University System of Ohio

June 30 | 09

Centers of Excellence

University of Toledo

Center of Excellence in Biomarker Discovery & Translational Bioscience

THE UNIVERSITY OF TOLEDO | BIOMARKER DISCOVERY TRANSLATIONAL BIOSCIENCE CENTER

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Executive Summary

Biomarkers are indicators that show a reliable, predictive correlation to differential patient responses and are essential to the realization of the quest for truly personalized health care. They are used as preclinical and clinical tools for evaluating safety and efficacy of health care; prevention, screening and early diagnosis; targeted therapy; and improved patient outcomes associated with substantially decreased healthcare costs.

The University of Toledo comprises eleven academic colleges and countless centers and academic programs that encompass the full educational, research and clinical spectrum. UT offers twelve undergraduate, 34 masters and 16 graduate/professional educational programs in the areas of health and biosciences. In addition, UT currently dedicates 1,941,457 sq feet for the education and research in bioscience. There are currently 80 ongoing NIH funded research programs in bioscience representing approximately 54% percent of the UT federally funded research programs.

The University of Toledo (UT) has remarkable consolidated and focused expertise in the biosciences and biomarkers to create The UT Center of Excellence (COE) in Biomarker Discovery & Translational Bioscience. We have united twelve key contributors and 46 supporting investigators from four UT colleges and from all five Featured Academic Services Tracks (FAST's) in clinical science as well as basic science as follows:

- Hormone-Related Cancer Biology & Diagnostics
- Cardiovascular & Metabolic Disease
- Infection, Immunology & Transplantation
- Neuroscience & Neurological Diseases
- Kinetic-Related Sciences & Disorders

These UT-COE key contributors have proven track-records for extramural funding ($12 million total base) and publication (an average impact factor h-Index of 19). The association of UT with the College of Medicine, and the College of Medicine with UT Medical Center, the UT Physicians faculty practice (UTP) and the UT Medical Assurance Company (UTMAC) provides the necessary exemplary environment for translational research. With this collaboration we have been morphing our translational research culture to recognize and harvest biomarkers. We define biomarker harvesting as systematic:

- Identification of potential biomarkers for appropriate translational research programs
- Protection of intellectual property of the biomarker

- Initiation of validation of the biomarker in human tissue
- Successful technology transfer and regulatory approval
- Commercialization and economic development

The biomarker market is expected to reach $20B by 2015. During 2007, the externally benchmarked economic impact of The University of Toledo College of Medicine (UT-COM) and its academic health care industry on the State of Ohio equaled $5.3 billion. Further, the UT-COM and its core and non-core teaching hospital affiliates accounted for over 57,000 Ohio full time equivalent positions and $177.6 million in total state tax revenue. Graduates of UT-COM that remain in Ohio to establish medical practices account for an additional economic impact of $65 million annually. On this economic platform, we currently have eleven demonstrated candidate biomarkers discovered by UT investigators, which provide excellent substrate for further validation, development and subsequent commercialization into the Ohio economic base. In the backdrop of a strong culture of entrepreneurship and collaboration, we are poised to continue to extend the number of bioscience spin-offs from the current eight (four of which are biomarker focused). We will continue to build a robust bioscience cluster and stimulate further economic development, boost programmatic growth of regional biotech/pharmaceutical industry, and create new high-tech job opportunities in Ohio.

Biomarker research isn't without challenges. The biology of biomarker discovery is multifactorial and simple genetics cannot account for variability of responses or phenotypes. There are also major issues around human tissue access, assay technology and appropriate interpretation of highly complex data. The Jacobson Center for Clinical & Translational Research (J-CCTR) continues to build on our culture of collaboration and promote the necessary integrated approach that combines clinical and basic science researchers, epidemiologists, and clinical research coordinators. In addition, UT has multiple bioscience core laboratories to focus specifically on biomarker discovery and development:

- Genomics/Proteomics,
- Biostatistics/bioinformatics
- Flow cytometry
- Advanced imaging
- Tissue banking
- Drug development
- Technology transfer

We also apply a strong business perspective to develop strategies, create project plans, establish milestones and report progress.

Sixteen strategic faculty recruitments within the last five years of scientists with bioscience and biomarker expertise, $2M endowment of J-CCTR, $1.1M in Translational Bioscience Research Stimulation Awards, and plans for additional dedicated clinical trial research space indicates an ongoing and strong commitment by UT to this center. Further significant investment by UT with matching extramural funding is required to

expedite the process of biomarker discovery, harvesting and commercialization, and to ensure quality, speed and cost-effectiveness of biomarker validation on an ongoing basis. With a combination of formal state (University System of Ohio) designation and continued funding, we have the potential within five years to rival benchmarked universities such as Mt. Sinai Medical Center, the Duke Clinical Research Institute's Advanced Biomarker research unit, and others.

Our specific aims in the next five years for the COE are to:

- Recruit 9 additional renowned and highly respected biomarker discovery and commercialization experts
- Create a Biomarker Validation Core Lab Facility equipped with state-of-the-art biobank and 'omics technology and associated technicians and epidemiologists,
- Develop additional biosciences graduate programs in translational research
- Double our extramural biomarker research funding
- Quadruple our funding in intellectual property protection and technology transfer

The outcome will be milestones in 2015 that include: 50 biomarker-related invention disclosures, 25 patents, and 10 license agreements and 1-2 viable spin-offs per year.

The **Mission** of The University of Toledo Center of Excellence in Biomarker Discovery & Translational Bioscience is to improve the human condition through biomedical innovation resulting from effective multi-disciplinary and inter-professional:

- Excellence in biomedical research and education with a focus towards biomarker discovery; and
- Distinctive entrepreneurship to bring innovations to the community.

The **Vision** is that The University of Toledo will be recognized as a leader in biomedical research with distinction in biomarker discovery, thereby transforming health and biomedical science.

The University of Toledo is grateful to the Ohio Board of Regents and all involved with the University System of Ohio for soliciting this visioning work and for the opportunity to successfully marry the successful centers of excellence of the institutions of the University System of Ohio with the economic development of our region and our state. Our dedication to these interdependent successful outcomes is hopefully clearly expressed in the materials previously presented and in the documents and references contained in the documents that follow.

1 Center of Excellence Concept

1.1 Center of Excellence Selection Process

The University System of Ohio Strategic Plan for Higher Education clearly outlines the vision for excellence through mission differentiation. In today's competitive market, each institution must develop distinctive missions and Centers of Excellence that attract people, technology and capital. The University of Toledo (UT) has a well-deserved reputation for being Focused, Flexible, Facile & Fast Moving, and has responded to this call with the following proposal to designate a Center of Excellence in Biomarker Discovery & Translational Bioscience.

UT initiated a process to identify potential Centers of Excellence (COE) in April, 2008. Following a thorough study of the requirements, we established criteria for designation of UT-COE's. These selection criteria were shared with the Board of Trustees and with the Chancellor, and are provided below in Table 1. A ranking grid was developed, and was made for 36 internally and externally suggested COE's. Analysis of the assessment grid resulted in the identification of 6 potential UT-COE's. These recommendations were shared with the UT Board of Trustees, the Chancellor and the Department of Development. We have since been aligning UT directions and resources accordingly.

UT Strategic Alignment
USO Strategic Alignment
Regional (NWO) Alignment
National Reputation
Extramural Support
IP Transferability Record
Economic Impact
Transformational Nature
Educational Alignment
Facilities Alignment
Instrumentation Alignment
Faculty Number & Distribution
Faculty Leadership
Interdisciplinary Study
Extramural Collaborations
Growth Potential
Competitive USO Risk
Relationship to Ohio Economy
External Metrics & Benchmarks
Enduring Sustainability

Table 1 UT-COE Selection Criteria

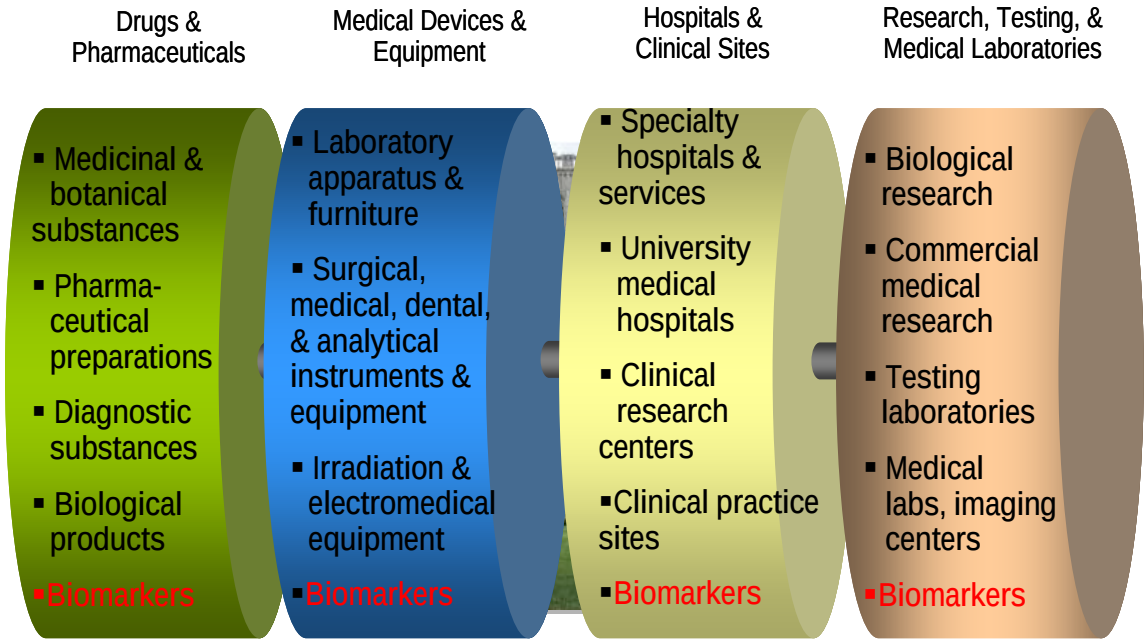
The identification of a COE for Biomarker Discovery & Translational Bioscience at UT is evident based on the attributes of academically outstanding faculty and students, innovative science and technology, and funding to support the needed physical infrastructure to attract and retain highly talented students, post-doctoral associates, senior research faculty, and industrial scientists. Furthermore, the focus on biomarkers provides excellent opportunity for economic development. We have World-Class Academic Talent that links to Connections to the Local Economy, which then links to Economic Advancement. Outstanding higher education drives our significant clinical contributions, both of which drive our translational research, which in turn drives economic advancement.

1.2 Biomarker Discovery & Translational Bioscience

1.2.1 Economic Development

The FDA definition of a biomarker, also adopted by NIH, is '*A characteristic that is objectively measured and evaluated as an indicator of normal biologic or pathogenic processes or pharmacological responses to a therapeutic intervention.*' Biomarkers fit neatly into the important, large and growing sector of health and bioscience in the US, Ohio and the regional economy, covering a very wide range of businesses, as shown below. Note that Biomarkers fit into each category of businesses. There is strong evidence for this COE to create economic development in the region and the state. More details will be found in Section 3.

Figure 1 Bioscience Business Categories



Biomarker Discovery & Translational Bioscience

1.2.2 Alignment

Biomarker Discovery & Translational Bioscience is aligned with the new University of Toledo's three-part mission and strategic vision, and accounts for a highly significant proportion of the breadth and corporate structure, number of graduate and undergraduate programs, faculty and funding, and academic productivity of UT. The number and proportion of University of Toledo colleges, educational programs, research, space, job creation, economic development and service to the community indicates significant commitment to Translational Bioscience.

- The mission of The University of Toledo is to improve the human condition; to advance knowledge through excellence in learning, discovery and engagement; and to serve as a diverse, student-centered public metropolitan research university.
- The vision of the University of Toledo is to be a transformative force for the world. As such, the University will become a thriving student-centered, community-engaged, comprehensive research university known for its strong liberal arts core and multiple nationally ranked professional colleges, and distinguished by exceptional strength in science and technology.

1.2.3 Focus

The University of Toledo's narrower and deeper focus in our Featured Academic Services Tracks (FAST) of Hormone-Related Cancer Biology & Cancer Diagnostics; Cardiovascular and Metabolic Disease; Infection, Immunology and Transplantation; Neurosciences and Neurological Diseases; and Kinetic-Related Sciences & Disorders creates true excellence in Biomarker Discovery & Translational Bioscience research,

education and clinical programs. As a result, of this focus, 87% of all federally funded research is now directed towards these key areas[1]

The metrics provided in the following sections will demonstrate:

- Highly organized interdisciplinary translational research programs
- Benchmarked excellences in basic, translational and clinical research
- Featured Academic Services Track focused programs
- Highly focused faculty teams and research laboratory cores
- Research tightly linked to educational and clinical programs
- Remarkable business, legal, engineering and education support systems
- Closely linked workforce development education & licensing resources
- Extensive collaborations with medical institutions and bioscience companies in Ohio, nationally and internationally
- Extensive external support systems through UT Innovation Enterprises (UTIE), Regional Growth Partnership (RGP), BioOhio, the UT Institutional Review Board (IRB), and Clinical Trial Organizations
- Business and community collaborations and support

The intersection between the many bioscience programs in research, education and economic development is in Biomarkers. We have taken on biomarker discovery as a strategic focus, building on existing expertise and opportunities for UT and for Ohio.

1.3 Value

Biomarkers provide a reliable, predictive correlation to differential patient responses – essential to personalized medicine and can be used for:

- Preclinical and clinical trial tools for safety and efficacy
- Prevention, Screening, Early Diagnosis
- Earlier therapy, targeted therapy, most effective therapy
- Improve patient outcomes, reduce waste through more appropriate selection of treatment choices
- Enhance safety, cost-effective targeted health care

  "*The concept of Personalised Healthcare (PHC) is being driven by the idea of improved patient outcomes and also to contain soaring healthcare costs. It is only when the right patients receive the right treatment that the true value of PHC is realised. To achieve this, biomarkers that are quantifiable need to be identified to select the right patient populations. The challenges of implementing this new research strategy are complex and would require a multifaceted approach."*[2]

  "Cancer is a great place to use genetic and genomic biomarker strategies, because ultimately cancer is a disease of the genome, and it is in a very real way mechanistically linked to events that happen there," says Ken Carter, President and CEO of Avalon Pharmaceuticals, Germantown, Md. Genetic damage can be found in every cancer cell, and so, theoretically, can potential biomarkers for drug targets. The approach has already proven fruitful: drugs like Herceptin and Erbitux would

have been dismal failures without the HercepTest and the EGFR pharmDx test to sift through thousands of patients and find the potential responders.[3]

The Biomarkers Consortium http://www.biomarkersconsortium.org is a novel public-private partnership that brings together government, pharmaceutical and biotechnology industry, patient advocacy groups, private organizations and the public, managed by the Foundation for the National Institutes of Health. While the missions of the various partners vary, the need for biomarkers brings them together to advance discovery, development and qualification of biomarkers for use across the spectrum of biomedical research and practice. This unique collaboration highlights the value of biomarkers in the quest to improve the human condition.

An example of how biomarkers are being used successfully today as a form of personalized medicine is in the treatment of breast cancer. Patients with breast cancer in which the gene *ERBB2* (also known as *HER2* or *NEU*) is amplified (that is, extra copies are present) benefit from treatment with Herceptin, whereas when the gene encoding the estrogen receptor is expressed by the tumor, the patients respond to treatment with tamoxifen instead.[4]

1.3.1 Benchmarking Biomarker Discovery

Biomarkers have been a focus for pharmaceutical industry over the last decade, but few academic institutions have biomarker discovery centers. Harvard's NeuroDiscovery Center http://www.harvard.edu/biomarker recently launched a Biomarker Discovery program, dedicated to discovering and validating biomarkers specifically for neurodegenerative diseases. Mount Sinai has the Personalized Medicine Research Program http://www.mountsinai.org, the purpose of which is to enable and foster breakthrough research to define, on a molecular level, the common disorders so that diagnostics and therapeutics can be targeted to specific patient populations. Their focus is on the genetic basis for deferential responses to medication. As such, they have an extensive biobank and core laboratories to support genomic research, which are keys aspects of biomarker research. OSU has a Center for Personalized Healthcare http://cphc.osu.edu/, where they are using biomarkers in the treatment of patients, but not for research. The Duke Clinical Research Institute (DCRI) Biosignatures Advanced Biomarkers research unit http://www.dcri.duke.edu/ provides scientific expertise and operational support for the incorporation of biospecimen collection, routine laboratory and biomarker testing, and advanced molecular biomarker research. The Advanced Biomarkers unit uses high-throughput "omics" technology in all phases of clinical research, biomarker discovery, and biomarker development; and offers consultative skill in scientific, operational, logistical, and protocol development. This is a highly achievable aspiration of the UT-COE for Biomarker Discovery & Translational Bioscience to continue along these lines.

Larger, research-based universities focus on basic science and tend to eschew applied science, such as biomarker identification and development. However, most bioscience research results in the discovery of one or more potential biomarkers or signals of biological processes. There is a high and growing demand for biomarkers as commercially viable products.[5] Through leadership in the UT-COE for Biomarker

Discovery & Translational Bioscience, we will identify and utilize these biomarkers for economic advancement. We are changing our research culture to recognize and harvest biomarkers. We define biomarker harvesting as systematically protecting intellectual property and initiating validation in human tissue, and working through technology transfer and regulatory approval systems for commercialization and subsequent economic development. Examples of success in this area are included in Section 4. Unlike larger universities, we have successfully begun this culture shift due to the smaller size, co-location and excellent relationships between clinical and pre-clinical investigators.

2 Scope of Activities

The **Mission** of the UT-COE in Biomarker Discovery and Translational Bioscience is to improve the human condition through biomedical innovation resulting from effective multi-disciplinary and inter-professional:

- Excellence in biomedical research and education with a focus towards biomarker discovery; and
- Distinctive entrepreneurship to bring innovations to the community.

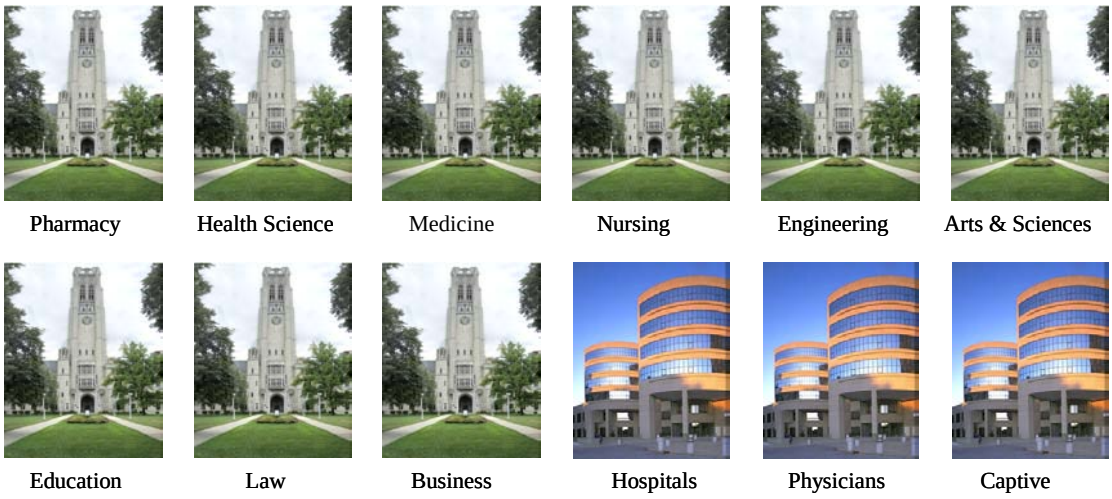
The **Vision** is that The University of Toledo will be recognized as a leader in biomedical research with distinction in biomarker discovery, thereby transforming health and biomedical science.

2.1 An Integrated Community

Biomarker Discovery & Translational Bioscience is a component of an integrated community of six colleges (Medicine, Nursing, Health Science & Human Service, Pharmacy, Arts & Sciences Dept of Biological Sciences and Department of Chemistry, and Engineering Department of Bioengineering), with highly constructive interactions with the remaining three colleges of Business (College of Businesses Center for Technological Entrepreneurship and Innovation), Law and Education. Space and faculty are dedicated to bioscience, linked to undergraduate, graduate and professional education, and coexisting with UT clinical care programs.

Biomarker Discovery & Translational Bioscience at UT also reaches the UT Medical Center, UT Physicians group and the Insurance Captive. There are only ~100 academic health science centers with strong Translational Bioscience in the US, and few have the key components for biomarker discovery and development that we will describe in the following sections. All have a huge regional scholarly and economic impact. Research, education and clinical care are closely linked. Great universities are associated with great medical schools, and great medical schools are associated with the best hospitals. These university medical centers obtain the majority of federal bioscience grants and contracts; recruit and retain the finest research and clinical scientists; recruit and retain the finest students, residents and fellows; provide extensive community outreach and clinical services; and establish extensive public and private partnerships. Translational bioscience from bench to bedside to community is feasible from within UT, fostered by a culture of collaboration and entrepreneurship, and supported by the Center for Drug Design and Development and J-CCTR, and is certainly unique to NW Ohio.

Figure 2 University of Toledo Bioscience Entities



2.2 Research Centers and Core Facilities Associated with the UT-COE

Ten major bioscience centers at UT are listed below. Biomarker research and commercialization occurs or can potentially take place in all of these research centers.

Major Bioscience Research Centers UT:

- Cancer Center
- Center for Creative Instruction
- Center for Diabetes and Endocrine Research (CeDER)
- Center for Drug Design and Development
- Center for Successful Aging
- Engineering Center for Orthopaedic Research Excellence (ECORE)
- Heart & Vascular Center
- Institute for the Development and Commercialization of Advanced Sensor Technology (IDCAST)
- Ohio Center for Innovative Immunosuppressive Therapeutics (OCIIT)
- Paired Kidney Donation Program

These programs and the UT-COE for Biomarker Discovery & Translational Bioscience are supported by many core resource research facilities, including the following, which are critical for biomarker research.

Core Facilities at UT:

- Advanced Microscopy & Imaging Core Lab Center*
- Bioengineering Electron Microscopy Facility
- Bioinformatics Core Lab Facility*

- Center for Drug Design and Development (CD3)
- College of Businesses Center for Technological Entrepreneurship and Innovation (CTEI)
- Flow Cytometry Core Lab Facility
- Jacobson Center for Clinical & Translational Research (J-CCTR)
- Ohio Crystallography Consortium*
- Proteomics Core Lab Facility
- Tissue Bank Core Lab Facility
- Tissue Typing Core Lab Facility
- UT Innovation Enterprises (UTIE)

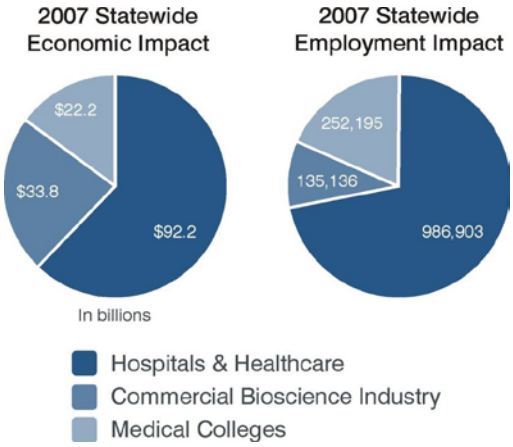
*State consortium located at UT

3 Prospects for Driving Economic Advancement

3.1 Bioscience Economic Contribution and Employment Impact[6]

The Ohio Bioscience Growth Report for 2007-2008 http://bioohio.com, produced by BioOhio, provides many metrics indicating the emergence of Ohio as one of the leading bioscience states in the nation. Bioscience economics accounted for $146.2B and accounted for employment of 1,374,000 people in the state of Ohio in 2007. Ohio's research medical centers added much needed jobs; they directly or indirectly employed 252,195 Ohioans in 2007 (Figure 3). UT is the only such center in NW Ohio and therefore plays an important role in the regional economy.

Figure 3 Ohio's Statewide Impact of Bioscience in 2007



The direct and indirect contributions of medical colleges to the Ohio economy and employment are shown in Figure 4.

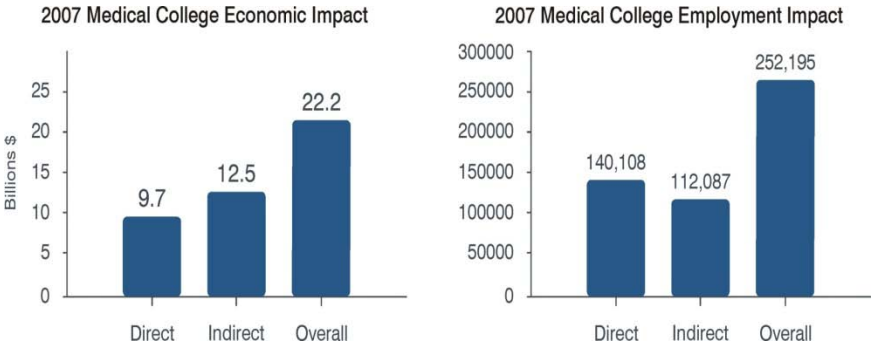


Figure 4 Direct and Indirect Impact of Medical Colleges on Ohio Economy and Employment

Biomarker Discovery & Translational Bioscience is an important, large and growing sector of the US, Ohio and the regional economy. Metrics supplied by BioOhio show increasing:

- Corporate, clinical & research bioscience trends in Ohio
- Workforce development & employment trends in Ohio
- Corporate earnings & economic impact in Ohio

- Corporate start-ups & spin-offs in Ohio
- Clinical health care & bioscience trials in Ohio
- Health profession education impact in Ohio

The influence of bioscience on the economy is far-reaching and provides exceptionally good-paying jobs, particularly when we look at medical colleges. In 2004, the average annual wage of $65,775 for bioscience employees was significantly greater than the total US private sector annual wage of $39,003 (Table 2).

Table 2 US Average Annual Wages per Employee, 2004

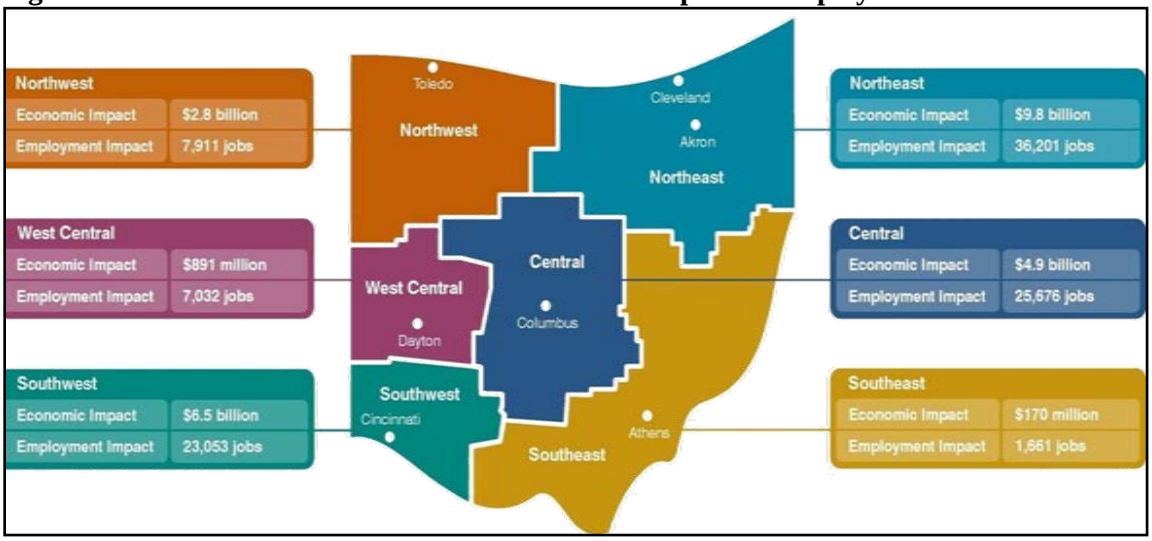
Drugs and Pharmaceuticals	**$**	**79,303**
Finance and Insurance	$	69,889
Total Biosciences	**$**	**65,775**
Research, Testing, & Medical Laboratories	**$**	**65,414**
Agricultural Feedstock & Chemicals	$	63,383
Professional, Scientific, & Technical Services	$	62,411
Information	$	60,530
Medical Devices & Equipment	**$**	**56,449**
Manufacturing	$	47,705
	$	40,297
U.S. Total Private Sector	**$**	**39,003**
Transportation & Warehousing	$	38,758
Real Estate & Rental & Leasing	$	37,167
Health Care & Social Assistance	$	36,606
Retail Trade	$	24,337

source: Battelle calculations based on Bureau of Labor Statistics, QCEW program data from the Minnesota Implan Group. Data Include Puerto Rico.

3.2 Bioscience Research and Economic Development[5]

In Northwest Ohio, Health and Bioscience accounted for $2.8B and 7,911 jobs but clearly there is enormous opportunity for growth (Figure 5). The UT-COE is ideally situated to provide significant economic enhancement in the region, as an employer and through technology transfer.

Figure 5 Commercial Bioscience: Total Economic Impact & Employment in Ohio



Funding for bioscience research and development increased $1.46M from 2004-2007 to $2.48B in just the state of Ohio. It is clear that bioscience is an important, large and growing sector of the US, Ohio and Regional economy. There is very little growth in NSF and NIH grants, but VC/Angels, IPO and Acquisitions funding grew substantially (Figure 6).

Figure 6 Ohio Bioscience Development Funding Growth

Funding Type	2007	2006	2005	2004
	Funding in Millions $			
VC/Angels	$296	$114	$98	$91
IPO	$188	$12	$49	$0
SBIR/STTR*	$27	$27	$29	$22
State Biomedical Partnerships (Third Frontier)	$135	$155	$75	$51
Matching Corporate Funds for Biomedical Partnerships	$92	$273	$112	$111
NSF Bioscience Grants	$12	$10	$15	$36
NIH Institutional Grants	$628	$627	$717	$691
Other Healthcare Equity Financing	$13	$0	$112	$12
Acquisitions	$1,089	$75	$279	$0
Total Bioscience Funding	**$2,480**	**$1,293**	**$1,486**	**$1,014**
* estimate based on 2006 figure				

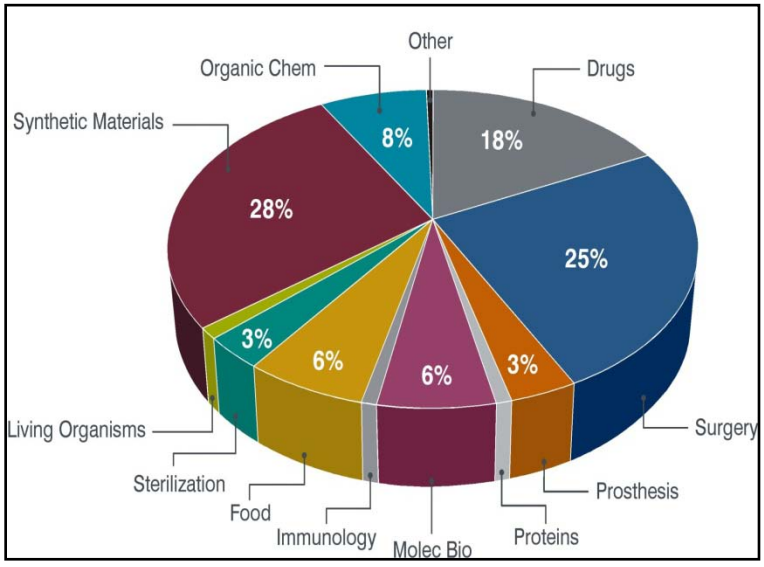


Figure 7 2001-2007: Ohio's Bioscience Patents by Type

Patents have been filed from the state of Ohio since 2001 in many different bioscience areas, but a large number are in Surgery and Drugs (Figure 7). UT can and has contributed to patents in most of these areas. More data on UT's bioscience technology transfer success will be provided later in Section 3.4.2.

As the Ohio University R&D expenditures doubled since 2001, the number of new bioscience company starts grew from 12 in 2001 to 65 in 2009 (YTD). This is a 5.4-fold increase, which was supported by a 13.5-fold increase in capital raised over the same time period (Table 3). We can speculate further growth over the next decade.

Table 3 Ohio Bioscience Growth and Support

Statistic	1991	2001	2009	Relative Growth 2009/2001
Number of bio entities in Ohio	170	352	1141	3.2
University R&D expenditures	$285M	$481M	$1.1B	2.3
New company starts	12	12	65	5.4
Private capital raised for new starts	NA	$14M	$189M $473M IPO/Acq	13.5
Bioscience capital sources in Ohio	4	8	63	7.9

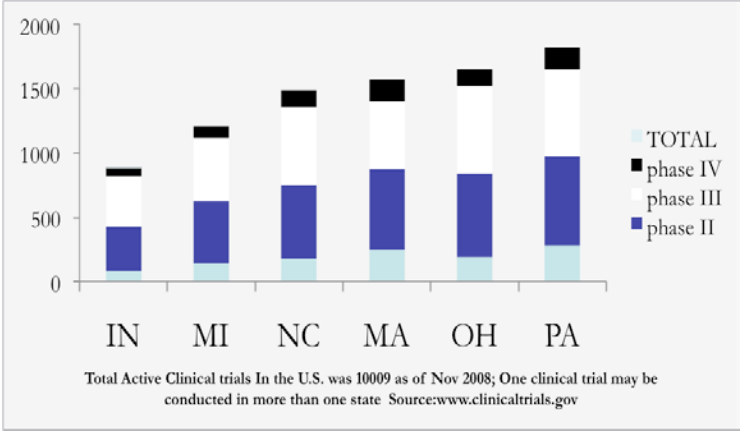


Figure 8 Total Active Clinical Trials in the U.S. 2008

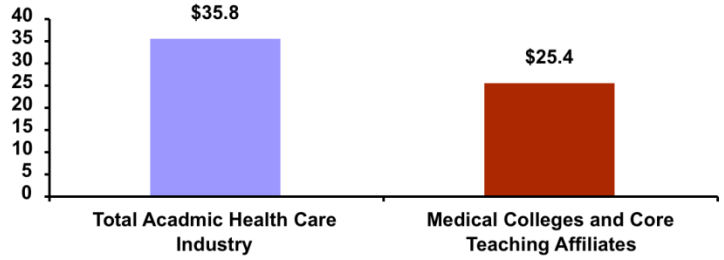
Another measure of economic impact of bioscience is the conduct of clinical trials in the state. One out of six clinical trials conducted in the United States includes study sites in Ohio (Figure 8). This indicates not only existence of the appropriate patient populations in the state, but also the willingness of these patients to participate in clinical trials, which in turn implies greater trust in our medical providers than other parts of the country. This also suggests that we should have the ability to conduct and complete translational research studies in our region.

3.3 TrippUmbach Economic Analysis[7]

3.3.1 Ohio Academic Health Care and Medical Colleges

TrippUmbach http://www.trippumbach.com is a well-known consulting firm which has conducted economic impact studies for hundreds of health care institutions and medical colleges throughout the country. They prepared an analysis of the economic impact of Ohio's Academic Health Care in 2008 http://www.medicinemeansbusiness.org/2008.htm. They reported that combined economic impact of Ohio's entire academic health care industry, the seven Ohio-based medical colleges and all of their core and non-core teaching hospitals equaled $35.8 billion in 2007 (Figure 9).

Figure 9 Economic Impact of Ohio's Academic Health Care

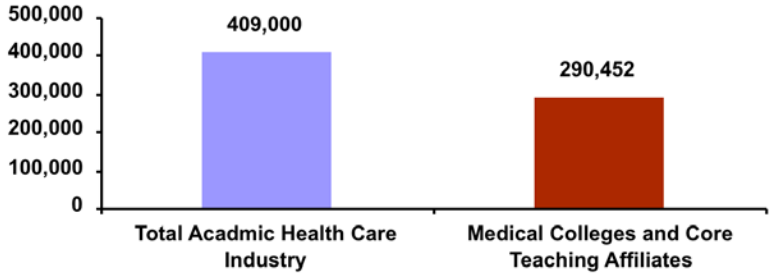


The combined economic impact of businesses operating within the State of Ohio in the wholesale, retail, tourism, service and manufacturing sectors benefit from the direct expenditures of the institution and its staff on goods and services.

With the total state business volume in 2007 of approximately $737.0 billion, the academic health industry accounts for nearly 5% of total economic expansion. More than one in every 20 dollars in the total Ohio economy is attributable directly and indirectly to academic healthcare.

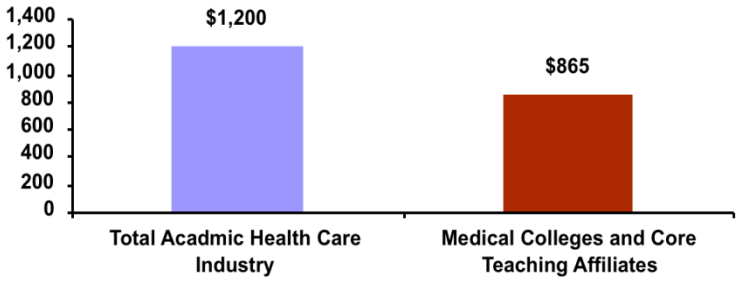
Ohio's medical colleges and teaching hospitals are also major employers, providing quality sustainable employment to a diverse group of workers.

Figure 10 Ohio's Employment by Academic Health Care



In 2007 alone, nearly 409,000 FTEs in Ohio were directly and indirectly related to the overall academic health care industry (Figure 10). Stated another way, nearly 1 in every 15 workers in Ohio was directly or indirectly employed by a medical school or teaching hospital in 2007.

Figure 11 Ohio State Taxes Generated by Academic Health Care



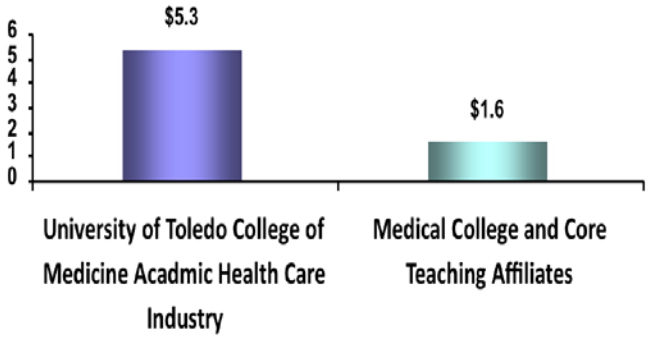
Academic health centers are also major generators of state tax revenue. In 2007, more than $1.2 billion in state taxes were generated by Ohio's medical colleges and teaching hospitals (Figure 11).

During FY 2007, Ohio provided $66.3 million in state funding to support medical education. For every $1.00 provided by the state in direct support for Ohio based medical colleges, $18.10 was returned in tax revenue.

3.3.2 UT Highlights[6]

During 2007, the economic impact of The University of Toledo College of Medicine (UT-COM) and its academic health care industry on the State of Ohio equaled $5.3 billion (Figure 12).

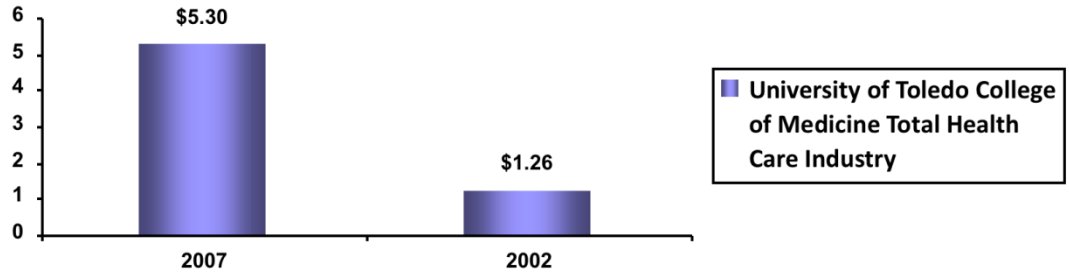
Figure 12 UT's Economic Contribution to Ohio in 2007



Further, the UT-COM and its core and non-core teaching hospital affiliates accounted for over 57,000 Ohio full time equivalent positions and $177.6 million in total state tax revenue. Graduates of UT-COM that remain in Ohio to establish medical practices account for an additional economic impact of $65 million annually.

The economic impact of UT-COM equaled $5.3 billion in 2007 (Figure 13). This represents an increase of approximately $4 billion dollars since 2002. This significant growth is attributed to increased investment and the increase in the number of teaching affiliates since 2002. Businesses operating within the State of Ohio in the wholesale, retail, service and manufacturing sectors benefit from the direct expenditures of UT-COM.

Figure 13 UT's Total Economic Impact



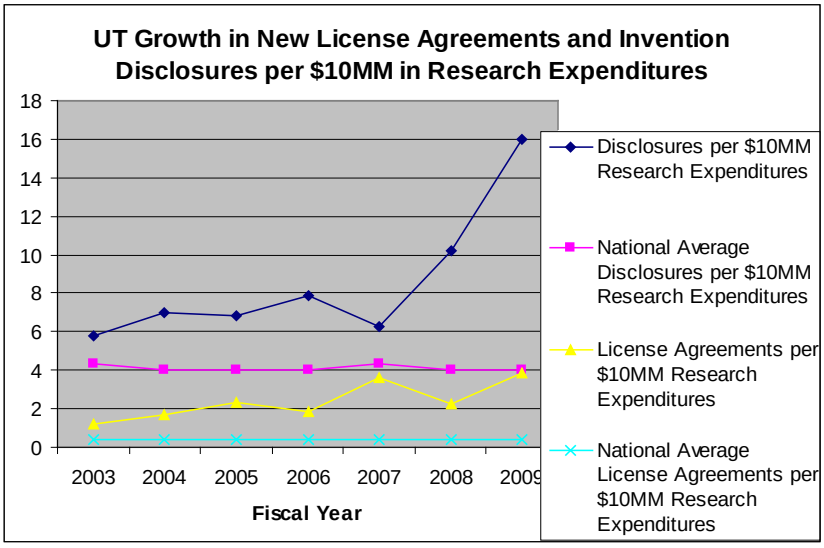
The UT-COM is also a major regional employer, providing quality sustainable employment to a diverse group of workers. Dramatic levels of economic expansion created by UT-COM and its affiliates create demand for additional employment in the

state's economy. The "employment-multiplier" related to the economic impact of UT-COM and its affiliates are responsible for thousands of additional Ohio jobs.

3.4 Entrepreneurship at UT[4]

3.4.1 UT Tech Transfer Statistics

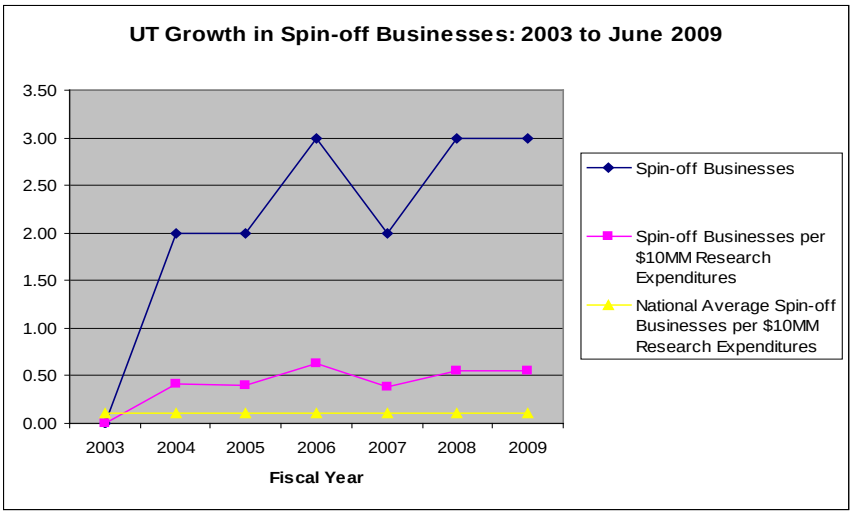
Figure 14 UT Tech Transfer in Relation to Research Expenditures



The University of Toledo has had a successful culture of entrepreneurship. The national average of license agreements per $10M research expenditure is approx 0.5. In the last decade, UT's average has been consistently higher, and in 2009 we had 3.82 licensing agreements for each $10M of research expenditure (Figure 14).

Figure 15 UT Spin-Off Businesses

There has also been a strong growth in business spin-offs from UT, which is well above the national average relative to research expenditures.



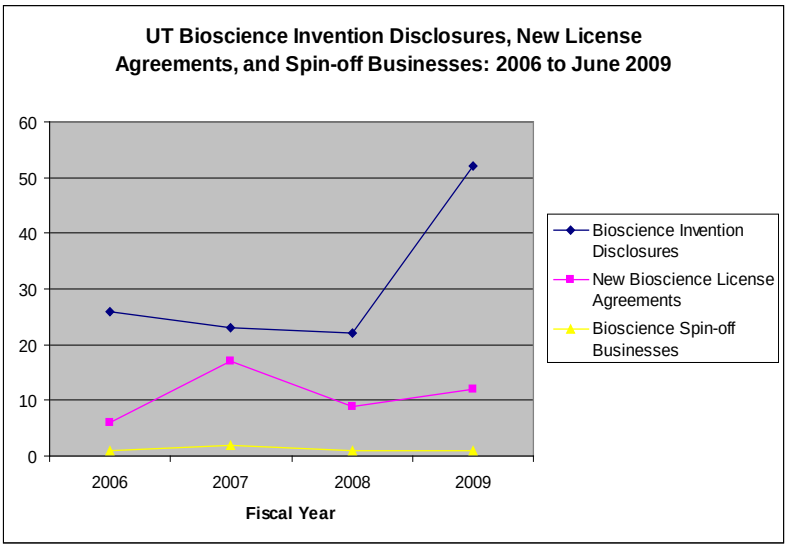
3.4.2 UT Bioscience Tech Transfer Statistics

The contribution of bioscience to UT entrepreneurship is significant, with a range of 49% to 68% of the invention disclosures and 57% to 89% of license agreements being in bioscience over the last 4 years (Table 4).

Table 4 UT Bioscience Research and Technology Development Statistics: 2006 through June 2009

Metric	2006	2007	2008	2009
UT Invention Disclosures	38	33	55	88
Bioscience Invention Disclosures	26	23	22	52
New UT License Agreements	9	19	12	21
New Bioscience License Agreements	6	17	9	12
UT Spin-off Businesses	3	2	3	3
Bioscience Spin-off Businesses	1	2	1	1

Figure 16 UT Bioscience Tech Transfer



This year's spike in bioscience invention disclosures (Figure 16) predicts a sharp growth in bioscience license agreements and spin-off companies in the next few years, as these discoveries mature towards commercialization.

3.4.3 UT Commercialization & Business Experience

The UT Innovation Enterprises (UTIE) is a group consisting of staff from research development, technology transfer, and business and workforce development to assist all levels of entrepreneurial need. UTIE works to assist faculty and outside businesses with commercialization needs. A brief list of services include: grant matching and grant assistance, sponsored research and contracted research, global business development, business incubation, and business locations.

UTIE's ability to drive economic advancement is shown with its proven track record in transferring technology. UT now has 14 active spin-offs. Of the 14 University of Toledo spin-out companies, 8 of them are bioscience related. Half of these companies - ***Gene***

Express, ***Hi-Genomics***, ***Freedom Meditech***, and ***ADS Biotechnology*** – are involved in biomarker research and development.

- **Gene Express** – a biotech company providing gene assays to assist pharmaceutical and biotech companies with biomarker and drug development and expression analysis. This company now has 15 Employees and expecting $5.0 Million Private Equity Investment.
- **Cognitive Pharmaceuticals, Ltd. and Mithridion, Inc**. – have merged forces to develop drugs for Alzheimer's disease and other serious Central Nervous System disorders. Upon completion of the merger, Mithridion announced the closing of a Series B round in the amount of $2.3 million, which will be used to commence clinical trials of Mithridion's first drug candidate, MCD-386.
- **Hi-Genomics** – is a virtual company with technologies in tissue culture and genetic transformation that couple high output, rapid, genotype independent regeneration to high frequency DNA transfer using either Agrobacterium or biolistic transformation. They have successfully sublicensed technology to Agrivida.
- **Turning Point, LLC** – a manufacturing and marketing firm that produces a state-of-the-art golf exercise and therapeutic device. Successful manufacturing partnership established in 2007. Now developing phase II prototype Product introduction expected 2nd Q 2008.
- **Spinal Designs** – a marketing firm that provides products and services to orthopedic surgeons. Virtual company with success in sublicensing technologies.
- **Freedom Meditech** – a medical device company developing and commercializing a non-invasive glucose (a biomarker) measurement technology for use by persons with diabetes. The company is working to secure $1.7M of Series A financing preparing for pilot human clinical studies.
- **ADS Biotechnology** – a start-up focused on developing a revolutionary approach for the treatment of threatening clinical conditions. The company's primary product, pegylated albumin, is a therapeutic colloid-type blood volume expander agent that is superior to human serum albumin.
- **Esclapeus Biopharmaceuticals** – a start-up focused on developing a small molecule intervention for obesity.

The potential for commercialization of biomarkers is great as the interest in biomarkers is high and growing, from NIH to non-profit disease-specific foundations, pharmaceutical and device companies, and small biotechs such as Biomarker Strategies http://www.biomarkerstrategies.com/. There is a prediction that the biomarker market, worth $5.5B in 2007, will be worth more than $20B by 2015, with a focus on diagnostics.[8]

Even the National Institutes of Health plans to fund small businesses that will develop technologies for advancing the means of diagnosing, treating, and preventing liver disease, including biomarker research, and molecular diagnostics and reagents, among others.[9]

3.4.4 Current Candidate Biomarkers for Potential Commercialization

Major national peer-reviewed research funding garnered by UT investigators in the health sciences has resulted in the identification of many novel predictive and diagnostic biomarkers (Table 5). These candidate biomarkers have a high potential clinical and commercial impact. The nature of the biomarkers is diverse and includes proteins in the blood stream or urine, molecular signatures obtained from tissue biopsies, mutations in certain genes (gene polymorphisms) and arrangements of the DNA sequence within particular regions of a chromosome. The potential clinical utility of the biomarkers includes: (i) identification of individuals at high risk for certain diseases, (ii) early detection of diseases that cannot be treated effectively because they are typically too advanced at the time of diagnosis, (iii) prediction of response to different treatments in order to determine the most appropriate treatment opt ion for a patient and (iv) the ability to monitor disease response and disease recurrence during or after treatment.

Table 6 provides a summary of eleven examples of candidate biomarkers already discovered by UT investigators. These biomarkers are in immediate need of further validation and development, and provide excellent opportunities for commercialization. Each represents a critical step in the development of personalized health care.

Table 5 Candidate Biomarkers Discoveries by UT Investigators

Biomarker and Source	Disease	Applica-tion	Investiga-tor	Funding Source	Stage of Biomarker Validation
Bone marrow specimens; Adipocyte marker proteins: PPARg2, FABP4, UCP1-3, and osteoblast marker proteins: Runx2, Dlx5, Col1, alkaline phosphatase and osteocalcin	Bone loss due to anti-diabetic drugs; Age related osteoporosis	Assessmen t of bone quality and fracture risk; Assessmen t of bone regenerativ e potential in individuals with a risk of compromis ed fracture healing, such as the elderly or diabetic patients on TZD therapy.	Beata Lecka-Czernik, Ph.D. , Department of Orthopaedic Surgery	NIH/NIA	Human bone marrow samples will be collected from patients undergoing orthopaedic surgeries at the UTMC and analyzed by real time PCR for expression of gene markers - pending IRB protocol approval

Biomarker and Source	Disease	Applica-tion	Investiga-tor	Funding Source	Stage of Biomarker Validation
Breast cancer tissue that is tamoxifen resistant; Responsive to glyceollin I	Breast Cancer	Monitoring disease and therapeutic options	Paul Erhardt, Ph.D., Center for Drug Design & Developme nt	Ongoing US Dept Agricultur e	In vivo studies underway
Raf kinase inhibitor protein (RKIP); a protein inside cells that is decreased or lost in aggressive tumors measured in tumor biopsies	Breast Cancer and Prostate cancer	To predict the course of the disease	Kam Yeung, Ph.D. Department of Biochemistr y and Cancer Biology	NIH/NCI	human tissue
Endogenous cardiotonic steroids and Na/K-ATPase; measured in blood and in red blood cells	Cardiovascular disease	To predict adverse cardiovascu lar events in patients with renal artery stenosis (RAS)-induced hypertensio n	Zi-jian Xie, Ph.D. Department of Physiology and Pharmacolo gy	NIH	pending
CEACAM1; a protein in liver; changes in the protein levels and also CEACAM1 gene mutations	Diabetes and other Obesity related diseases	To predict risk and onset of insulin resistance and obesity which precede overt disease	Sonia Najjar, Ph.D., Department of Physiology & Pharmacolo gy	NIH, US Dept of Agricultur e, American Diabetes Associati on	found to be reduced in the liver of obese individuals
WDNM1-like; a protein in the blood produced by white adipocytes, hepatocytes,macroph ages	Inflammation and Obesity	To determine risk of obesity related diseases	Cynthia Smas, D.Sc., Department of Biochemistr y and Cancer Biology	Discover y was the offshoot of a previousl y funded NIH NIDDK grant.	In vitro studies of regulation, function and correlation with inflammatory status are ongoing.

Biomarker and Source	Disease	Application	Investigator	Funding Source	Stage of Biomarker Validation
Antibodies, sensitized "memory" B cells (mB), and functional populations of donor-specific T cells in recipients; mRNA and protein expression for the signature markers measured in blood cells	Kidney transplant rejection	Selection of matching kidney donors and recipients; Monitoring transplanted recipients; Improving long-term survival for kidney transplants; Avoiding transplanting allografts to previously sensitized recipients	Stanislaw Stepkowski, DVM, Ph.D., D.Sc., Department of Medical Microbiology and Immunology	NIH/Paired donation program	Human peripheral blood lymphocytes (PBL) from donors and recipients prior- and post-transplantation. Biopsies from transplanted kidneys.
Gene expression signature; mRNA profile of MYC, p21, and E2F1 expression in fine needle aspirate biopsy of suspected lung cancer to increase accuracy of lung cancer diagnostic tests	Lung cancer	To improve accuracy of lung cancer diagnosis from cytologic samples obtained at fine needle aspirate	James Willey, M.D., Department of Medicine	NIH/NCI CA103594	Two case control studies have been completed and support that the test improves diagnostic accuracy compared to existing cytomorphologic tests. Another larger study is planned*
Gene expression signatures; mRNA profile of antioxidant genes (GPX1, GPX3, GSTP1, GSTM3, GSTT, mGST, Catalase, Superoxide dismutase) and DNA repair genes (ERCC4, ERCC5, XRCC1) from normal airway epithelial cells	Lung cancer	To determine risk for lung cancer; To personalize approach to early detection of lung cancer	James Willey, M.D., Department of Medicine	NIH/NCI CA95806 ES005719-04 George Isaac Cancer Research Fund	Confirmed in two case-control studies. Prospective nested cohort study about to begin.*

Biomarker and Source	Disease	Applica-tion	Investiga-tor	Funding Source	Stage of Biomarker Validation
miRNA biosignatures of oxidative stress; the complement of small RNA molecules in blood cells	Neurotoxicity due to drug abuse and chronic stress; neurodegenerative disease including Parkinson's disease and ischemia and stroke	Detection of the disease states and assessment of their severity	Bryan Yamamoto, Ph.D., Department of Neurosciences	NIH DA07606	tissue and plasma measures
Folate receptor types –α and –γ; soluble forms in the blood	Ovarian cancer, Breast cancer, Lymphoma	To detect ovarian and breast cancers well before clinical manifestation of the diseases; To monitor the recurrence of lymphoma following surgical treatment	Manohar Ratnam, Ph.D., Department of Chemistry and Cancer Biology	NIH R01 CA140690, NIH R01 CA080183, NIH R01 CA103964, NIH R01 CA095673, Eli Lilly and Co. Totalling $3M in direct costs	human tissue
Prostate cancer tissue that is hormone independent; PAM enzyme is over-expressed	Prostate Cancer	Monitoring disease and therapeutic options	Paul Erhardt, Ph.D., Center for Drug Design & Development	Prior US Army, Submitted RO1	In vivo studies completed

*Invention disclosure completed patents submitted IP licensed to Gene Express

UT has many mechanisms and resources for technology transfer, entrepreneurial development, and commercialization activities in the bioscience area. With the combined resources of UT Innovation Enterprises and the Regional Growth Partnership, entrepreneurs can find the full spectrum of assistance. We also work closely with BioOhio and the Third Frontier, as well as many other regional and national businesses.

The Regional Growth Partnership (RGP) http://www.rgp.org/ is a private-sector-driven and funded economic development organization based in Toledo that operates two programs

for technology development, Launch and Rocket Ventures. Launch is a service resource to technology-based entrepreneurs and start-up companies providing business planning and business development assistance. Rocket Ventures is a pre-seed, early-stage venture fund for technology-based entities/companies in Ohio.

4 Faculty Members Associated with the Center

4.1 COE Faculty

We have identified 12 Key Contributors (Table 6) and 46 Supporting Investigators (Table 7) for the COE for Biomarker Discovery & Translational Bioscience. Key Contributors are senior investigators in biomarker research who will play leadership roles for the UT-COE. They are all highly regarded scientists with strong funding and publication records, and significant contributions to bioscience with a strong interest in biomarkers. They represent all the FAST areas and three colleges across UT. Two of these faculty members were recruited within the last five years to UT as strategic hires.

Biosketches for our key contributors and supporting investigators are attached as Appendix A to this report. Further descriptions of their biomarker research are provided in Appendix C.

Table 6 Key Contributors

Name	Title	College	Department	Expertise
Cooper, Christopher	Prof and Chief	COM	Medicine: Cardiovascular	Renal artery stenosis, cell-based therapies for critical limb ischemia
Erhardt, Paul	Prof and Director	PHAR	Center for Drug Design & Development	Small molecule diagnostics, treatment and preventative agents with an emphasis upon hormone related cancers.
Leaman, Douglas	Assoc Prof and Chair	A&S	Biological Sciences	Our lab has used gene array technology to identify candidate IFN- and virus-stimulated genes that regulate cellular apoptotic or antiviral responses. Some of these genes can then serve as candidates for therapeutic targeting or use as predictors of disease state or therapeutic effectiveness. At least one of the proteins we are studying appears to serve as a biomarker for cancer progression, perhaps functioning as a tumor suppressor. Studies to test this are in progress.
Lecka-Czernik, Beata	Professor	COM	Orthopedics	a) Age-related bone loss. b) Bone loss as a result of anti-diabetic therapy with TZDs; c) Bone marrow stem cell differentiation during aging and diabetic disease; d) Bone fracture healing in elderly and diabetics

Name	Title	College	Department	Expertise
Najjar, Sonia M	Prof and Director	COM	Medicine: Diabetes	Pathenogenesis and underlying mechanisms of obesity-related diseases: a) Type 2 diabetes b) Metabolic syndrome, which includes visceral obesity atherosclerosis and hypertension c) Non-alcoholic steatohepatitis (NASH) d) The molecular link between obesity and cancer
Ratnam, Manohar	Professor	COM	Biochemistry	In my laboratory, we have identified soluble forms of the folate receptor (FR) proteins as potential serum markers for the early detection and monitoring of several types of cancer. Soluble FR type α is a marker for serous and endometriod cancers of the ovary, which constitute approximately 90 percent of the cases of ovarian cancer and also for nearly half the cases of breast cancer. FR type γ, which is a secreted protein, is a potential marker for lymphoma. We are developing assays for these proteins that are superior to current methods. A significant finding that we have reported, based on animal model studies, is that the level of expression of FRα in tumors that are positive for this protein may be greatly increased by administering an innocuous amount of dexamethasone, resulting in a corresponding increase in the level of the serum marker; this treatment strategy could enhance the detectability of FRα-positive ovarian and breast tumors and could be used to screen women at high risk for these types of cancer. Translational studies are planned.
Shapiro, Joseph	Prof and Chair	COM	Medicine: Nephrology	How renal disease leads to cardiovascular disease. The focus is on the signaling of cardiotonic steroids through the Na/K-ATPase
Shemshedini, Lirim	Professor	A&S	Biological Sciences	sGCα1, which plays an implicated role in the proliferation of prostate cancer cells and recently identified anti-p53 activity, may be very important in the initiation and progression of prostate cancer and thus be a potential biomarker for and therapeutic target of prostate cancer
Takashima, Akira	Prof and Chair	COM	Medicinal Microbiology & Immunology	Immunobiology of dendritic cells, which are professional antigen presenting cells that govern host immunity

Name	Title	College	Department	Expertise
Tietjen, Gretchen	Prof and Chair	COM	Neurology	vWF antigen, CRP, and fibrinogen as promising markers of endothelial function and associated with migraine
Willey, James	Professor	COM	Medicine: Pulmonary	Biomarkers for lung cancer risk, lung cancer diagnosis, lung cancer response to treatment; methods for biomarker development, including Standardized NanoArray PCR for Gene Expression Profiling of Lung Cancer
Xie, Zi-Jian	Professor	COM	Physiology & Pharmacology	Biomarkers of Cardiovascular Disease. We have identified that the plasma membrane level of Na/K-ATPase controls cell growth and function. Thus, it can be used as a biomarker for cancer and cardiovascular diseases. Similarly, since the surface level of Na/K-ATPase is regulated by endogenous cardiotonic steroids, the plasma and urine ouabain and marinobufagenin concentration can be used as an indirect indicator.

The Supporting Investigators have past/current funding in bioscience with a focus on biomarker research, a significant growing interest in biomarker research, and/or significant core lab leadership. Note that four of the Supporting Investigators were included in the Section 3 summarizing their biomarker discoveries. Fourteen of these 46 COE faculty members were recruited as strategic hires within the last 5 years.

Table 7 Supporting Investigators

Name	Title	College	Department	Expertise
Askari, Amir	Prof and Chair	COM	Physiology & Pharmacology	Digitalis-Induced Signaling by Cardiac Na+/K+-ATPase
Blumenthal, Robert	Professor	COM	Medicinal Microbiology & Immunology	Bioinformatics; Biomarkers of key bacterial pathogens
Bryant-Friedrich, Amanda C.	Assoc Prof	PHAR	Medicinal & Biological Chemistry	Discovery of novel biomarkers for the early detection of cancer based on DNA adducts derived from biological degradation products of oxidative stress
Cameron, Brent D	Assoc Prof	ENG	Bioengineering	Role for rhodopsins in dampening auditory cortex activity following tinnitus
Chin, Khew-Voon	Assoc Prof	COM	Medicine	Small molecule targeting adipogenesis
Diakonova, Maria	Asst Prof	A&S	Biological Sciences	JAK2-PAK1 axis is a novel biomarker for the breast cancer detection

Name	Title	College	Department	Expertise
Dong, Fan	Assoc Prof	A&S	Biological Sciences	Molecular mechanisms involved in the development and progression of hematopoietic malignancies
Elmer, Lawrence	Assoc Prof	COM	Neurology	Parkinson's Disease collaborative study of genetic linkage, 'PROGENI'
Fedorov, Alexei	Assoc Prof	COM	Medicine	Non-Coding RNA biomarkers for Autistic Spectrum Disorder
Gaba, Colette		COM	Pediatrics	Genetic epidemiology of lung lancer: Gene identification in high risk families
Geisler, John	Assoc Prof	COM	Ob/Gyn Oncology	Proteomic interrogation of tissue samples from patients with ovarian cancer for biomarker discovery
Godfrey, Donald	Professor	COM	Surgery	Amino acids and acetylcholine in central auditory plasticity
Goel, Vijay K	Prof and Chair	ENG	Bioengineering	Kinematics, kinetics and stresses and strains as biomarkers
Hassoun, Ezdihar	Professor	PHAR	Pharmacology	Determining various biomarkers of oxidative stress, such as reactive oxygen species, lipid peroxidation, DNA damage, antioxidant assessment
Hill, Jennifer		COM	Physiology & Pharmacology	Hypothalamic leptin and insulin signals aligning metabolic state and fertility
Isailovic, Dragan	Asst Prof	A&S	Chemistry	Analysis and discovery of potential glycan and protein biomarkers by mass spectrometry and light microscopy.
Jankun, Jerzy	Professor	COM	Urology	Pilot study of assays for detection and drug for PAI-1 deficiency
Jayasuriya, Ambalangodage	Asst Prof	COM	Orthopedic Surgery	Dual Release of Osteogenic Factors to Enhance Bone Regeneration
Joe, Bina	Assoc Prof	COM	Physiology & Pharmacology	Biochemistry and genetics of hypertension
Khuder, Sadik	Professor	COM	Medicine	Biostatistics

Name	Title	College	Department	Expertise
Kirchhoff, Jon R	Prof and Assox Chair	A&S	Chemistry	Detection and analysis of the neurotransmitter acetylcholine and measurement of the transport of its metabolic precursor, choline; sensors for sensitive and selective detection of biologically active thiols
Komuniecki, Richard	Jacobson Professor of Biomedical Research	A&S	Biological Sciences	Using a non-parasitic nematode, Caenorhabditis elegans, as a model with signaling pathways that have clear counterparts in humans, he hopes results may be applied to the development of new medications for conditions such as schizophrenia, depression and migraines.
Liu, Ming-Cheh	Assoc Prof	PHAR	Pharmacology	Vitellogenin-1, cytochrome P-450 1A1 (CYP1A1), and zona pellucida 2 (ZP2), all expressible by cultured zebrafish liver cells, as biomarkers for screening industrial, medical, and environmental chemicals for estrogenicity.
Manahan, Kelly	Assoc Prof	COM	Ob/Gyn Oncology	Investigation of cancer-associated PCNA in epithelial ovarian cancer tissue specimans for biomarker discovery
Martin, Steven J.	Professor & Chair	PHAR	Pharmacy Practice	Procalcitonin as a biomarker for bacterial infection related to sepsis, and therapeutic biomarker for antibiotic discontinuation
Mauro, Vincent F	Professor	PHAR	Pharmacy Practice	Assuring that acute coronary syndrome patients and chronic heart failure patients are discharged on appropriate medications proven to enhance their survival
Messer, William S	Prof and Chair	PHAR	Pharmacology	Molecular screening for M5 muscarinic-receptor modulators
Mrak, Robert	Prof and Chair	COM	Pathology	Biomarkers for Alzheimer disease and other neurodegenerative diseases

Name	Title	College	Department	Expertise
Nadaraja, Arunan	Prof and Interim Chair	ENG	Bioengineering	Development of a molecular sensor platform for biomarker detection
Nauli, Surya M	Asst Prof	PHAR	Pharmacology	Biomarker discovery and validation on research challenge topic to identify the normal and diseased proteome of subcellular organelles of relevance to NIDDK diseases
Pierre, Sandrine	Asst Prof	COM	Physiology & Pharmacology	CEACAM1 in the Regulation of cardiac fatty acid metabolism and myocardial lipotoxicity
Pizza, Francis Xavier	Professor	HSHS	Kinesiology	Biomarkers that regulate the interplay between leukocytes and skeletal muscle cells after exercise
Rees, Michael	Professor	COM	Urology	Innate cellular lectin-mediated binding of xenoantigens, identification of biomarkers for zoonotic viral infections related to xenotransplantation, identification of biomarkers predicting survival of kidney transplants
Skrzypczak-Jankun, Ewa	Assoc Prof	COM	Urology	Structure-function relationship of proteins and enzymes, molecular basis of diseases: human lipoxygenase as biomarker in cancer, PAI-1 in coagulation.
Slama, James T.	Professor	PHAR	Medicinal & Biological Chemistry	Link between CD38 deficiency and diabetes and possibly immunodeficiency. CD 38 is used as a bio-marker for the development progression of chronic lymphocytic leukemia.
Smas, Cynthia	Assoc Prof	COM	Biochemistry	Role of a transcriptional regulator, ID1, in prostate cancer progression to androgen independence
Stepkowski, Stanislaw	Professor	COM	Medical Microbiology & Immunology	Antibodies, sensitized “memory” B cells (mB), and functional populations of donor-specific T cells in recipients; mRNA and protein expression for the signature markers measured in blood cells

Name	Title	College	Department	Expertise
Tamburinno, Marijo	Prof and Chair	COM	Psychiatry	Genetic, developmental and neuroimaging predictors of deployment-related PTSD: a prospective case-control study
Tian, Jiang	Asst Prof	COM	Medicine	Identification of Na/K-ATPase as a biomarker of cardio-renal syndrome
Vazquez, Guillermo	Asst Prof	COM	Physiology & Pharmacology	Role of TRPC3 channels in atherosclerosis
Vestal, Deborah J	Assoc Prof	A&S	Biological Sciences	Evaluation of hGBP-1 as a marker for paclitaxel resistance in ovarian cancer
Viola, Ronald	Professor	A&S	Chemistry	Surfactant-based screens for membrane protein investigations
Wall, Katherine A	Professor	PHAR	Medicinal & Biological Chemistry	CD38 deficiency in human populations and link to diabetes, immunodeficiency, obesity, or signaling defects. CD 38 is used as a bio-marker for the progression of chronic lymphocytic leukemia.
Westerink, MA Julia	Professor	COM	Medicine	Elderly immune response to *pneumococcal* polysaccharide
Williams, Frederick E	Professor	PHAR	Pharmacology	Influence of human gene variants in glutathione associated proteins on the effects of developmental MeHg and EtHg exposure by looking at various biomarkers of oxidative stress; superoxide anion, lipid peroxidation, and antioxidant systems
Yamamoto, Bryan K	Prof and Chair	COM	Neuroscience	Determinants and consequences of methamphetamine and NDMA neurotoxicity
Yeung, Kam C	Asst Prof	COM	Biochemistry	RKIP regulation as a potential for tumor metastasis suppression
Zyrek-Betts, Jill	Asst Prof	COM	Pathology	Tissue Bank

4.2 Bioscience Faculty

The potential for biomarker discovery, validation and development can be vastly expanded when we consider the totality of researchers in bioscience at UT. There are 1709 faculty members (523 full-time) in Bioscience at six colleges of UT and they are

located in 1,941,457 square feet of office and laboratory space across both campuses (Appendix D1).

Of these, 295 UT faculty members are currently funded to do research in Bioscience.[4] They come from 20 Departments and occupy more than 100,000 square feet of office and laboratory space throughout the two campuses (Appendix D2).

5 Graduate Programs Associated with the Center

There are ten Doctoral Programs in Bioscience at UT, with 276 students who participated in the 2008-2009 school year. Graduates from any one of these programs across four colleges are potential contributors towards future research in Biomarker Discovery & Translational Bioscience.

Table 8 Bioscience Graduate Degree Programs

Degree Program	Degree	Number of Students
Doctor of Philosophy		
Biological Sciences		
Cell Molecular Biology	Ph.D.	54
Chemistry		
Chemistry	Ph.D.	55
Engineering		
Biomedical Engineering	Ph.D.	1
Biomedical Sciences		
Cancer Biology	Ph.D.	20
Cardiovascular & Metabolic Diseases	Ph.D.	31
Infection, Immunology and Transplantation	Ph.D.	17
Neurosciences and Neurological Disorders	Ph.D.	8
Exercise Science	Ph.D.	15
Health Education	Ph.D.	25
Psychology	Ph.D.	50
Total Ph.D.	**10**	**276**

There are 34 Masters Programs in Bioscience offered at UT, with 727 students who participated in the 2008-2009 school year (Appendix D3).

In addition, UT offers certificate programs in: Bioinformatics & Proteomics/Genomics, Biostatistics and Epidemiology, Epidemiology, Health Care Policy and Administration, and Public Health and Emergency Response.

We would like to develop a Ph.D. program in Translational Research, as well as a Clinical Research Masters Program (see Section 11.2).

6 Professional Programs Associated with the Center

There are six professional doctorate programs in Bioscience at UT, with a total of 1002 students who enrolled in the 2008-2009 academic year. Graduates from any one of these programs are potential contributors towards future research in Biomarker Discovery & Translational Bioscience.

Table 9 Bioscience Professional Degree Programs

Degree Program	Degree	Number of Students
Medicine	M.D.	628
Pharmacy	Pharm.D.	213
Medicinal Chemistry	D.M.C.	21
Nursing Practice	D.N.P.	9
Physical Therapy	D.P.T.	76
Occupational Therapy	O.T.D.	55
Total Professional Doctorates	**6**	**1002**

A total of 1935 students participated in graduate studies at UT in the last academic year.

7 Undergraduate Programs Associated with the Center

There are 12 undergraduate programs in Bioscience at UT, with an enrollment of 4549 students in the 2008-2009 academic year (Appendix D4).

8 Outside Collaborating Entities

There are many examples of educational, research and clinical partnerships in the Bioscience areas. Many of these extend far from the domain of higher education into government, economic development, finance and well into the private sectors. Appendix B includes letters of support from some key outside collaborators. These supporting collaborators include:

8.1 Hospitals and Universities

In addition to many clinical and educational collaborations with the two other hospital systems in the city of Toledo (ProMedica Health System and Mercy Health Partners), and with the St. Joseph Mercy Health Care System in SE Michigan, we are actively conducting research with most of the universities and associated hospitals in Ohio. There are UT Bioscience awards from FY07 thru 6-10-09 with subcontracts to 159 Educational Institutions and Non-Profits (Appendix D5), and there are UT Bioscience awards (FY07-09) on which UT is on a subcontract from 33 Educational Institutions or Non-Profits (Appendix D6). The institutes we are collaborating with include Case Western, Cleveland Clinic, Duke, Ohio State University, Mount Sinai Medical School, Northeastern Ohio Universities College of Medicine, Stanford University, University of Michigan, and Washington University.

8.2 Pharmaceutical / Device Companies

UT has established relations and contracts for clinical trials with more than 130 pharmaceutical and device companies since 2005. In many cases, we have worked directly with a CRO (shown in parentheses) on behalf of the industry sponsor (Appendix D7). We have excellent relationships with local companies such as NAMSA.

8.3 Incubation Facilities and Technology Park[4]

UT Innovation Enterprises operates numerous facilities for entrepreneurial activity. The incubation facilities have a proven track record in building successful businesses. In the last four years there have been 13 companies in UT incubators accounting for 132 jobs equating to more than $8,910,000 in new wages. Two incubators at UT will provide bioscience related companies' opportunities to innovate and commercialize. On UT's main campus, a 40,000 sq ft mixed-use technology incubator is located directly next to UT's College of Engineering and takes advantage of the multi-disciplinary activity between medicine and engineering. The Biomedical incubator (35,000 sq ft), on the UT's Health Science Campus, is completely dedicated to the growth of bioscience related companies. The biomedical incubator has unique commercial advantages with proximity to both the American Red Cross headquarters as well as the 180 acres of Technology Park and companies located within. These types of connections allow bioscience start-up

companies find local locations and grow local jobs in the community. The relationship between UT, UTIE, and RGP at the intersection of the Biomedical Incubator will be an impetus for further development of the Bioscience Cluster in NW Ohio.

9 Supporting Scientific, Scholarly, and/or Creative Activities

9.1 Publications

Table 10 COE Key Contributor Publication Metrics

COE Key Contributor	Publications*	Citations	h-index
Cooper, Christopher	21	1587	11
Erhardt, Paul	74	2051	21
Leaman, Douglas	50	1804	22
Lecka-Czernik, Beata	26	1001	13
Najjar, Sonia M	45	1075	15
Ratnam, Manohar	57	2206	23
Shapiro, Joseph	92	1915	23
Shemshedini, Lirim	25	801	14
Takashima, Akira	106	3618	37
Tietjen, Gretchen	37	458	12
Willey, James	57	2316	24
Xie, Zi-Jian	63	2255	26

*Publications include peer reviewed articles and reviews, but not corrections, meeting abstracts, editorials, or proceedings papers

The COE Key Contributors have published their work widely, and their work is well cited, as shown in Table 10. Their total number of publications (not including duplicates due to co-authorship) is 605. The h-Index is a relative merit indicator, a measure of an author's productivity and impact, simultaneously. The index itself is the number of publications by an author which have been cited at least that many times. A value for h of about 10-12 might be a useful guideline for tenure decisions at major research universities. A value of about 18 could mean a full professorship, 15–20 could mean a Society Fellowship, and 45 or higher could mean membership in the National Academy. The h-Index ranges from 11 to 37 for the Key Contributors with an average of approximately 19.

Specific publications by the COE Faculty (Key Contributors and Supporting Investigators) are provided in Appendix A.

The potential to expand biomarker discovery and translational bioscience is evident in the quality of the bioscience faculty. There were 4379 peer-reviewed publications by faculty on the Health Science Campus in 2006-2008, averaging over 500 journal publications per year. This does not include publications from the departments of Biological Sciences, Chemistry or Bioengineering (Appendix D8)

9.2 Journal Editors and Reviewers

Evidence of national recognition of expertise is in editorship of journals and being asked to participate as a reviewer. Ten Key Contributors are editors or reviewers of at least one journal.

Table 11 COE Key Contributor Professional Journal Activities

Key Contributor	Journal
Cooper	• Editorial Board for the Journal Vascular Medicine, 2006 • Editorial Board for Vascular Disease Management, 2006
Erhardt	Editorial Advisory Board Member of Pure and Applied Chemistry 2004-2006)
Lecka-Czernik	• Reviewer for: Nature Medicine, Nature Clinical Practice Endocrinology & Metabolism, Nature Clinical Practice -Rheumatology, Journal of Clinical Investigation, Aging Cell, Stem Cells, Journal of Bone and Mineral Research, Journal of Endocrinology, Journal of Molecular Endocrinology, Journal of Clinical Endocrinology and Metabolism, Journal of Cellular and Molecular Medicine, Bone, Expert Opinion on Investigational Drugs, Expert Opinion on Therapeutic Patent, Pharmacogenomics, American Journal of Physiology – Endocrinology and Metabolism, Physiological Genomics, PPAR Research, Experimental Gerontology, FEBS Letters. Differentiation Editorial Board of PPAR Research (from 2006); • Editorial Board Open Longevity Science (from 2008) • Guest Editor for PPAR Research special issue PPARs and Bone Metabolism (2006)
Najjar	Editorial Board Member - Molecular Endocrinology
Ratnam	reviewer for: Nature Medicine, Molecular Biology of the Cell, The Journal of Biological Chemistry, Journal of Clinical Investigation, Blood, Cancer Research, Molecular Pharmacology, Biochemistry, Journal of Molecular Biology, Nucleic Acids Research, American Journal of Physiology, Biochemical Pharmacology, Biochimica et Biophysica Acta, Journal of Nutrition, Archives of Biochemistry and Biophysics, Gynecologic Oncology, Cell Proliferation, Gene, Developmental Dynamics, Int. J. Cancer, Biotechnology & Applied Biochemistry
Shapiro	Editorial Board Member of: Kidney International (from 2002), Frontiers in Bioscience (from 2002), Biological Research in Nursing (from 2002), of American Journal of Medicine (from 2005), American Society for Artificial Internal Organs (from 2005), Arterial'naya Gipertenziya – The Arterial Hypertension (from 2006)
Takashima	Associate Editor, *Journal of Immunology* (1997-2001) Volume Editor, *Chemical Immunology*, Vol. 79: Gamma-Delta T cells International Advisory Board, *Journal of Dermatology* (from 2000) Section Editor, *Journal of Immunology* (from 2001-2005) Associate Editor, *Journal of Investigative Dermatology (from 2002)* Regional Editor, *Journal of Dermatological Science (from 2002)* Consulting Editor, *Journal of Clinical Investigation (from 2006)* Editorial Board, *Journal of Dermatological Science (from 2008)*
Tietjen	Associate Editor, Headache
Willey	Editor-in-Chief, Gene Regulation and Systems Biology (from 2006) Editor-in-Chief, Cancer Informatics (from 2009)
Xie	Guest Associate Editor, Cellular Molecular Biology (2006)

9.3 Participation in National Panels or Fellowships

Further evidence of our UT-COE Key Contributors' high national standing in their fields is found in the following two tables.

Table 12 COE Key Contributor Fellowships and Participation on National Panels

Key Contributor	National Panel
Cooper	Elected Fellow, American Heart Association, Council of High Blood Pressure Research, 2004
Erhardt	• Chairman IUPAC Working Party on Metabolism Databases and Their Potential Utility in the Development of New Drugs • Founding member for American Association of Pharmaceutical Scientists Prodrugs Focus Group • Elected President of IUPAC Division VII Chemistry and Human Health in 2002
Lecka-Czernik	Medical Science Monitor International Reviewers Panel (from 2002);
Najjar	Chair, Special Emphasis Panel (SEP) ZRG1 EMNR-J (03) "Metabolic Regulation"
Tietjen	• National Institute of Neurological Disorders and Stroke, United States Department of Health and Human Services Performance and Safety Monitoring Board, Division of Stroke and Trauma (from 1999) • Executive Board Member, Section on Headache and Facial Pain, American Academy of Neurology (2002-2005) • Chairman, Section on Women's Issues in Headache, American Headache Society (2001-2003) • Board Member, American Headache Society (2002-2008) • Executive Board Member, Association of University Professors of Neurology (2002-2007) • Member, Education Committee, American Neurological Association (from 2008)

Table 13 COE Key Contributor NIH Study Section Participation

Key Contributor	NIH Study Section
Erhardt	SBIR awards pertaining to Drug Design and Development
Leaman	• NIH/NIAID, ZAI1-BDP-I-J3 and ZAI1-BDP-I-J4 (Jan. 2009) • Ad Hoc Reviewer, NSF (2006/2007), NIAID (2006) • RAID Review panel, (Nov. 2005) • NIAID ZAI VSG-1 (S2) Special Emphasis Panel, (June 2004) • Ad hoc study section member - NIH/NCRR Comparative Medicine Review Committee, (2002/2003)
Lecka-Czernik	NIH Peer Review Study Section, ad hoc member: Cellular Mechanisms of Aging and Development
Najjar	• Standing member at Integrative Physiology of Obesity and Diabetes (IPOD) study section • Ad Hoc reviewer, NIH study sections: NCI, NIDDK B subcommittee, MADO, CADO

Key Contributor	NIH Study Section
Ratnam	• Regular Member of NIH Study Section BMCT, April 2007- March 2011 • Regular Member of NIH Study Section Experimental Therapeutics-1, July 1,1997-June 30, 2001 • Ad hoc reviewer for NIH Study Section BMCT • Ad hoc reviewer on NIH Study Section ET-1 • NIH Special Emphasis Panels, May 1999, April 2000, August 2000, and December 2000, December 2003, June 2004, December 2004, August 2005
Takashima	NIH ACTS Study Section (from 2006)
Willey	SPORE in Lung and Genitourinary Cancers, Emerging Technologies in Cancer Research, IMAT (from 2005)
Xie	• Regular Member of NIH CMBK Study Section (2005-2009) • Ad Hoc member, Hypertension and Microcirculation Study Section (2005)

9.4 Seminars and Symposia at UT

Biomedical research at The University of Toledo is a vibrant and vigorous environment marked by numerous seminar series and other scholarly activities in every department. These activities involve visiting scientists, faculty, postdoctoral scientists, graduate and undergraduate students. The lifeblood of the research environment is in the postdoctoral fellows and graduate students that populate the numerous research laboratories on both campuses of the university. Hence most of the supporting scientific, scholarly and creative activities revolve around the efforts of these young researchers. The abundance of seminars and research presentation events are such that multiple biomedical seminars occur weekly somewhere on campus. A listing of most of these events is shown below. Many of the Bioscience Departments have programs that support education and research (Appendix D9)

9.5 Entrepreneurship

As previously described, UT has many resources for assisting entrepreneurial efforts. Many of these efforts that support scientific or scholarly activity relate to incentive and grant programs for faculty. Many other creative and collaborative opportunities exist in partnership with the RGP. These include business plan and development services, entrepreneurial award recognition, and funding and federal grant informational sessions.

UT encourages entrepreneurial activity through several unique research award programs available to biomedical disciplines. These include:

- deArce Memorial Endowment Fund in Support of Medical Research and Development (up to $100,000)
- Interdisciplinary Research Initiation Awards (up to $100,000)
- Phase 0 SBIR/STTR Program ($4,500)
- Proposal preparation for Federal Grants (5,000)
- Publications Subvention Program ($1,000 for publishing scholarly manuscripts)

The University of Toledo Innovation Enterprises also partners with the RGP and Gorillas and Gazelles to present and honor local entrepreneurship of new technology-based and other businesses in the community through the Entrepreneurial & Business Excellence Hall of Fame awards. These are a series of 8-9 awards recognizing business that have had a significant impact on local the local community.

For those faculty who start-up their own company or are working with other start-up companies, the RGP and the College of Businesses Center for Technological Entrepreneurship and Innovation (CTEI) work together to provide various services including: feasibility studies, financial analysis, marketing plans, and presentation videos.

UTIE also partners with the RGP to operate an Alumni development network program that brings interested Alumni into the network for supporting entrepreneurial development.

Entrepreneurial Boot Camp is also a partnership between UT and the RGP. This is a one-day training event providing topics important to start-up companies including: building a foundation for your business, financing your business, lessons learned from successful entrepreneurs, sales and marketing, legal and accounting, and human resources and operations. UT also actively participates in RGP's TechConnect events which are networking events bringing together

10 Management Plan

The UT-COE for Biomarker Discovery and Translational Bioscience will be managed through J-CCTR, under the direction of Debra E Gmerek, Ph.D.

Dr. Julius Jacobson, III and his wife Joan recently provided a $2M endowment to UT. The purpose of the Jacobson Center is to:

- Promote and facilitate translation of health & bioscience basic research into the clinic, focusing on FAST clinically important areas.
- Monitor and support potentially viable discoveries and stimulate the clinical translation and commercialization process, including biomarkers.

Jacobson Center will promote the necessary integrated approach that combines clinical and basic science researchers, clinical research coordinators, core laboratories (genomics, proteomics, biostatistics/bioinformatics, flow cytometry, imaging, and tissue bank), and technology transfer and regulatory approval systems. We will also apply a strong business perspective to develop strategies, create project plans, establish milestones and report progress.

Dr. Gmerek joined UT in January, 2009. She also serves in the role of Associate Dean for Research for the College of Medicine. She holds a Ph.D. in pharmacology, and came to UT with more than twenty years of experience in translational and clinical research and drug development, most recently with Parke-Davis/Pfizer.

The role of the Administrative Director for the COE in Biomarker Discovery & Translational Bioscience will include:

- Strategy & Operations of the Business Plan
- Leadership of monthly meetings of the Key Contributors
- Quarterly meetings with the COE Advisory Board
- Development of biomarker-focused seminars and symposia
- Identification of potential funding opportunities
- Development of the Biomarker Validation Core Lab Facility
- Continuous interactions with Faculty, Core Facilities, Tech Transfer, and other related internal and external stakeholders
- Budget management
- Progress reports

During the UT-MUO merger process, a sophisticated web based strategic planning and implementation application was developed, tested and implemented by the UT Center for Creative Education. This application has been extensively used for strategic planning and operations in business and academic areas for over two years. We will use the UT Strategic Planning Prism https://myutplan.utoledo.edu for strategic planning, tracking and

management. We will also develop a database for monitoring and tracking the biomarker projects. This will be linked to a detailed business and project plan. Microsoft Project will be used to manage, track and report established milestones.

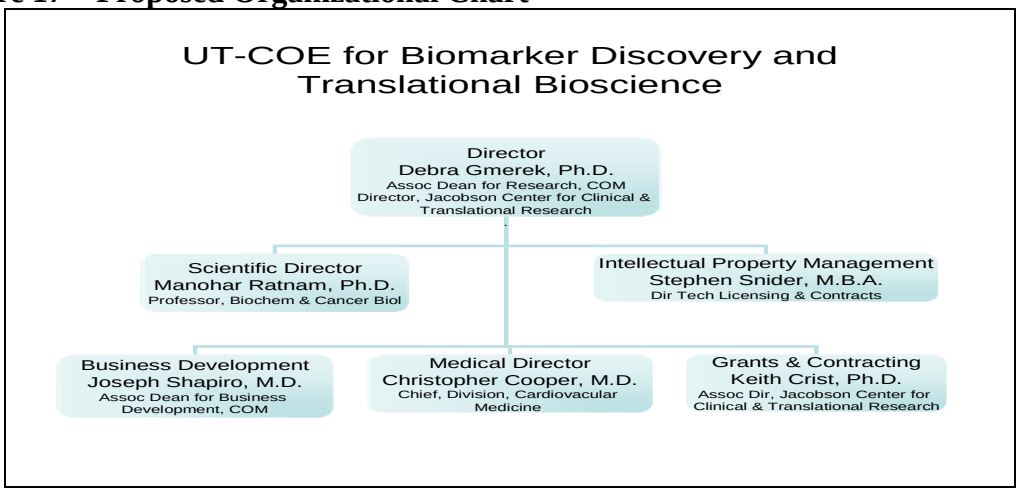
The UT-COE for Biomarker Discovery & Translational Bioscience will be scientifically led by Manohar Ratnam, Ph.D. and Christopher Cooper, M.D. will be the Medical Director for the COE. We will use future funding to hire an internationally recognized expert in the field of biomarker research and development to be the Scientific Director. This will improve our ability to be recognized as a national leader in biomarkers and attract additional experts in the field.

Dr. Ratnam has an impressive record in obtaining federal and private funding for his work identifying soluble forms of the folate receptor (FR) proteins as potential serum markers for the early detection and monitoring of several types of cancer. Dr. Cooper is the Director of the UT Heart and Vascular Center. He is the Primary Investigator for four ongoing grant-funded clinical trials including the Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL), and NIH-funded ($28M) multicenter clinical trial. Dr. Cooper's Clinical Coordinating Center maintains stored patient-related samples for risk stratification and biomarker evaluations.

The role of Scientific Director and Medical Director for the COE in Biomarker Discovery and Translational Bioscience will include:

- Providing leadership in biomarker and translational research
- Establishing process and ethics guidelines for biomarker discovery, validation and commercialization at UT
- Advising faculty on scientific matters
- Consultation for the COE Administrative Director
- With the Administrative Director, establishing short- and long-term goals for the COE

Figure 17 Proposed Organizational Chart



This organization will also be supported by a Biomarkers Commercialization Consultants group, which will include Frank Calzonetti (Assoc VP for Economic Development),

Dan Kory (Assoc VP for Tech Transfer), Jim Trempe (Sr. Dir for Research Administration), Jeffrey Gold (Provost), and representatives from BioOhio and RGP as appropriate.

The UT-COE will also convene an Advisory Board of regional and national experts in the area of biomarker discovery, development and commercialization to provide strategic recommendations for new hires, sources for funding, and short- and long-term goals.

Proposed Advisory Board

- Johnny L. Early, RPH, Ph.D. Dean, College of Pharmacy
- *Stephen Eck, M.D., Ph.D. NIH Biomarkers Consortium Executive Committee (representative: pharmaceutical/biotechnology industries) Vice President, Translational Medicine & Pharmacogenomics Eli Lilly and Company
- Jeffrey P. Gold, M.D. Provost and Executive Vice President for Health Affairs, Dean, College of Medicine
- *James W. Jacobson, Ph.D. Acting Associate Director, Cancer Diagnosis Program, DCTD, NCI
- *Maren R. Laughlin, Ph.D., Program Director for Metabolism and Insulin Resistance, and Functional and Molecular Imaging, NIDDK
- *Hugh A. Sampson, M.D. Professor and Dean of Translational Biomedical Science at the Mount Sinai Medical Center.
- Beverly J. Schmoll, PT, Ph.D., FAPTA Dean, College of Health Science & Human Service
- *Sudhir Srivastava, Ph.D., MPH, Chief, Cancer Biomarkers Research Group, Division of Cancer Prevention, NCI
- *Ruth A. VanBogelen, Ph.D., Director, Biomarkers & Proteomics, NextGen Sciences, Inc

*not yet contacted

11 Resource Management and Funding Plan

Current funding for the COE is associated with the various colleges, departments and centers from which the faculty resides, and comes from intra- and extramural sources. In addition, UT has provided extra funding for Biomarker Discovery & Translational Bioscience through the Translational Stimulation Awards, described in Section 11.1.

11.1 UT Translational Research Stimulation Awards

In January 2007 the University of Toledo established the Translational Research Stimulation Awards (TRSA). These translational research seed grants for two years and $100,000 were developed to bridge the gap between basic research and clinical research at the university. The program encourages faculty members to cross disciplines, departments, centers, institutes and colleges to conduct studies that emphasizes translational research — in which basic science discoveries are brought to the bedside to improve patient care.

Since its inception, eleven awards have been granted for a total of $1.1 million dollars of support. This extraordinary level of support has opened up new avenues of investigation as well as the establishment of intramural and extramural collaborations. Moreover this program is consistent with the National Institutes of Health's Roadmap for Medical Research by emphasizing translational research by urging the elimination of barriers between scientists and practitioners and fostering the education of future clinical and translational scientists.

11.2 UT Staffing and Space Allocation

Commitment to the COE is also evident in strategic hiring of 16 strong bioscience researchers with biomarker expertise, and the hiring of the director and allocation of a $2M endowment to J-CCTR. The second floor renovation of the Health Education Building, which houses Medical Microbiology & Immunology, is funded 50% by the COM, and the COM Strategic Plan calls for an additional outpatient building with specified space for clinical trials work.

11.3 Extramural Funding

Sustainability of the COE will depend on successful procurement of matching extramural funding from federal, state, and private sources. However, there are many sources available for funding the area of biomarker research, discovery, validation and development. Appendix D10 describes NIH funding sources specifically for biomarker validation. Funding is also available for biomarker discovery, validation and commercialization from disease-specific non-profits and from venture capital firms.

11.4 Future Investments

First and foremost, we must continue to hire first-rate, well-funded scientists with expertise in biomarker discovery, validation and development. While this strategy is being implemented as we replace faculty who leave through natural attrition, we will require matching funds to supplement existing faculty and move this progression towards greatness along at a faster rate.

We currently have at least eleven candidate biomarkers discovered by UT investigators, which provide excellent substrate for further validation, development and commercialization. This COE will provide the framework by which the next steps for the biomarker candidates can take place. Further intramural and extramural investment is required to expedite the process, and to ensure quality, speed and cost-effectiveness of biomarker validation on an ongoing basis. Biomarker research hasn't been without challenges. Biology is multifactorial and simple genetics won't solve the problems. There are major issues around human tissue access, assay technology and appropriate interpretation of complex data.[10] Human tissue sample access, state-of-the-art assay technologies, and appropriate analysis of data are essential for validation of biomarkers for regulatory purposes.

11.4.1 Short-Term Investments

Therefore, in the short term (1-3 year horizon), significant investments are needed to achieve the greatest potential of this COE. These are described in the following table. Approximately $350,000 is needed for equipment plus $740,000/yr in salaries.

Table 14 Short-Term Investments for UT-COE

Requirement	Current State	Future State	Estimated Budget	Funding Source
Scientific Director	Current faculty are fully committed to current teaching and research obligations	Highly respected and well-funded scientist with biomarker expertise provides leadership, scientific direction, and brings national credibility and respect to the UT-COE	$250,000/ yr	UT and matching extramural funding
Expanded Tissue Bank	Opportunistic collection of solid tumors, not automated	Collect blood, urine and DNA for all UT Hospital surgical patients. Automated sample storage & retrieval linked with Electronic Medical Records. Full-time technician	$150,000 equip; $40,000/yr staffing	matching extramural funding
Updated Proteomic/Genomic Core Lab Facility	Equipment is out-of-date	State-of-the-art facility with part-time Director and technical support	$175,000 equip; $100,000/ yr staffing	matching extramural funding

Requirement	Current State	Future State	Estimated Budget	Funding Source
Epidemiologist	Biostatisticians and epidemiologists at UT are fully committed to teaching and personal research obligations; not experts in bioinformatics	Full-time epidemiological expertise available to support bioinformatics core	$150,000/yr	matching extramural funding
Biomarker Validation Core Lab Facility	Biomarker expertise is distributed randomly across the UT campuses, and researchers are focused only on their personal projects.	The biomarker strategy will result in identification of potential biomarkers in the bioscience laboratories across the university. A Biomarker Validation Core Lab Facility would bring efficiency and quality to the verification and validation of biomarkers, thereby expediting commercialization. This facility would bring together aspects of the Tissue Bank, Proteomics/Genomics/Bioinformatics Core. It would require dedicated space, a part-time Director and several expert technicians.	$250,000/yr	matching extramural funding

11.4.2 Medium-Term Investments

In the medium time-frame (2-5 years), investment is needed to support development of several programs that will build the biomarker franchise through training new translational scientists and provide support for intellectual property protection.

- **Ph.D. Program in Translational Research**
  L. John Greenfield, Jr., M.D., Ph.D. is the Director of the existing UT College of Medicine M.D./Ph.D. Program. The M.D./Ph.D. program educates physician-scientists, a unique breed of physicians who complement the clinical practice of medicine with active research in basic and/or clinical science. This program will continue but we want to offer opportunities to develop highly skilled translational researchers without requiring the, what can be prohibitive, length of time required to complete a combined degree.

  Having recently been awarded a highly prestigious Howard Hughes Medical Institute (HHMI) grant in the area of medical education, Dr. Akira Takashima has recently submitted a proposal for a HHMI Grad into Med grant to support a Translational Medicine in Infection, Immunity & Transplantation (TM-IIT) Program. We will

design the program to overcome two major shortcomings in today's graduate education: lack of two-way collaborations between basic biology and clinical medicine and narrowly focused emphasis on molecular knowledge. We will train the next generation of scientists to understand human biology and pathology as well as issues related to clinical translation and regulatory compliance and who can readily translate scientific knowledge into clinically applicable forms. The TM-IIT Program will be aligned with the ongoing interdisciplinary research initiative in a targeted clinical area (infectious and immunological diseases). Our specific aims are: 1) to recruit qualified students who are committed to translational research, 2) to provide cohesive training for their readily preparedness for working in a clinical setting, 3) to broaden their view in terms of research objectives, clinical applications, and career goals, and 4) to further foster collaborations among participating faculty using our students as a biological glue. Our objective is not to create a mini MD/PhD program, but to provide limited and focused medical education/training in a targeted clinical area. This will empower our students to apply advanced knowledge to be gained during the doctoral studies and thesis projects to solving medically critical problems. The relatively restricted scope should allow us to accomplish our aims in a time- and cost-efficient manner and to evaluate the outcomes in an objective fashion. Moreover, once proven to be successful, our new certificate program should serve as a small-scale/high-impact model that can be easily implemented by any graduate program in US medical schools.

Taking this proposal a step further will create a Ph.D. program in Translational Research, which could be associated with any of the FASTs, as all of our Biomedical Ph.D. programs are currently. At OSU and University of Michigan, students wishing to obtain a Graduate Specialization Transcript Designation in Translational Research (OSU) or a Postdoctoral Translational Scholars Program (UM) must complete additional coursework, training, and/or research experience following the Integrated Biomedical Science Graduate Program. This Ph.D. in Translational Research would integrate clinical expertise into the program from the beginning, as described in the previous paragraph, thus saving both time and expense as a student. Furthermore, this program would encourage collaborative, multidisciplinary teamwork, which is a requirement for effective translational research.

Funding for this program would come from the Howard Hughes Foundation plus a NIH Clinical Research Curriculum Award (K30) http://www07.grants.gov/ and matching funds.

- **Clinical Research Masters Program**
  An 18-credit graduate certificate program in Biostatistics and Clinical Research already exists at UT through the Department of Public Health & Homeland Security. The Clinical Research Masters Program (CRMP) is intended to be a 2-year program with a specialized curriculum that educates healthcare professionals for academic careers in clinical research and lead to a Master of Science degree in Clinical Research Design and Statistical Analysis.

The CRMP provides opportunities for education in clinical research design and hands- on clinical research under the guidance of an individual scientific advisory committee. Through this program, trainees acquire biostatistical skills and knowledge in specific areas of clinical research (drug development and clinical trials, health services research and translational research); learn how to properly design a clinical research study, follow requirements for human subject protection, and ethical principles and research integrity essential for the conduct of human subject research. Trainees also gain experience in the preparation of well thought-out grant applications and how to navigate the research funding options. The program strongly emphasizes mentoring and guidance in career development. The CRMP would be based in the COM Jacobson Center for Clinical & Translational Research and Department of Public Health & Homeland Security, and supported by an NIH K30 and matching funds.

- **Funding program for discovery patents for biomarkers**
  Funds to support patent applications are already a problem at UT. With a total annual budget of $440K (not specific for biomarkers), UT is already unable to support patents for every invention disclosure or discovery across the University. If we can reach our goal of 50 biomarker discoveries a year, with 25 patents, and assuming it takes 2-4 years to get to the next stage of commercialization, and assuming that we must also file patents internationally to attract investors, then we will need approximately $1.2M over a 3 year period just to support the patents. Significant extramural funds are needed to support intellectual property protection as it is critical to the future economic development of biomarkers. A wise investment!

12 Sponsored Program Activity Associated with the Center[4]

The UT-COE for Biomarker Discovery & Translational Bioscience Key Contributors have a total of extramural funding in 2007-2009 of over $24M, which averages to about $8M/year altogether for the 12 investigators. This includes private as well as Federal funding.

Table 15 Key Contributor Funding for 2007-2009

Name	Extramural Funding In Dollars
Cooper, Christopher	5,293,554
Erhardt, Paul	1,662,483
Leaman, Douglas	891,560
Lecka-Czernik, Beata	759,831
Najjar, Sonia M	847,521
Ratnam, Manohar	1,331,107
Shapiro, Joseph	15,000
Shemshedini, Lirim	10,229,145
Takashima, Akira	1,967,345
Tietjen, Gretchen	567,419
Willey, James	18,000
Xie, Zi-Jian	891,764
Total	$24,474,730

The Supporting Investigators have jointly contributed $22M in extramural funding in 2007-2009, averaging another $7.3M annually to the COE. This includes private as well as Federal funding. Altogether, the COE faculty contributed $46M in total funding over the last three years.

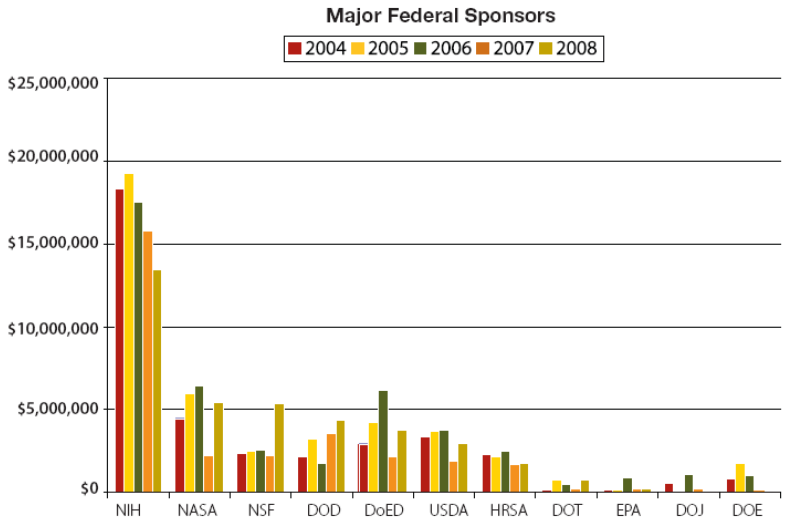
The FAST Health & Bioscience research accounted for $44.64M in UT Federal funding in the past 3 years to date. Clearly, biomarker research is a large component of our research.

Table 16 UT Bioscience Federal Funding by FAST

FAST	**2007-2009**	2007	2008	2009 YTD
Hormone-Related Cancer Biology & Cancer Diagnostics	**$7,599,868**	$3,598,081	$2,289,134	$1,712,653
Cardiovascular & Metabolic Disease	**$14,708,017**	$6,936,092	$4,269,891	$3,502,035
Infection, Immunology & Transplantation	**$11,665,995**	$4,598,811	$3,885,982	$3,181,202
Neuroscience & Neurological Disease	**$9,654,030**	$2,365,386	$4,038,809	$3,249,835
Kinetic-Related Sciences & Disorders	**$1,016,739**	$35,200	$426,366	$555,173
TOTALS	**$44,644,649**	**$17,533,569**	**$14,910,182**	**$12,200,898**

As of 5/20/09, there were 97 funded NIH grants for 80 projects, a total $18.9M of support for all of bioscience at UT. This does not include funding from other Federal and State agencies, or from private sources.

Figure 18 UT Federal Funding by Sponsor



Health and Bio-science represented 54% of UT Federal funding in 2008/2009, the majority of which was from NIH, but also accounts for some of the NSF, DOD, and other Federal funding sources. The total bioscience funding in FY 2008 was $28.5M.

Figure 19 UT Federal Funding by College

Other than a spike in the College of Arts & Science in 2005, the College of Medicine brings in the largest amount of Federal funding, all of which is related to health and bioscience. A segment of funding from A&S (Biological Sciences and Chemistry) and Engineering (Bioengineering) is in also bioscience.

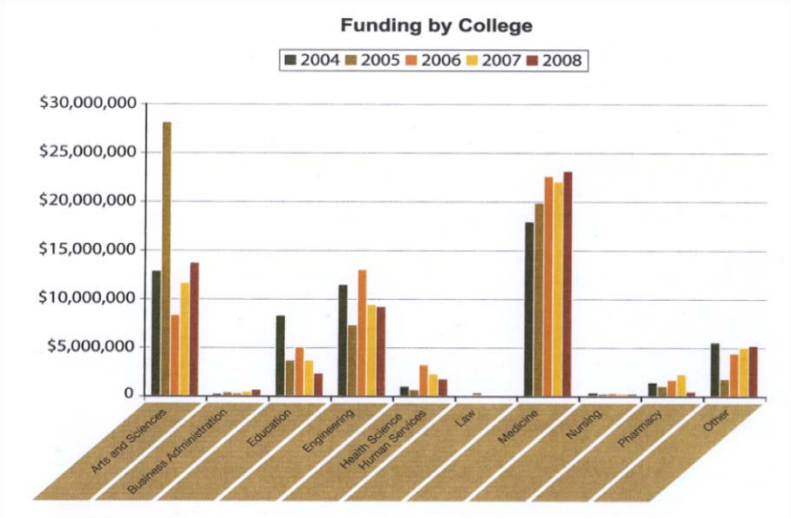
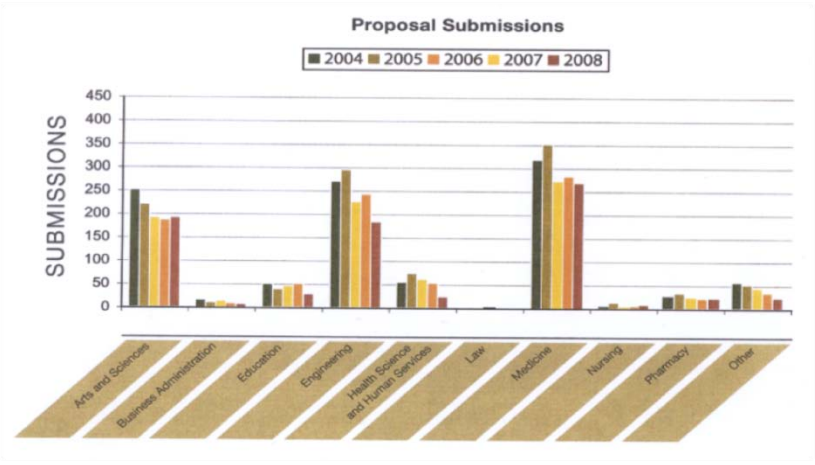


Figure 20 UT Federal Grant Submissions by College

Health and bioscience also accounts for 49% of all Federal grant submissions. In 2009 YTD, 246 grant applications in health and bioscience have been submitted with a budget totaling $48.73M.



13 Suggested Metrics that Define Excellence for the Center

Sixteen strategic faculty hires within the last five years, of scientists with bioscience and biomarker expertise, $2M endowment of J-CCTR, $1.1M in Translational Research Stimulation Awards, and plans for dedicated clinical trial research space indicate a strong commitment by UT to this COE. Further significant investment by UT with matching extramural funding is required to expedite the process, and to ensure quality, speed and cost-effectiveness of biomarker validation on an ongoing basis. We have the potential within five years to rival benchmarks such as Mt. Sinai Medical Center and Duke Clinical Research Institute's Advanced Biomarker research unit.

The key metrics that will define success for a COE in Biomarker Discovery & Translational Bioscience are:

- Biomarker Validation Core in operation
- Faculty recruitment
- Funding – NIH, state and private
- Intellectual Property – invention disclosures, patents, licenses, and spin-offs

Our specific aims in the next five years are: 1) to recruit nine renowned and highly respected biomarker experts, 2) create a Biomarker Core Laboratory equipped with state-of-the-art biobank and 'omics technology and associated technicians 3) develop graduate programs in translational research, and 4) to double our research funding from $15M to $30M per year, and quadruple our funding to support intellectual property protection and technology transfer.

Full funding for the COE as described in Section 11 will bring us to an annual budget of approximately $36M/year. As a result, the number of biomarker invention disclosures, patents, licenses and spin-offs will increase dramatically. Our 2015 target is 50 biomarker-related invention disclosures, 25 patents, and 10 license agreements and 1-2 viable spin-offs per year.

Figures and Tables

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Appendix A: Biosketches
Appendix B: Letters of Support
Appendix C: Description of Biomarker Research at UT
Appendix D: Reference Tables