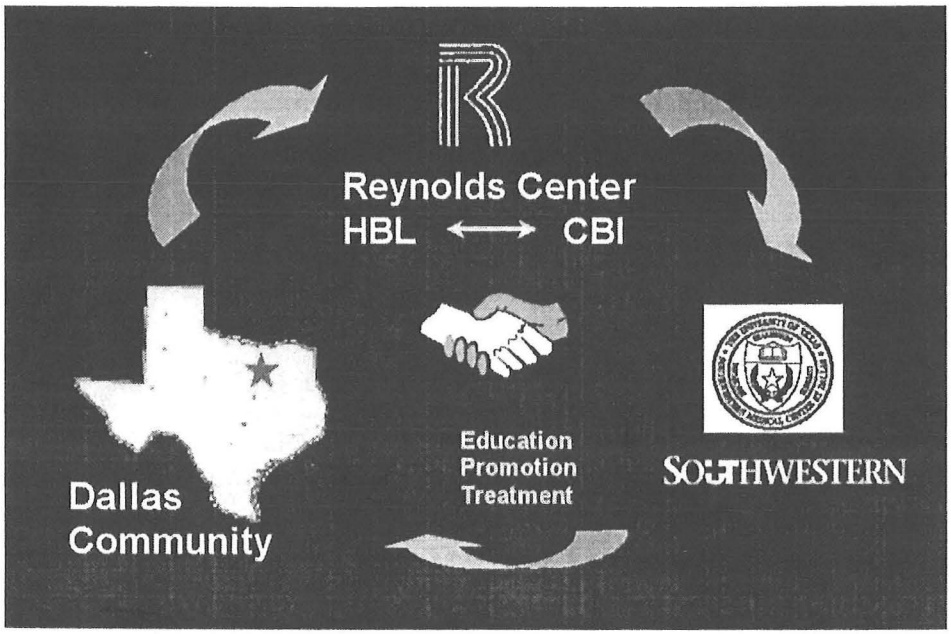
The Reynolds Center for Clinical Cardiovascular Research at UT Southwestern Medical Center: Preventing Heart Disease in Dallas County



INTERNAL MEDICINE GRAND ROUNDS

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Research Interests: gene regulation in cardiac and skeletal muscle, myogenic stem cells, genomics of CV disease, biotechnology

"This is to acknowledge that R. Sanders Williams, M.D. has disclosed no financial interests or other relationships with commerical concerns related directly or indirectly to this program. Dr. Williams will not be discussing "off-label" uses in his presention."

Unmet Challenges of Cardiovascular Disease

Ischemic heart disease was recognized by physicians as a disease entity as the 20th century began (1), and by mid-century it had emerged as a leading cause of death and disability among citizens of the United States and other industrialized nations (2). Throughout the 1970s and 1980s, advances in our understanding of the complex pathogenesis of this disorder led to effective preventive and therapeutic strategies that have produced tangible declines in age-adjusted mortality rates (6, 17). The high prevalence of coronary artery disease and its attendant complications has demanded an immense allocation of medical and financial resources. Technologically based therapeutic measures such as thrombolytic drugs for acute coronary occlusion, coronary artery bypass surgery and percutaneous transluminal coronary angioplasty have become available virtually everywhere in this country. After the etiological roles of certain risk factors were identified, powerful new drugs have been developed to reduce blood pressure or to lower plasma cholesterol. Public awareness of behaviors that raise or lower the probability of developing coronary artery disease has led to marked changes in activities of daily living within some segments of the population, and in laws governing labeling or regulation of foodstuffs and tobacco products. New industries have emerged to serve the public's demand for behavioral or dietary aids that are believed to lower risk for heart disease. Although examples of profiteering, excessive zeal, or downright charlatanism abound within this historical movement, for the most part the biomedical enterprise can, and should, take pride, in the accomplishments of the last century with respect to the battle against heart disease (19). Most of the central conceptual and therapeutic advances stand on firm scientific ground.

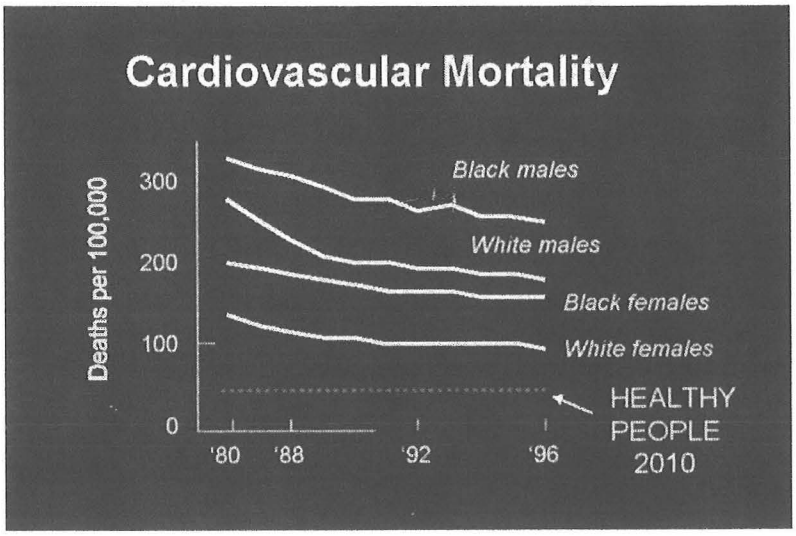


Fig. 1. Age-adjusted mortality from cardiovascular disease stratified by ethnic group and gender (6).

Pride in these scientific achievements and in our current clinical capabilities, however, carries a present danger of complacency. In many respects we have failed to achieve the impact on public health that the progress of the last third of the century seemed to predict.

Around 1990, the U.S. Department of Health and Human Services developed a working document called "Healthy People 2000" (3), stating a goal that cardiovascular deaths within the U.S. population should be reduced to less than of 50 deaths per 100,000 by the year 2000. This goal was based in part on extrapolation of the downward trend throughout the 1980's in cardiovascular mortality rates in white males, the demographic group in which most data were available.

As shown in Fig. 1, this goal remains distant. The rate of decline in cardiovascular mortality in white males throughout the 1990's slowed from that achieved in the early 1980's, and that rate was not matched in females of any ethnic group or in black male Americans (6, 16, 18, 20, 21). Fig. 1 also illustrates that, despite declining mortality in all of the four demographic groups shown, the gap between blacks and whites widened rather than narrowed between 1990 and 1996 (6-9). As the millennium has arrived with the goal of Healthy People 2000 unattained, the DHHS clock has been reset to 2010 (4).

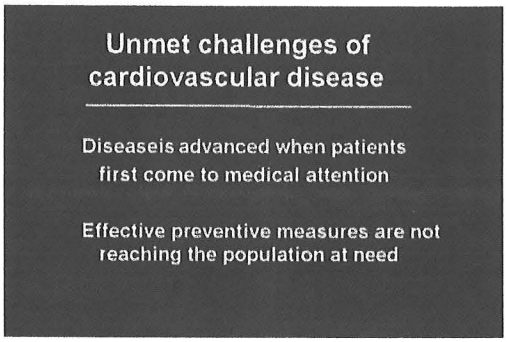


Fig. 2. Considerations that limit success in reducing cardiovascular risk.

In the midst of important therapeutic and preventive advances, what accounts for these rather disappointing trends? The case studies presented in this Grand Rounds illustrate two of the major difficulties (Fig. 2). Coronary atherosclerosis and/or left ventricular hypertrophy are often asymptomatic until the diseases are far advanced, and patients come to medical attention only following a catastrophe. While we have therapeutic measures that are effective in extending the lifespan of individuals who survive a cardiac arrest or myocardial infarction, or who are treated successfully for heart failure, these interventions are unlikely to have major impact from a public health perspective when applied only at stages when features of the disease are irreversible.

A second difficulty is apparent from studies that have assessed the degree to which major risk factors for coronary artery disease and/or heart failure are identified and controlled within defined populations. Such analyses provide sobering results irrespective of socioeconomic and ethnic differences, but are particularly disappointing within urban minority groups. An enormous number of individuals have treatable abnormalities but fail to achieve adequate control, even when they have ready access to medical followup (10, 11, 14).

What Are the Appropriate Responses?

If we are to achieve the goals of Healthy People 2010 with respect to cardiovascular disease, and if coronary artery disease really is to be "Gone with the century" as Drs. Brown and Goldstein have encouraged us to consider (15), what is needed? To focus the question more specifically on the academic medical enterprise, how should we as individuals and as a leading research institution respond to these unmet needs? Is it sufficient to go about our business as clinicians and investigators in a traditional manner or are new modes of professional activity and institutional organization required?

About a year ago, the National Heart Lung and Blood Institute asked some leading cardiovascular specialists to ponder these questions and to come up with some recommendations that would serve as guidelines for action by the research community, and for setting priorities for research support provided by the NIH. This committee called itself the SPARK Working Group, to emphasize their role in initiating new approaches. Some results of their deliberations are illustrated in Figures 3 and 4. They concluded that while virtually all segments of the cardiovascular research enterprise were thriving, effective communication among research disciplines was lacking. Molecular and cell biologists studying problems relevant to cardiovascular disease often seem to inhabit a different universe from those engaged in clinical epidemiology or clinical trials. These disciplines are separated not only by differences in scientific culture and language, but often by the geographic and administrative organization of the academic workplace. The SPARK group proposed that new initiatives should encourage cross-disciplinary communication to integrate results from basic molecular biology into more complex systems extending from cells to tissues to organ systems to intact humans to populations, serving the common goal of enhancing cardiovascular health (Fig. 3). They proposed further that some restructuring of academic units would be required to "enable" this process, specifically by rethinking the process by which new investigators are trained, by capitalizing on new technologies in selected areas, and by emphasizing genetic studies in well-defined populations (Fig. 4).

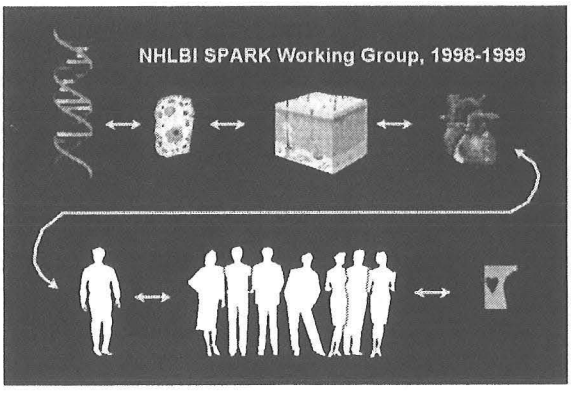


Fig. 3. Recommendations of the SPARK Working Group: Encourage cross-disciplinary communication that integrates results from basic molecular biology into more complex systems extending from cells to tissues to organ systems to intact human individuals and populations (16,22).

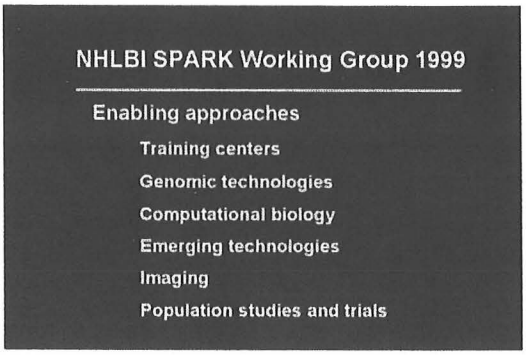


Fig. 4. Recommendations of the SPARK Working Group: New approaches to training of investigators, new technologies, with an emphasis on genetics and population studies (16,22).

Leading figures within the cardiovascular research community such as Dr. Valentine Fuster and Dr. Scott Grundy have added other perspectives. In 1999 Dr. Fuster observed that "Our challenge is to integrate basic and applied science, foster group collaboration, and bring together funding from government, industry, public or private corporations, and individuals to meet the changing needs of society (16)." Dr. Grundy pointed out that more effective approaches to stratify degrees of risk so that specific-risk reducing strategies can be targeted most efficiently is "at the core of primary prevention (24)".

Prior to the publication of these recommendations from the NHLBI SPARK Working Group, a different panel of experts had reached many of the same conclusions when asked by the Donald W. Reynolds Foundation of Las Vegas, Nevada to advise that foundation as to how they might make a tangible impact to reduce death and disability from cardiovascular disease within the American public. In the fall of 1998, the Reynolds Foundation announced a national competition for a grant to establish a Center that would address the problems we are discussing. In their Request for Applications they stated:

> "Advances in cardiovascular disease prevention and treatment require progress across the broad spectrum of activities ranging from fundamental laboratory science, clinical research, health services research, technology transfer, device and drug development and strategies that will facilitate prevention . ... [to] encompass the following goals:
>
> a) Contribute to new knowledge that will speed progress toward a cure for atherosclerotic heart disease.
> b) Effectively translate new knowledge into applications that will improve health and prevent cardiovascular diseases.
> c) Demonstrate new intellectual and organizational strategies for facilitating translational research and clinical trials, health services research, epidemiology and biostatistics in atherosclerotic heart disease to achieve scientific advances that will lead to the improvement of health.

d) Demonstrate effective programs for the education and training of clinical investigators who will become leaders in research in atherosclerotic heart disease.
e) Create innovative and productive approaches for collaborating among scientists at multiple institutions and across disciplines in the conduct of translational and patient-oriented research."

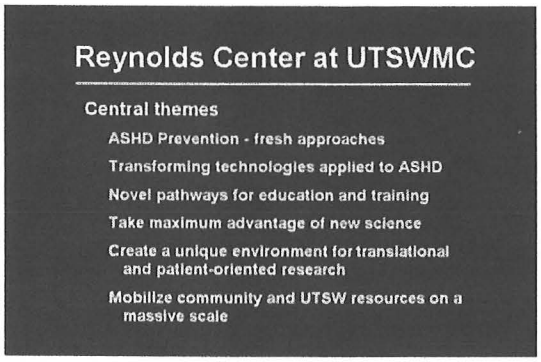
The Reynolds Foundation contracted with The American Heart Association to review the applications and to decide who would receive funding. The peer review committee was lead by Dr. Kenneth Shine, the President of the Institute of Medicine of the National Academy of Sciences. The announcement of this opportunity was timely in relation to the how several of us at UT Southwestern Medical Center were thinking about these global problems, and we prepared our proposal between December 1998 and April 1999. The final application included over 850 pages, merging the efforts of more than 40 of our faculty. We were encouraged when the recommendations of the NHLBI SPARK Working Group appeared to corroborate the fundamental approaches we had incorporated into the proposal. The primary architects of our plan were Drs. Helen Hobbs, Ron Victor, Eric Olson and myself, though many others made pivotal contributions. The review process culminated in June 1999 when we defended our proposal in a six hour face-to-face session with the review committee. A few days later we were notified that, alone among American medical centers, over 40 of whom had applied originally, UT Southwestern had been selected as the site for the D.W. Reynolds Center for Clinical Cardiovascular Research.

What is the Reynolds Center at UT Southwestern and how does it address the unmet challenges of cardiovascular disease?

A "cure" for atherosclerotic heart disease, defined conservatively as a ten-fold reduction in age-matched rates of morbid events resulting from ASHD in all segments of the American population, represents an important current goal of medical science. We argued that primary prevention of atherosclerotic heart disease at its inception through the elimination of hyperlipidemia, hypertension and diabetes, and prevention of heart failure provoked by ASHD, hypertension or diabetes, provide the most logical points of attack to achieve this end.

Since ASHD arises from a dynamic interplay between predisposing genetic variations and features of the social environment, successful strategies for reducing risk should accommodate both of these dimensions. Since progress in biomedical science is driven by technological advances, successful strategies should efficiently create and incorporate these innovations. Since existing modes of academic organization and operation have not solved the problem, successful new strategies should seek multidisciplinary synergism, drawing strength from individuals of highly disparate expertise. Our Center has been constructed on these premises. Our proposed translational research programs are designed to generate new technologies to be introduced into the clinical arena. Our Center will create intimate partnerships between top scientists accomplished in discovery biology and investigators skilled in translational and clinical research disciplines. Our

Center will seize opportunities provided by the Human Genome Project (23) and other advances in biomedical science and technology, and mobilize the collective expertise and resources of many individuals to make tangible progress towards a cure for ASHD.



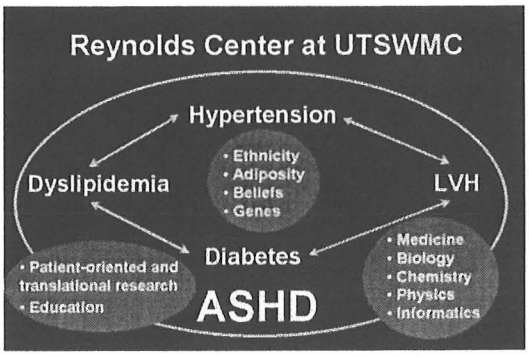


Fig. 5 & 6. Themes and interdisciplinary components of the Reynolds Center.

The burden of ASHD, heart failure, and their antecedent risk factors is uneven among different ethnic groups, and the gaps between higher and lower risk populations are increasing (Fig. 1). The need for new preventive measures and programs is particularly acute in urban minority neighborhoods. The creation of a Reynolds Center at UT Southwestern will have an immediate real life impact on health care in Dallas for high risk populations, with measurable benefits within the project period of the award. The ultimate impact we seek, however, is inclusive of all segments of our population in Dallas County and in the nation. We expect our Reynolds Center ultimately to produce tangible outcomes: 1) new devices, drugs and procedures of general utility to reduce risk for death from cardiovascular disease; 2) model programs that can be adapted in other urban communities for control of major risk factors; 3) a cadre of academic physician-scientists uniquely prepared to meet this challenge.

Summary of Reynolds Center Operations

The Center began operation on 10/1/99 with an initial grant of $24 million over four years. There will be an opportunity, based on strong initial performance, to extend the award to $60 million over 10 years. Our stated goals 1) to improve primary prevention of atherosclerotic heart disease (ASHD), and 2) to prevent or reverse heart failure resulting from ASHD. We believe that these goals can be achieved most effectively by breaking down traditional academic barriers between laboratory-based science and population- or patient-based investigation, and by incorporating the products of the ongoing revolution in molecular genetics and biotechnology as core elements of clinical and epidemiological research projects. Our strategic plan to achieve these goals calls for the development of novel conceptual and organizational paradigms in three areas of operation.

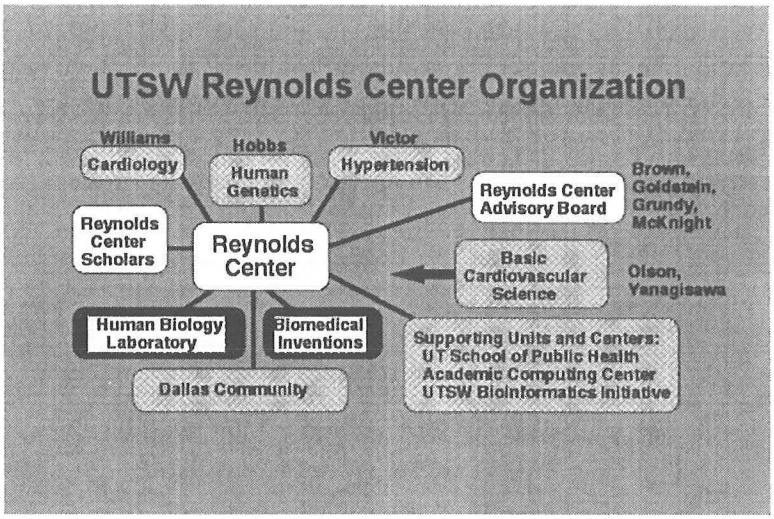


Fig. 7. Organizational Chart of the Reynolds Center.

1) The Human Biology Laboratory (HBL) or Clinical Research Unit (CRU): Under the operational leadership of Dr. Tom Andrews, a random, multiethnic population data base will be developed by testing of 7000 individuals aged 18-65 from Dallas County. Each subject will be characterized with respect to medical history, family history, blood pressure, fasting lipoproteins and other plasma constituents, EKG, MRI to assess cardiac mass and geometry, MRI to assess regional body fat, and EBCT to assess coronary calcification. DNA will be banked from each subject for genotyping. Subjects will be followed by telephone contact, and by automated tracking of hospital admissions to 47 area hospitals.

Subjects from the HBL population who manifest specific phenotypes will participate in one or more substudies that are funded by the original grant, and that call for additional testing. Importantly, the HBL is intended also to serve as a resource for additional studies to be proposed subsequently, and funded from other sources. We will welcome proposals from other investigators, from UTSWMC or elsewhere, for additional analyses using this population.

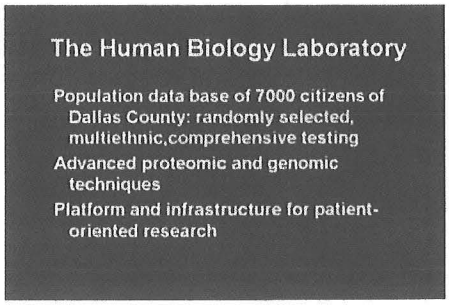
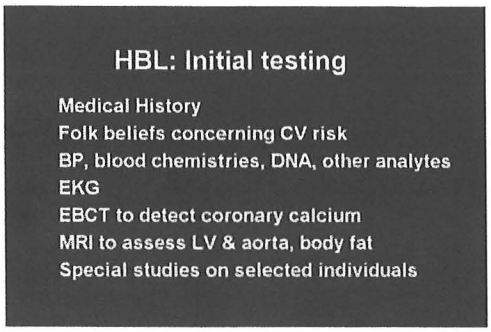


Fig. 8. Components of the Human Biology Laboratory (also called the Clinical Research Unit).



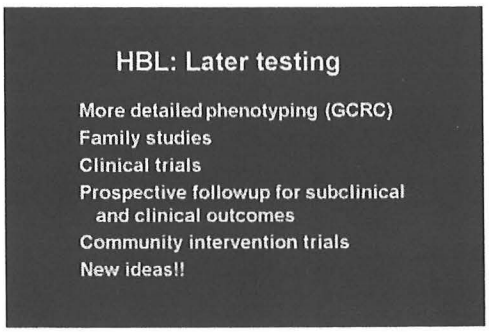


Fig. 9 & 10. Initial and later testing of the population.

The Human Biology Laboratory: Specific Project Goals

1) Elucidate novel risk factors and intermediate phenotypes that translate into new interventions to lower risk for ASHD.
2) Measure subclinical outcome variables that translate into novel interventions to reduce risk for ASHD.
3) Measure clinical outcome variables that translate into novel interventions to reduce risk for ASHD.
4) Develop novel strategies to prevent salt-dependent hypertension.
5) Develop novel strategies to prevent obesity-related hypertension.
6) Identify novel intermediate phenotypes and susceptibility genes that predict cardiac and vascular hypertrophy and remodeling.
7) Determine the metabolic mechanisms responsible for the lower plasma levels of TG, and higher plasma levels of HDL-C and Lp(a) in African-Americans, and identify the DNA sequence variants that contribute to these differences.
8) Identify intermediate phenotypes and DNA sequence variants associated with differences in lipoprotein levels, and determine if they more accurately reflect coronary atherosclerotic burden.

2) The Center for Biomedical Invention (CBI): A program of translational research will be initiated to develop new devices, drugs or procedures that improve prevention or therapy of atherosclerotic heart disease and its clinical sequelae. The CBI was conceived originally by Dr. Stephen Johnston and is designed to function as an incubator wherein fundamental discoveries are advanced to the point that they have sufficient practical and commercial potential to justify their transfer to pharmaceutical or biotechnology companies for further development and application. The CBI is explicitly multidisciplinary, and incorporates investigators of different backgrounds including chemistry, physics, engineering, and information sciences, as well as biologists and clinical investigators.

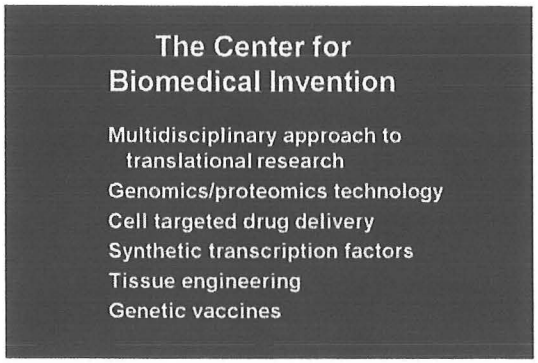


Fig. 11. Components of the Center for Biomedical Invention.

An initial series of focused translational research projects within the CBI are funded by the Reynolds Grant. The intent is for Reynolds funds to support projects to the point that they acquire independent funding from other sources, or are transferred to industry. As specific projects mature, Reynolds funds will be redirected to new inventions. The proposed translational research agenda includes several emerging areas of biomedical science – novel technologies for drug discovery, genomics, proteomics, cell and molecular targeting strategies, and stem cell transplantation – that ultimately will be focused on prevention of ASHD and its complications.

The Center for Biomedical Invention: Specific Project Goals

1) Develop novel therapeutic strategies targeted to skeletal muscles for the treatment of insulin resistance and diabetes.
2) Develop a device capable of rapid and inexpensive production of complex, high density microarrays of oligonucleotide or chemical libraries.
3) Develop synthetic transcription factors with potential as drugs to prevent atherosclerotic heart disease and its sequelae.
4) Develop techniques for selective delivery of drugs or DNA to cells of the liver, heart or coronary vasculature, so as to improve clinical therapeutics of atherosclerotic heart disease and heart failure.
5) Develop cell transplantation techniques for repair of damaged myocardium to prevent cardiac failure.
6) Develop novel inhibitors of hypertrophic signaling pathways and conduct preclinical testing in genetically engineered mouse models of heart disease.
7) Identify candidate genes for human genetic studies of cardiac hypertrophy and failure, and assess the functional consequences of sequence variants identified in human genetic studies.

3) Educational Programs: The Reynolds Center has an educational mission designed to prepare trainees for success in a rapidly changing research environment. Funding is available from the Center to support career development at several levels: junior faculty, fellows and students. Trainees will participate in an innovative and rigorous program pioneered by Dr. Charles Pak ("the Curriculum for Patient-Oriented Research") that includes formal course work biostatistics, study design, etc.), workshops, seminars, and preceptorships that can be integrated with advanced clinical training (e.g. cardiology

fellowship) and/or original research conducted in association with distinguished mentors. The emphasis is on patient-oriented research in the context of the HBL, or translational research in the context of the CBI, but trainees will gain some familiarity with both environments.

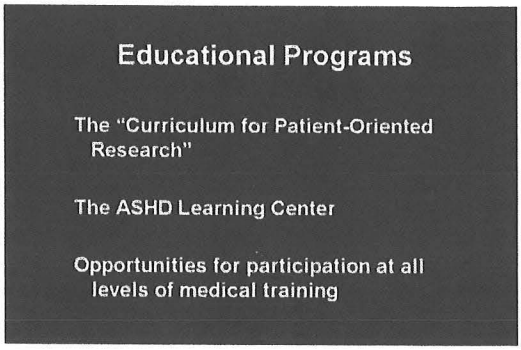


Fig. 12. Components of the educational programs of the Reynolds Center.

The Reynolds Scholars and Consultants: A distinctive feature of the Reynolds Center is the formal participation of outstanding senior scientists from other institutions. These individuals will function in an advisory capacity, and will direct original research in collaboration with UT Southwestern investigators. In addition, these individuals will take on mentorship roles with respect to Reynolds Center Fellows.

An example of the integration of Basic, Translational and Patient-Oriented Research

Gene-environment interactions as determinants of cardiac hypertrophy: Basic research has defined many of the fundamental molecular events by which the myocardium responds to changes in contractile load or neurohormonal stimulation. An important discovery in this area was made recently by Dr. Eric Olson and colleagues, who defined a role for the protein phosphatase calcineurin in the control of cardiac hypertrophy (13). The activity of calcineurin is modulated by changes in intracellular calcium evoked both by contractile demand and by the action of extracellular signaling molecules such as angiotensin II that bind cell surface receptors and trigger intracellular signaling cascades. The calcineurin pathway acts in concert with other signaling molecules in a complex cascade to control the functional activity of several transcription factors that serve as the terminal effectors to alter expression of genes involved in the hypertrophic growth process. A recent model of these interactions is shown in Fig. 13.

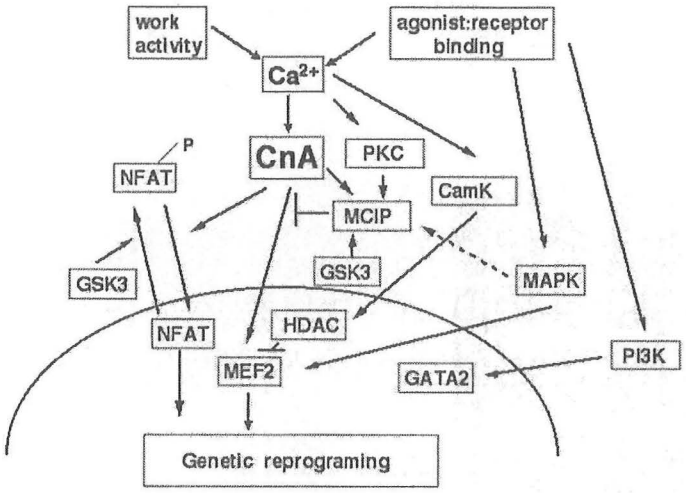


Fig. 13. Components of signaling pathways that control muscle phenotypes.

Translational research within the Reynolds Center seeks to provide us with measures (new drugs or gene therapies) to alter the activity of proteins within these pathways, thereby to control cardiac growth and prevent heart failure. In addition, we expect to advance technologies for assessing left ventricular mass and geometry through cardiac imaging (an effort led by Dr. Ron Peshock), and to pioneer new methods for assessing the sequence and expression of specific genes.

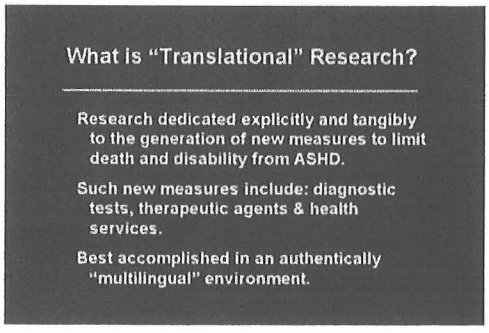


Fig. 14. A definition of translational research.

The latter effort relies in part on a technology developed locally by Dr. Skip Garner and colleagues called digital optical chemistry (Fig. 15). This invention combines photochemical methods for DNA synthesis with a computer-controlled micromirror device (from Texas Instruments) to generate microarrays that can be used to assess expression of genes or to define genetic variations among individuals. Currently in prototype phase, the DOC instrument promises to reduce the time and expense required to generate microarrays for genetic analysis by a factor of 100-1000 in comparison to current methods.

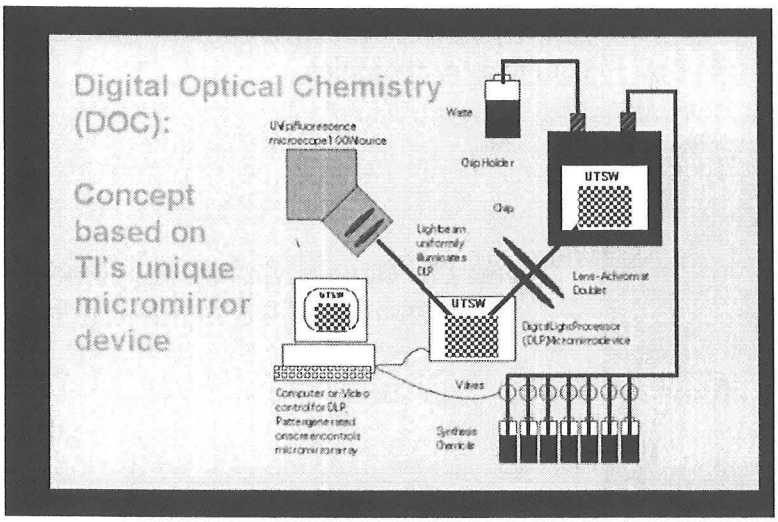


Fig. 15. Digital optical chemistry for construction of microarrays.

These and other technologies will link translational research within the Reynolds Center directly to several categories of patient-oriented research, illustrated in Fig. 16. We plan to explore gene-environment interactions as determinants of left ventricular mass within the Reynolds Center cohort in the manner illustrated in Fig. 17. Left ventricular hypertrophy is a major predictor of cardiovascular mortality in the presence or absence of concomitant coronary artery disease (12). Dr. Mark Drazner is leading this effort from the clinical end, with support from Dr. Richard Cooper, one of the Scholars from another institution, and from Dr. Ralph Shohet. The cardiac imaging studies included in the initial phase of testing of participants included within the random population sample of the Human Biology Laboratory will afford a precise measurement of left ventricular mass in each individual.

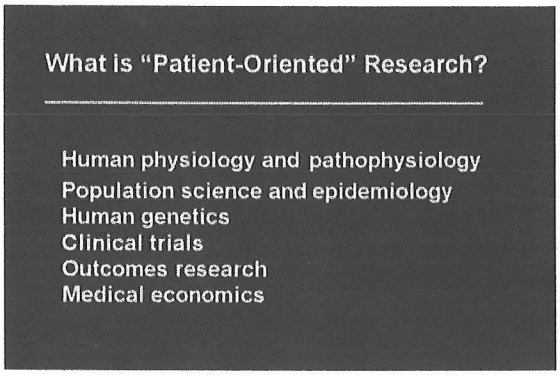


Fig. 16. Categories of patient-oriented research.

Based on information available from the literature, we will calculate for each individual the left ventricular mass predicted on the basis of blood pressure, body mass, adiposity and other clinical variables and compare this to the actual measurement defined by MRI. Those individuals with a left ventricular mass that deviates significantly from the predicted value are likely to carry genes that render them more sensitive or more resistant to hypertrophic stimuli than the average person. The likelihood of a genetic contribution will be increased further if such a deviation from the predicted value is heritable, i.e. also

found in first degree relatives. The genotype of persons with such extreme phenotypes will be determined using DOC (see Fig. 15) or other technologies.

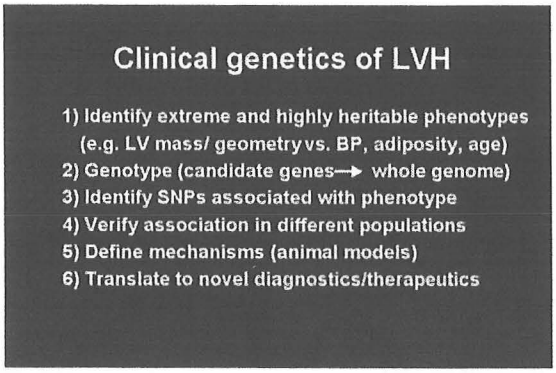


Fig. 17. Gene-environment interactions as determinants of left ventricular mass.

The specific genes to be interrogated initially will be limited to those already implicated in the pathogenesis of LVH and to additional candidate genes selected on the basis of a predicted pathogenic role (see Fig. 13). Ultimately, however, as the technologies improve, we expect to extend the genotyping analysis to an increasingly complete set of genes. In doing so, we will take advantage of progress within the Human Genome Project (23), using new locally developed tools for bioinformatics that are suitable for handing the massive data sets required for this type of investigation. A code called Panorama (Fig. 18) developed by the Garner group provides an example. Other informatic tools process and analyze microarray data, or predict sites within thehuman genome most likely to harbor polymorphisms that have a causal relationship to human diseasse. We are aware of the potential pitfalls of population based genome-scanning studies, and our study designs will be guided by the premise that a rigid and careful definition of the clinical phenotype is the first key to success (5).

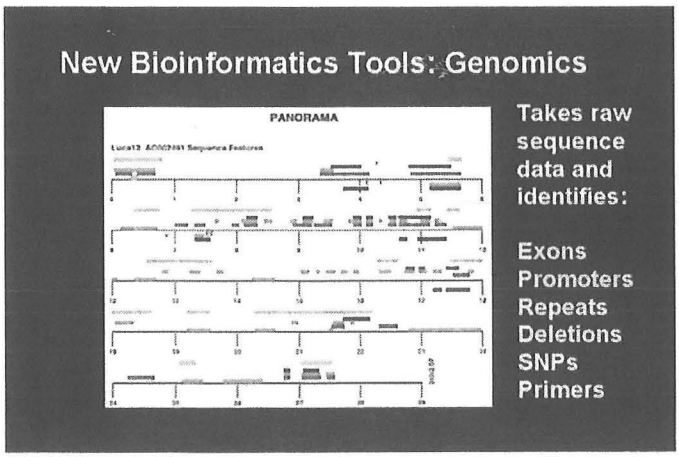


Fig. 18. Panorama, a bioinformatic tool for viewing the organization of a given gene.

What Do We Expect to Accomplish?

Our mission is to have a tangible impact on mortality and morbidity from atherosclerotic heart disease, heart failure and associated disorders, within the Dallas Community and nationwide. We have approached this formidable task in two phases, each of with will occupy about five years. The first period will be devoted to constructing and optimizing the three platforms – the Human Biology Laboratory, the Center for Biomedical Invention, and the Education Program – on which progress of the Center depends. Some tangible goals for this phase are stated in Fig. 19.

Fig. 19 & 20. 5 year and 10 year time horizons for the Reynolds Center.

If we are successful in launching this initiative, we expect both to renew the Reynolds Grant and to attract additional resources to carry on into a second and even more ambitious phase within the following 5 years. As shown in Fig. 20, in the second phase we will implement new programs of community intervention, the basis for which has been established in the first 5 years, and demonstrate their effectiveness by controlled trials within the community. We expect to involve an ever increasing number of trainees and faculty colleagues in this effort as it grows, and to link our local efforts to a network of similar initiatives at other institutions.

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Appendix I: The People of the Reynolds Center

Principal Investigators, Project leaders and Participating Faculty

R. Sanders Williams (cardiology)
Helen Hobbs (human genetics)
Ron Victor (hypertension)
Eric Olson (molecular biology)
Masashi Yanagisawa (molecular genetics)
Chris Newgard (diabetes)
Skip Garner (genomics & informatics)
Stephen Johnston (molecular biology)
Tom Kodadek (chemistry)
Bob Haley (epidemiology and biostatistics)
Ron Peshock (imaging)
Tom Sato (vascular biology)
Rhonda Bassel-Duby (molecular biology)
Jonathan Cohen (human genetics)
Ken Jialal (clinical chemistry)
Bob Meidell (cardiology)
Roger Unger (diabetes)
Anne Freeman (community intervention)
Ivor Benjamin (cardiology)
Micheal DeMaio (cardiac surgery)
Joan Reisch (biostatistics)
Makoto Kuro-O (biology of aging)
Gail Thomas (neurobiology)
Kathryn Sykes (CBI)
Kevin Luebke (CBI)
Kathlynn Brown (CBI)
DuWayne Willett (cardiology)
Cheryl Gariepy (molecular genetics)
Weiguo Zang (hypertension)
Zhen Yan (cardiology)
Barbara Moses (cardiology)

Reynolds Center Associates (Junior faculty with major roles):

Tom Andrews (HBL Director)
Deepak Srivastava (congenital heart disease)
Dan Garry (stem cell biology)
Ralph Shohet (genomics)
Rob Kowal (cardiac arrhythmias)
Nina Radford (womens' health)
Joe Garcia (transcription factors)
Mark Drazner (cardiac hypertrophy)

Other participating UTSW faculty:

Mike Brown (Co-chair of Scientific Advisory Board)

Joe Goldstein (Co-chair of Scientific Advisory Board)

Steve McKnight (Scientific Advisory Board)

Scott Grundy (Scientific Advisory Board)

Dan Foster (Scientific Advisory Board)

Dennis McGarry (Scientific Advisory Board)

David Garbers (Scientific Advisory Board)

Ron Anderson (Scientific Advisory Board)

John Rutherford (Chair of HBL Quality Control Committee)

David Hillis (Chair of Education Committee)

Reynolds Center Scholars and Consultants (other institutions)

Richard Cooper (Loyola University)

Jeffrey Leiden (Harvard University)

David Siscovick (University of Washington)

Stuart Schreiber (Harvard University)

Darwin Labarthe (Center for Disease Control)

Loren Field (Indiana University)

Adminstrative Staff

Cindy Lawson - Reynolds Center Administrative Director

Pat O'Brien - Assistant to Dr. Sanders Williams

Teresa Bosler - Network Supervisor

Laura Fuller - Assistant to Dr. Helen Hobbs

Anne-Marie January – Assistant to Dr. Stephen Johnston and the CBI

Wanda Simpson - Assistant to Dr. Eric Olson & Molecular Biology/Oncology

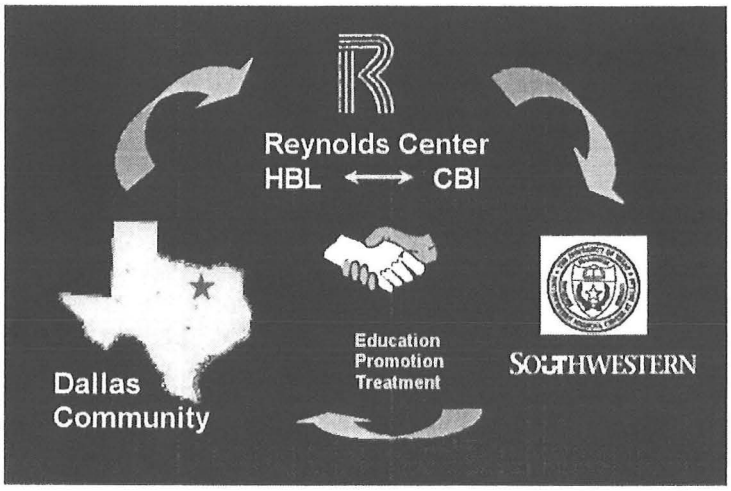
Stacey Siegh - Assistant to Dr. Ron Victor and the Division of Hypertension

Nicola Coburn - Assistant to Dr. Tom Andrews and the Human Biology Lab

Deborah Baker, RN - Phlebotomy Supervisor for the Human Biology Lab

Jeff Schageman, - Genomics Data Supervisor

Appendix II: Contact Information



Visit our Web page: cardiology.swmed.edu/reynolds

Call or email Ms. Pat O'Brien (Reynolds Administrator)
(214) 648-1421
O'brien@ryburn.swmed.edu

Get involved!

Opportunities for residents and students:
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- Educational resources of the Learning Center on H8

How do I get involved?

- Visit our Web Page
- Come to the Learning Center
- Get on our mailing list and participate in educational activities
- Talk with faculty about your interests

Get involved!

Opportunities for faculty:
- Participate in the educational activites
- Use the data base
- Use the infrastructure
- Get support for specific projects or career development