an environment for clinical excellence, but there is still a significant road to travel. HealthGrades, which uses in-patient claims data along with mortality and complication ratings to analyze 10 specialty areas, found that only in orthopedic, gastrointestinal, stroke, and pulmonary specialties does Arizona have three or more hospitals in the top 10%. Still, there is strong improvements in HealthGrade ratings taking place even from 2005 to 2006, with Arizona having at least one hospital in the top 10% for all of the 10 specialty areas in 2006, except in Critical Care. By comparison, in 2005 Arizona had no hospitals rated in the top 10% for Critical Care, General Surgery, Maternity Care, and Women’s Health.

Arizona also is still building up its residency training programs, which is a mark of the depth and breadth of

clinical excellence. In many specialty areas Arizona has no residency programs, such as allergy and immunology, physical medicine and rehabilitation, otolaryngology, and plastic surgery. In other medical specialty areas, the number of residents is quite low, particularly compared to Arizona’s share of overall national population, which stands at 1.8%. For instance, Arizona has 1% or less of the residents trained across the nation in anesthesiology, ophthalmology, orthopaedic surgery, pathology, radiation oncology, thoracic surgery, and urology.

Arizona’s clinical research activities, which often go hand-in-hand with clinical excellence, reflect a similar trend. Arizona does not meet the national average in number of NIH grants awarded for clinical research. Only 28% of

Arizona Lagging in Early Stage Clinical Trials

Trial Phases	Trials Recruiting in AZ		Trials Recruiting in U.S.	
	Number	% of Total	Number	% of Total
Phase I	51	7%	1,530	22%
Phase II	252	34%	3,141	45%
Phase III	373	51%	1,567	22%
Phase IV	62	8%	750	11%

Source: Clinicaltrials.gov, May 2006

Arizona NIH grants are for clinical research, compared to a 32% national average. Specialized NIH grant awards—physician scientist awards, clinical research curriculum awards, etc.—are significantly under-represented in the state. Arizona lags behind the leading bioscience sectors in Maryland, North Carolina, California, and Massachusetts in number of clinical trials. As well, the types of clinical trials that predominate in Arizona are telling about the state’s lack of innovation in translational research. Phase I and II clinical trials are early stages that establish safety and efficacy of a new treatment in humans and are

markers of innovation. The percentage of Arizona clinical trials in Phase I is much lower than the national average (7% vs. 22%), and while this gap is smaller for Phase II trials, Arizona's number is still low (34% vs. 45%).

ARIZONA OPPORTUNITIES AND STRENGTHS TO ADVANCE TRANSLATIONAL RESEARCH

While Arizona is not noted for its innovation or excellence in a clinical setting, a number of factors must be evaluated in determining the impact of these gaps on Arizona's translational research goals.


Arizona's relative youth in biomedical research is a contributing factor to its lack of high-powered medical centers and innovative output. While this results in a poor showing for the state in a number translational research metrics, it also means that Arizona's economic, organizational, and cultural practices are not firmly ingrained.

That Arizona is less entrenched in the old way of doing things gives it an advantage over current leaders in biomedical research who are tasked with having to retool systems that are weighed down in years of traditional approaches and attitudes.

Arizona's recent explosive population growth is also a positive sign for future clinical endeavors.

The type of population growth seen in Arizona in the 1990s (40%) and more recently directly translates into

Arizona outpacing nation in population growth



POPULATION CHANGE: 1990 – 2000		
	U.S.	Arizona
Total Population	13.1%	40%
Under 18 years old	13.7%	39.3%
65 years and older	12.0%	39.5%
Native Americans	26.4%	25.7%
Hispanics	57.9%	88.2%

Source: U.S. Census Bureau, 2004

a growing patient population. This growth should drive the development of new medical

centers that can be designed from the ground up to optimize clinical stages of translational research. A growing patient population also provides a broader spectrum of individuals for possible clinical trials as well as an increased number of individuals in special population groups, such as the elderly and Native American populations, that may provide niche areas of research focus for the state.

Arizona has identified core areas of research strength for focus and made significant gains in NIH funding in recent years. *Arizona's Bioscience Roadmap* identified research in neuroscience, cancer therapeutics, bioimaging, and bioengineering as core competency areas in the state. Other emerging areas include asthma, diabetes, agricultural biotechnology, and infectious diseases. Since *Roadmap* efforts were initiated, NIH funding to the state has increased substantially. Arizona has seen a growth in overall NIH funding of 30% from 2001 to 2004, 75% of its *Roadmap* goal of netting \$214 million in funding by 2007.

Arizona is developing a deeply rooted spirit of collaboration that is serving the state well in advancing translational research. The willingness of Arizona's institutions to work together to overcome obstacles is exemplified by the private sector, state and local government, foundation, and Native American interest groups that banded together to recruit the Translational Genomics Research Institute to the state. Through their efforts, a powerhouse of genomics, bioinformatics, and computational biology expertise is at hand to help drive bioscience research and discovery in the state. Arizona's collaborative tradition has been formalized and incorporated into the state's *Roadmap* strategy for bioscience success. A number of different collaborations have formed since the *Roadmap's* inception, most focusing multidisciplinary efforts on one of the core research areas identified by the *Roadmap*. Many of these collaborative

efforts have also embraced the idea of leveraging technology to facilitate the state's translational bioscience goals in these specific disease areas.

There are a number of areas of technological strength in Arizona that can be leveraged toward productive early and late stage translational research activity. Arizona has long been recognized in the physical sciences and has accumulated a pool of skills and knowledge in optics, electronics, computer science, applied physics, engineering, applied mathematics, and statistics that can be applied to novel bioscience solutions. These broad technology strengths are advancing progress in the state's core research areas through a number of different fields:

- Bioimaging
- Bioinformatics
- Tissue Banking and Molecular Diagnostics
- Drug Development

Bioimaging

The University of Arizona has one of the world's leading optics programs, making it a powerhouse of state-of-the-art equipment and expertise that can be harnessed in the development of new bioimaging techniques. Barrow Neurological Institute is advancing novel methodologies in magnetic resonance imaging, an endeavor that has led to a partnership with GE Medical Systems. Arizona State University is advancing flexible display technologies that can be used in future medical applications.

These new imaging technologies have become a key component in Arizona's core research areas of cancer therapeutics and neuroscience. The Arizona Alzheimer's Research Consortium has been pioneering the use of advanced imaging techniques to diagnose the early onset of Alzheimer's Disease. Arizona is pursuing research programs for the detection and management of many

cancers, including gastrointestinal and skin cancers, with aid of its experimental animal imaging core center, funded by the National Cancer Institute.

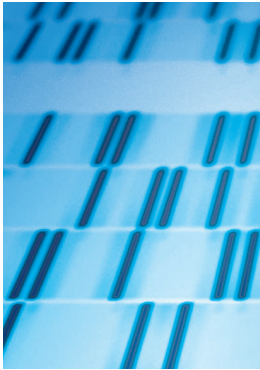
Technology enhancements in the use and transmission of imaging are underpinning the advancement of Arizona's telemedicine initiative. Arizona is home to one of the nation's premier telemedicine programs for providing modern medical technology and expertise to remote underserved locations.

Bioinformatics

The advent of the Translational Genomics Research Institute (TGen) brought world-class bioinformatics capacity to the state. ASU is set to expand that capacity with a new program in Biomedical Informatics. The university will offer an MS in Biomedical Informatics starting in 2007 and a PhD program starting in 2008.

Arizona's broader research strengths are being leveraged to allow the state to "lead with technology" in such fields as bioimaging, bioinformatics, and drug development.

The field of bioinformatics makes it possible to evaluate and draw conclusions from large-scale system studies in the biosciences, the type of studies that the NIH is particularly interested in promoting. Arizona's strong base in bioinformatics and computational biology should act as a cornerstone for molecular discoveries in a number of disease areas, including cancer and neuroscience. Such discoveries impact basic research science and offer key information necessary for the development of diagnostics and treatments for disease.



The Arizona Health Query (AZHQ) has developed, and continuously updates, a database of community health information to aid community leaders in making policy decisions about health care in the state. This database maintains secure, confidential, and individually identifiable information on patients that can be used to track benchmarks in community health over time, forecast future health needs in the state, and inform management and policy questions with current information.

Tissue Banking and Molecular Diagnostics

Demand for high quality, standardized human tissue samples for research continues to grow, particularly within the pharmaceutical industry and biotechnology companies. Arizona is in one of the strongest positions possible to capitalize on this opportunity. Arizona's Sun Health Research Institute has one of the world's leading brain banks. Other institutions, notably Barrow Neurological Institute (BNI) and the University of Arizona, also have important tissue banking activities. Similarly, the Southern Arizona VA Health Care System in Tucson is committed to improved molecular diagnostics and has made a significant investment in its tissue bank. This investment has paid off in the Southern Arizona VA being named the national tissue bank for the VA system. TGen and its strategic partner, the International Genomics Consortium, are advancing the collection and analysis of cancer-related tissues to identify molecular "markers" for new cancer drug discovery and molecular diagnostics. In partnership with Arizona State University, TGen is also advancing the use of nanotechnology in the development of innovative cell-based imaging approaches for diagnostics.

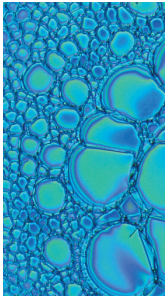
Drug Development

Arizona has become home to one of the leading initiatives to upgrade the use of technology in drug development, a key problem identified by the FDA's Critical Path report. The University of Arizona, SRI International, and the FDA have entered into a strategic partnership to form the Critical Path Institute (C-Path) in Tucson. This partnership will serve as "neutral ground" to test ideas to optimize drug development processes. C-Path and its partners will work to foster new standards and tools that will be considered by the FDA as it develops formal guidelines and "best practices" for the commercial development of drugs and medical products.

C-Path will seek to accelerate cancer drug development by incorporating FDA recommendations in novel clinical trial design and approaches.

Protocols may include harnessing biomarker technology to support design, monitoring and analysis of trials for the development of effective cancer drugs with greater assurance of safety.





Arizona's deeply rooted spirit of collaboration has served it well in laying the groundwork for translational research.

EXAMPLES OF ARIZONA'S EMERGING CULTURE OF COLLABORATION

• **The Arizona Alzheimer's Research Consortium (ARC)** is dedicated to the understanding, treatment, and prevention of Alzheimer's disease. The nine members of the Consortium—Arizona State University, Barrow Neurological Institute, Banner Good Samaritan Medical Center, Harrington Arthritis Research Center, Mayo Clinic, Northern Arizona University, Sun Health Research Institute, TGen, and the University of Arizona—are committed to “leveraging complementary resources” to fight this debilitating disease. The Alzheimer's Research Consortium is comprised of the Arizona Alzheimer's Research Center (AARC), a “statewide research laboratory without walls,” and the NIH-sponsored Alzheimer's Disease Core Center (ADCC). The ARC has pooled its strengths in brain imaging, computer science, and the basic, behavioral, and clinical neurosciences; in the process, it has become a national model for a comprehensive, multidisciplinary approach to research.

• **The Arizona Parkinson's Disease Center** is a three-year consortium that brings together leading investigators throughout the state to study early predictors of Parkinson's Disease as well as possible molecular targets for therapy. The Center is funded by the Arizona Biomedical Research Commission and pools research talent from Sun Health Research Institute, Mayo Clinic, Barrow Neurological Institute, Banner Good Samaritan Medical Center, Arizona State University, and TGen toward a better understanding of this debilitating neurological disorder.

• **Arizona's Critical Path Institute (C-Path)** was created in 2004 in response to the Food and Drug Administration's (FDA) call for innovative programs to accelerate the development of new medicines. Rising development costs and a drastic bottleneck in the number of medicines submitted to the FDA prompted the “critical path initiatives” and the development of Arizona's independent, non-profit C-Path institute with its mission to create a safer, smarter, faster way of developing medicines. C-Path founders—the University of Arizona, SRI International, and the FDA—bring together an arsenal of experience in pharmaceutical drug development, regulatory issues, and basic and clinical research to bear on this problem.

• **The unique strategic partnership between Scottsdale Healthcare, TGen, Mayo Clinic Scottsdale, and TGen's subsidiary, TD2**, brings together world-class researchers, clinicians, and cutting-edge technologies to combat cancer. TGen expertise in gene array technology and gene expression studies, the early stage and pre-clinical drug development capabilities of TD2 and the excellence of clinical research and patient care of Mayo Clinic and Scottsdale Healthcare have been brought together in a focused effort to speed the translation of research cancer biology discoveries into patient treatments. This partnership embodies all of



Sun Health Research Institute



Mayo Clinic

the key components necessary to perform the major stages of translational research and physically locates them together in a new 110,000 square-foot facility on the Mayo Clinic campus.

- **The University of Arizona Cancer Prevention Network** encompasses Arizona physicians from a number of different subspecialty areas committed to the prevention of cancer. The Network is part of the Arizona Cancer Center's Cancer Prevention and Control Program (CPC) directed by Dr. David Alberts. The CPC is dedicated to addressing all aspects of cancer prevention through basic, translational, clinical, and population-based research. The CPC develops research studies to determine environmental and genetic factors that affect cancer incidence and survival rates in general, high-risk, and minority population groups, conducts basic research to elucidate the underlying biochemical and cellular mechanisms associated with these factors, and performs clinical studies on the effectiveness of new prevention methods. The Arizona Cancer Prevention Network brings a fleet of surgeons, dermatologists, gastroenterologists, gynecologists, and urologists into service to meet the CPC goals.

- **The Arizona Telemedicine Program (ATP)** at the University of Arizona is a multidisciplinary program that harnesses telemedicine to provide health care services to rural areas as well as distance medical education and virtual clinics in a number of subspecialty areas. The Arizona Telemedicine Program has 27 sites

across Arizona, including those on Apache, Navajo and

Hopi reservations, that provide patient access to medical specialty services, education, and research programs. The ATP harnesses the power of telemedicine technology to provide consultation in 49 specialty areas as well as continuing education to the medical community.

- **The Center for Rehabilitation Neuroscience and Rehabilitation Engineering (RNRE)** at Arizona State University is comprised of a multidisciplinary team of scientists, clinicians, and engineers committed to leveraging engineering technology to solve physiological problems resulting from neurological disorders and injury. The wide range of expertise encompassed by the RNRE allows neurological disorders to be studied at every level. Studies at the RNRE range from elucidation of the basic cellular physiology of the brain's neural circuitry to the development and clinical testing of novel technologies to counter the debilitating effects of neural disorders. Part of the Biodesign Institute at ASU, the RNRE has won a number of NIH grant awards for its multidisciplinary research.

- **A collaboration between Northern Arizona University and the University of Arizona Cancer Center** will seek to address the problem of disproportionate cancer mortality rates among the Native American population. This collaborative effort has been awarded a \$7.5 million grant from the National Cancer Institute for a comprehensive approach to educating Native Americans in cancer-related issues and exposing Native American students to the fields of oncology and basic cancer research. The long-term goal of the NAU/AZCC collaboration is to increase the number of Native American healthcare workers in these fields who can cross the cultural barriers that have previously prevented members of this minority population from seeking cancer treatment.



TGen



Arizona Cancer Center



WHAT HAS ARIZONA ACCOMPLISHED SO FAR?

Arizona has already begun to integrate the “best practice” lessons and guidelines for translational research success into its own unique context. Along with the numerous collaborations that have been formed to pursue research in Arizona’s core competency areas and in areas of special population interest, policy, and infrastructure changes have been put in place to create a framework that will foster translational research as well as the state’s broader bioscience goals:

Proposition 301 was passed in 2000 in support of research and technology at Arizona’s institutes of higher education. The proposition has allowed an increase in university educational offerings in key areas, facilitated technology transfer activities, and established new multidisciplinary institutes, Arizona State University’s Biodesign Institute and the University of Arizona’s BIO5, for the study of diseases and their cures. Proposition 301 also provides the funding mechanism for community college training programs to meet the state’s need for technically skilled workers in the biosciences.

A \$440 million bond issue, passed in 2003, provided the funding to create needed bioscience building infrastructure. A dozen new bioscience-related research facilities at Arizona universities have been built with this money, among them the buildings that house ASU’s Biodesign Institute and UA’s BIO5.

Arizona has addressed the critical need for expanded UA medical school in Phoenix.

The University of Arizona College of Medicine-Phoenix is expanding and relocating to downtown Phoenix in collaboration with Arizona State University. The renovation of three historic buildings that will house the new medical school is ongoing, and the funding and planning are on track for the school’s first class of students to begin in fall

2007. The advent of the school will bring UA clinical expertise together with Phoenix’s technological strengths and facilitate their integration toward successful translational research.

Funding mechanisms have been instituted to seed multidisciplinary, translational research in the state. The Arizona Biomedical Research Commission (ABRC), particularly, has taken a leading role in this area. Since its inception in 1985, this state agency has granted nearly \$100 million to Arizona medical researchers and clinicians throughout the state. The ABRC changed its name from the Arizona Disease Control Research Commission and shifted its mission to fostering the sort



of multidisciplinary, multi-institutional collaborations that will help make Arizona a world-class leader in biomedical research. The ABRC grant awards are targeted to discovery and early stage transla-

tional research projects requiring seed money to generate the proof of concept and feasibility data necessary to compete for the larger pool of federal support dollars. Recent ABRC awards have gone primarily to collaborative projects involving one of Arizona’s four areas of research strength—neuroscience, cancer therapeutics, bioengineering, and bioimaging. As well, the Commission favors projects that “lead with technology” by applying Arizona’s technological strengths in novel ways to solve biological problems. These multidisciplinary, technology-driven projects embody Arizona’s translational research goals and are closely aligned with FDA and NIH federal funding strategies to foster translational research.

FASHIONING A SUSTAINABLE ARIZONA TRANSLATIONAL RESEARCH SYSTEM

In order for the state to reach its overarching bioscience goals and to set a model for the nation in efficient translation of its basic research, Arizona must be systematic in its approach. Leaders in the state have already recognized the pivotal role that translational research must play in producing the kind of diagnostics and cures for disease that will drive improvements in state healthcare and serve as an economic base. This is evidenced by the change in focus of the Arizona Biomedical Research Commission to provide seed funding for translational, multidisciplinary projects in the state. However, **stand-alone interventions will not be enough to create the sort of sustaining translational research system that can keep pace with Arizona's changing translational research needs.** Advances in specific areas of its basic research, as well as changes in the economic and healthcare climate in the state, may necessitate a future shift in focus in disease area studied and/or a change in emphasis on specific stages of translational research. Arizona must fashion a statewide translational research system that has broad portability and can sustain such changes.

The “best practice” lessons from translational leaders must continue to be integrated into the particular context of Arizona institutions and organizational structures. The spirit of collaboration in the state that has already seen the formation of a number of multidisciplinary, multi-institutional collaborations must be formalized, with policy, resources, and infrastructure put in place to foster and guide such interactions across the translational research spectrum. Most importantly, the creation of such a sustainable system will require active facilitation and monitoring to ensure that interventions mesh into an efficient overall framework.

The formation of a major organizing mechanism

is proposed to provide this necessary oversight and facilitation. Arizona leaders, representing a broad base of Arizona institutions and a commitment to an umbrella initiative to create a sustaining translational research system in the state, have guided the development of a number of initial recommendations to reach this goal. At the forefront is the proposed formation of an Arizona Translational Resource Network (AZTransNet).

ARIZONA TRANSLATIONAL RESOURCE NETWORK (AZTRANSNET)

AZTransNet will facilitate the policy, infrastructure, and cultural changes necessary to build a statewide capacity for collaboration, one that encompasses Arizona's near- and long-term translational research goals and integrates “best practice” lessons from translational leaders into the specific context of the state. Industry, universities, non-profit research institutes, hospitals, medical centers, and private practice physicians will all be brought to the table under this statewide coordinating mechanism.

AZTransNet will have a fact-based understanding of the gaps in the current translational research system in terms of infrastructure and policy and foster interaction between the specific groups that can fill those gaps. This facilitation may require that AZTransNet seek funding support for specific interventions and shared services required by a subset of the institutions under its umbrella. In certain instances, AZTransNet may act as an organizing mechanism for pass-through of funding for larger collaborative efforts. Beyond funding for specific interventions, AZTransNet will require limited direct funding to support its roles in facilitation and coordination.

ARIZONA TRANSLATIONAL RESOURCE NETWORK (AZTRANSNET)

Purpose: AZTransNet will be a *facilitating and coordinating organization* and *honest broker* with the goal of advancing translational and clinical research activities in Arizona.

Role: AzTransNet will advance the activities set out in the Arizona Translational Research Pathway.

Participation: AzTransNet will seek to work with all biomedical research institutions in Arizona engaged in translational and clinical research across universities, non-profit research organizations, and hospitals and medical centers, as well as interact with private physician practices and private industry. The directions and policies of AzTransNet will be set by participating organizations.

Funding: AzTransNet will seek grants from foundations and government, and may fund specific efforts with support from member and participating institutions.

SPECIFIC RECOMMENDATIONS FOR TRANSLATIONAL RESEARCH SUCCESS

Under AZTransNet, a number of specific initial interventions are recommended to create a sustainable translational research system. A few of these recommendations fill gaps in the current translational research system at the extremes of the translational continuum—facilitating initial early stage discovery and late stage commercialization and marketing. Most of the interventions, however, focus on bridging the gap between the basic researcher and the clinician and on fostering clinical trials research. This gap is the widest and most pressing to fill in order for Arizona to meet its immediate and near-term translational research goals.

In the near term, Arizona has identified a set of activities to promote clinical research and collaborative activities involving:

- Creation of an **Institutional Review Board (IRB) Networking Forum**. Institutional Review Boards (IRBs) are charged with protecting human subjects used in research. Each organization that deals with some aspect of human subject research—whether it is the study of samples from tissue banks, the study of clinical patient epidemiology from records, or actual clinical trial administration—has an IRB responsible for regulating the conduct of that research. Experiments involving any aspect of human research require prior approval from an IRB, and these projects are subject to the IRB guidelines on use and disclosure of health information, conflict of interest, and research misconduct.

The formation of an IRB Networking Forum will help Arizona IRBs address a number of challenges. IRBs within different institutes, and even multiple IRBs found within the same large academic or health care centers, can have somewhat different policies, oversight requirements, and procedures for obtaining project approval. Collaborations that span multiple institutes and disciplines often require the approval of more than one of these IRBs. The differing policies and guidelines of the IRBs can make the task of obtaining project approval painstaking for the researcher and present a challenge to the IRB ability to maintain oversight. As well, a number of challenges are being presented to IRBs in the form of new regulatory requirements, calls for streamlining from the FDA and NIH, and new areas of bioscience research that present uncharted territory for regulation.

The IRB Networking Forum will allow informal discussion among IRB staff, directors, board members, institutional legal counsel, and research directors about common regulatory issues faced. **It is the mission of the IRB Networking Forum to create a sense of community and develop trust between those running and serving on different IRBs so that barriers to communication can be lowered and compatible policy and procedures developed across Arizona's IRBs.**

- Institution of **Technical Policy Development Retreats** that focus on specific policy and supporting document needs of IRBs. Each retreat will provide education on topics directly relevant to a particular policy or document to be developed and breakout sessions will facilitate discussion and refining of documents. The topic proposed for the first retreat is “serum and tissue repositories”; the specific goals of the retreat will be to produce template institutional policy on access to serum and tissue repositories, informed consent documents for donation to repositories, a HIPAA authorization form, and template research application form that can be used by all Arizona IRBs.
- Formation of an **Arizona Clinical Research Consortium** to increase clinical research activities in Arizona across the breadth of institutions conducting research, such as universities, non-profit research organizations, hospitals and medical centers, and medical groups. The Consortium would be responsible for coordination, facilitation, and awareness-building activities directed at increasing the ability of Arizona institutions to recruit more patients for clinical trials and reducing the time from first contact by a research sponsor to first enrollment of patients in the trial by creating a framework in which community physicians and clinical research leaders can collaborate.

- Advancement of **guidelines on approaches to complex business practices** that can pose barriers to collaboration in biomedical research, such as indemnification, intellectual property, cost sharing, and credentialing. Early resolution of these issues will allow collaborative efforts to continue more smoothly and efficiently.
- Development of a **community-based participation guide for advancing collaborations with Native American and Hispanic/Latino population groups.** The guide will educate the community on what to expect from researchers and advise researchers on the required participatory approach for a specific community. Formation of the guide will require open dialogue between Native American and Hispanic/Latino leaders, researchers, and healthcare providers.
- Establishment of an **Arizona Community Institutional Review Board** to provide IRB support for independent



research sites that lack in-house IRBs and studies that span multiple research sites. Arizona currently lacks the resources necessary to provide IRB support to all of the physicians, hospitals, research centers, and academic institutions

conducting human subject research. This human subject research is predominantly for medical-related clinical research, but often community colleges and smaller four year colleges who lack their own IRB are involved in behavioral and social science-oriented research involving human subjects. Many hospitals and independent research sites, lacking the expertise necessary to navigate the complexities of instituting their own IRBs, instead contract with commercial IRBs based

outside of Arizona. These IRBs have substantially higher costs than institutionally-based IRBs and, arguably, less knowledge of local community laws, medical practice standards, and demographics. An Arizona Community Institutional Review Board would provide these independent sites with an alternate mechanism to obtain the IRB support that they need, lowering costs and keeping research studies in the state. Studies that span multiple research sites require IRB approval from each site's designated IRB, causing such studies to incur substantial costs along with the time and effort associated with coordinating multiple IRBs. The Arizona Community Institutional Review Board would provide a mechanism for more efficient review of these multi-site studies.

Longer term initiatives will include:

- Development of specialty capabilities for **clinical research advisory services** in target disease areas.

Such services will help guide early stage clinical research with advice from knowledgeable basic and



clinical researchers, clinicians, and experienced program managers. An example, in the cancer area, of such clinical research advisory services is

TGen's subsidiary, TD2,

and its partnership with Mayo Clinic, Scottsdale Healthcare, and the UA Cancer Center to transition basic genomics discoveries into clinical trial testing of new diagnostics and treatments for cancer.

- Development and implementation of a **web-based information tool** for basic and clinical researchers. This web-based tool will include a series of searchable

databases on individual research interests, new funding opportunities as they become available, and pharmaceutical, biotechnology, and medical device industry interest in specific pre-clinical and clinical trials. These databases will allow individual researchers to quickly identify potential collaborators, keep abreast of new seed funding and federal granting opportunities for translational research, and match clinical trial capacity with industry partners.

- Development of an innovative, **statewide clinical scholars program** in Arizona in target disease areas. The program will include mechanisms for the recruitment and retention of leading clinical researchers to the state and their integration into a quality training program for future physician researchers. Training of clinical researchers will incorporate hands-on exposure of residents and young clinical faculty members to clinical research within novel clinical research academies or incubators. A few (3-4) eminent clinical research scholars from across the state will be identified in each target disease area to lead this effort. These incubators will work closely with the disease-specific translational research alliances to ensure efficient collaboration between basic researchers, clinical researchers, and clinical practitioners.
- Creation of a **network of site managers** to facilitate communication among investigators and assist in the identification of early stage discovery projects.

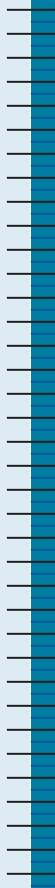


SUMMARY

Under the auspices of *Arizona's Bioscience Roadmap*, the state has made great progress toward fashioning a framework within which to accomplish its broader bioscience goals. It has become clear that translational research must play a key component in this framework in order for Arizona to maximize its investments and transform its biomedical research base into an economic and healthcare driver for the state.

Arizona's commitment to building a sustainable, quality translational research system is manifested in its initiative to form Arizona's Translational Research Pathway. This pathway will capitalize on Arizona's current research strengths, fill gaps in policy and infrastructure in its existing translational research system, and guide the integration of "best practice" lessons from translational leaders into Arizona's unique translational research context.

While the formation and implementation of Arizona's Translational Research Pathway is still in its infancy, a number of initial recommendations under this plan for Arizona translational research success have already been formulated. The creation of an organizing mechanism in the form of AZTransNet, along with specific interventions to fill critical gaps in Arizona's ability to perform preclinical and clinical research, should lay a strong foundation for future translational research excellence in the state.



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