Carolina Center for Genome Sciences
&
Department of Genetics

Five-year Report
2000 - 2005

Dr. Terry Magnuson, Director and Chair

Submitted to the Office of the Dean
School of Medicine
University of North Carolina at Chapel Hill

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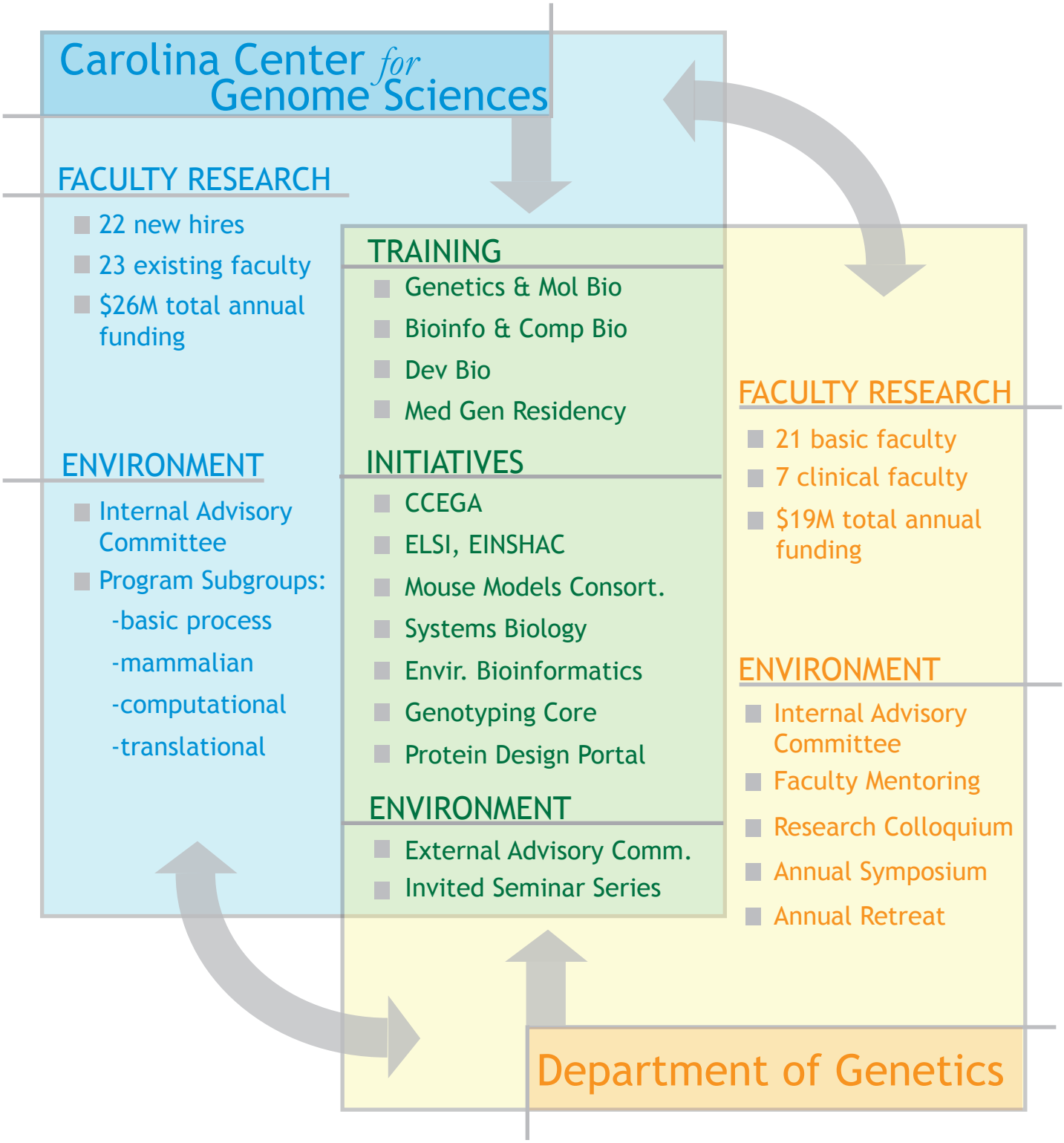
I. Introduction

Genomics is the comprehensive analysis of the entire genetic blueprint of an organism. Genomics was born through technical advances in the last decade leading to facile DNA sequencing of entire genomes of organisms beginning in 1995, with the sequence of the first free-living organism, a bacterium called *Haemophilus influenzae*, containing 1.8 million base pairs of DNA. Since then, an explosion of sequence information has emerged from organisms as diverse as bacteria, yeast, flies, mice and plants. In April 2003, the largest and most ambitious project to date—the human genome—was finally completed, with all 3 billion base pairs spelled out. This was clearly a landmark scientific and technological achievement, but it is merely the beginning of the long road of discovery that lies ahead. Genomics encompasses the work required to make sense of all this raw sequence data. We can now begin to ask questions that were never possible before: Which genes are turned on in cancer cells that are off in normal cells? How many targets does a particular drug or pesticide have? Why do certain drugs work for some patients but not others? What are the genes that make mice different from humans? Indeed, how does one define the human species at its most fundamental level? Answers to these and many other important questions will be forthcoming as vast amounts of sequence data are analyzed and interpreted by genomic researchers from many different basic and applied disciplines.

Terry Magnuson was recruited in July of 2000 with the charge of developing a vision that would provide the foundation for research and training in the genome sciences that would propel UNC-Chapel Hill to the forefront of the genomic revolution in the 21st century. Dr. Magnuson's biography and *curriculum vitae* can be found in Appendices 1.1 and 1.2, respectively. The plan put forward to the Chancellor and the UNC System Board of Governors was to create the Carolina Center for Genome Sciences (CCGS) (http://genomics.unc.edu/) as a campus-wide umbrella organization to coordinate and stimulate growth in basic and applied genomics research, education and training at the interface between biology, chemistry, physics, computer science, mathematics, the social sciences, public health and medicine. Because this new knowledge will form the basis for novel, individualized treatment and prevention strategies for human disease, and thus have a profound effect on how medicine will be practiced in the future, a critical part of the plan was the creation of a new Department of Genetics in the School of Medicine (http://www.med.unc.edu/geneticsdept/). The new department was envisioned as a springboard from which mammalian/human geneticists would serve as the translational arm for genomic medicine, bringing practical applications from genomics into the clinical arena. Although the CCGS and the Department of Genetics have clear, distinct missions, there is compelling synergy and organizational overlap such that both programs require close coordination to achieve maximum success (see Figure on next page for overview of the two programs). Thus, it was decided that one person should lead both efforts. This report summarizes our progress during the last four years and describes future areas of programmatic growth.

II. Background

Carolina Center for Genome Sciences: In July 2000, the Chancellor created 18 new faculty positions for the CCGS. These positions were funded with recurring salaries to be split equally between the CCGS and the respective home departments where their primary academic appointments would be held. Start-up funds were provided for each position. Soon after these commitments were made, a plan for distributing the positions among the academic departments was presented by the CCGS Director and approved by the participating Deans of the academic units involved. These include the College of Arts and Sciences (6.5 positions), the School of Information and Library Sciences (1 position) and the five Health Affairs Schools: Medicine (4.5 positions), Public Health (3 positions), Dentistry (1 position), Pharmacy (1 position) and Nursing (1 position). The School of Public Health added funds from their own resources to create another three genomics positions (splitting the 3 CCGS positions among 6 faculty).



Schematic Summary of CCGS/Genetics Five-year Report (2000-2005)
Under the leadership of Terry Magnuson, two distinct but synergistic entities were created to establish an innovative research and training environment that effectively integrates basic and clinical research in genetics/genomics with healthcare and public policy. The Carolina Center for Genome Sciences and the Department of Genetics have recruited an outstanding mix of new hires and existing UNC faculty to form a solid research foundation. Faculty from both CCGS (blue) and Genetics (yellow) have worked together with Dr. Magnuson and his administrative organization to build new research initiatives, training programs, and a research environment that takes full advantage of their combined strengths (green).

Thus, the total number of new faculty recruited to campus is now 22 (including those with partial positions). The home departments and the CCGS conducted the faculty recruitments and all 22 positions have been filled (Appendix 2.1). In addition to these new appointments, 23 existing faculty (Appendix 2.2) who contribute to key components of our mission were invited to join the CCGS. The total external funding for the entire CCGS faculty is $26,044,380 of which $12,322,047 are funds brought in by the 22 recruited with CCGS funds (Appendix 2.3). The biosketches of the entire CCGS faculty can be found in Appendix 2.4.

The Department of Genetics: The Dean of the School of Medicine created 10 new faculty positions for the Department. These positions were funded with recurring salary dollars. In addition, a Howard Hughes Medical Institute grant provided start-up funds that were supplemented by the Dean's office. To provide the necessary synergy between the CCGS and the Department, the 4.5 CCGS positions assigned to the School of Medicine were placed in the Department of Genetics and they were used for recruitment of human geneticists. Additional partnerships with the Lineberger Comprehensive Cancer Center, the Neuroscience Center, the Vaccine Institute and the Program in Molecular Biology and Biotechnology have allowed us to expand our primary faculty to a total of 14 tenure-track, 1 clinical-track and 4 research-track appointments (Appendix 3.1). Sixteen of these faculty are new recruits to the campus and three are transfers from other UNC departments. Ten additional faculty (Appendix 3.2) have joint (secondary) appointments, drawn primarily from clinical department faculty conducting genetics-related research and/or clinical work. The external funding for the Genetics primary faculty is $18,944,976 (Appendix 3.3). The biosketches of both the primary and secondary faculty can be found in Appendix 3.4.

In summary, the CCGS and Department of Genetics have recruited all of the 32 allotted new faculty to UNC-CH in 5 years. The distribution of faculty rank and research interests will be displayed in a set of tables as the program is described.

III. CCGS Organization & Research Programs

The genome science revolution is increasingly interdisciplinary, requiring expertise in animal and plant molecular biology, structural biology, genetics, cell biology, developmental biology, microscopy and imaging, bioanalytical, and combinatorial chemistry, applied biotechnology, clinical medicine, mathematical modeling, computer science, bioinformatics and computational biology. The CCGS focused its faculty recruitment on four thematic research areas (basic process genomics, computational genomics, mammalian genomics, and translational genomics) that builds upon existing research strengths at UNC-Chapel Hill and encompass the growing obligation to educate students in this new arena. The CCGS also plays a major organizational role in ensuring synergy in research and teaching across academic units.

CCGS Organization: To coordinate these efforts an Associate Director for Research as well as an Internal Advisory Committee (IAC) were appointed. The IAC consists of the Director, Associate Director for Research and six program leaders representing the four thematic research areas. This group meets weekly to discuss all aspects pertaining to CCGS operations. All other CCGS faculty belong to one of the four research programs, each of which meets once every other month to discuss research-related issues. On alternating months, Center-wide faculty meetings are held where program leaders summarize recent issues and research initiatives discussed in their respective programs, and one faculty member presents his/her research to the rest of the Center.

CCGS Internal Advisory Committee

Position	Name
Director	**Terry Magnuson, PhD**
Associate Director for Research	**Mary Sym, PhD**
Program Leaders	**Jeff Dangl, PhD** - Basic Process Genomics **Jim Evans, MD, PhD** - Translational Genomics (Medical Genetics) **David Threadgill, PhD** - Mammalian Genomics **Alex Tropsha, PhD** - Computational Genomics (Proteomics) **Marcia Van Riper, PhD** - Translational Genomics (ELSI) **Fred Wright, PhD** - Computational Genomics (Statistics & Bioinformatics)

CCGS Research Programs:

- **Basic Process Genomics -** Basic discoveries and tools developed in biology and chemistry provide a foundation upon which many advances in applied genomics and technologies have emerged. Many of the faculty in the Basic Process Genomics group work with model organisms such as yeast, *Drosophila*, and *Arabidopsis* whose genomes are extensively characterized at the genetic and molecular level. The ability to perform comprehensive and rapid genomic analyses and manipulations in these organisms allows researchers to ask many fundamental questions about how genes are regulated, how proteins interact, how cells communicate, and how organisms develop and evolve. Such questions necessitate the development of important computational, molecular, micro/nanofluidic and chemical tools to facilitate large-scale analysis and high-throughput assay development.

Basic Process Genomics Group

Name	Research Interests
Greg Copenhaver, PhD Assistant Professor of Biology	Chromosome structure and function in *Arabidopsis*, meiotic recombination, centromere function.
Jeff Dangl, PhD (program leader) Professor of Biology	Host-pathogen interactions in *Arabidopsis*, plant immune system, bacterial pathogenesis.
Corbin Jones, PhD Assistant Professor of Biology	*Drosophila* genome evolution and adaptation; statistical and bioinformatic tools for evolutionary genomics.
Jason Lieb, PhD Assistant Professor of Biology	Genome-wide mapping of protein-DNA interactions using microarrays, genome organization, chromatin structure and function.
Rihe Liu, PhD Assistant Professor of Medicinal Chemistry	Defining interactions on a proteomic scale, mRNA display, enzyme-substrate interactions, protein degradation.
Mike Ramsey, PhD Professor of Chemistry	Microfabricated chemical instrumentation, micro- and nanofluidic technologies.
Steve Rogers, PhD Assistant Professor of Biology	Functional genomics, high-speed resolution imaging, cytoskeletal organization in *Drosophila.*
Todd Vision, PhD Assistant Professor of Biology	Plant comparative genomics, evolution of genome organization.
Muhammad Yousaf, PhD Assistant Professor of Chemistry	Applications of surface chemistry and material science to cell biological problems: cell adhesion, migration, cell-cycle regulation, membrane enzymology.

- **Computational Genomics** - One of the great challenges in this era of genomics is to extract meaningful biological information from extremely large, complex, and noisy datasets. Whether the goal is to find genes linked to complex traits, or to understand sequence structure-function relationships, or to decipher transcriptional networks, there is a critical need for novel computational and theoretical analyses of biological processes. The Computational Genomics group brings together faculty with expertise in a diverse but synergistic fields such as bioinformatics, statistics, data mining, machine learning, protein folding, and mathematical modeling. Many of these faculty have close collaborations with experimental biologists and geneticists in order to develop, test and optimize their computational tools. One of the major roles of the CCGS is to foster these types of relationships and to bridge communication among faculty with different expertise towards a common goal.

Computational Genomics Group

Name	Research Interests
Nikolay Dokholyan, PhD Assistant Professor of Biochemistry	Protein folding and aggregation, molecular dynamics simulations methodologies.
Tim Elston, PhD Associate Professor of Pharmacology	Mathematical modeling of complex biological systems, intrinsic noise and stochastic events in biological processes.
Morgan Giddings, PhD Assistant Professor of Microbiology & Immunology	Computational and experimental proteomics, genome annotation, drug resistance.
Mayetri Gupta, PhD Assistant Professor of Biostatistics	Statistical and computational approaches to find patterns or motifs in genome sequences, gene regulatory modules, interaction networks.
Brad Hemminger, PhD Assistant Professor, School of Information & Library Sciences	Genomic and medical database design and analysis, informatics, datamining, digital libraries.
Brian Kuhlman, PhD Assistant Professor of Biochemistry	Computational and experimental approaches for protein design, specificity of protein-protein interactions.
Yufeng Liu, PhD Assistant Professor of Statistics & Operations Research	Statistical methodologies for general classification problems, machine learning, support vector machines.
Alex Tropsha, PhD (co-program leader) Professor of Medicinal Chemistry	Computational analysis of protein structure/function relationships, computer-assisted drug design, structural annotation of genomes.
Wei Wang, PhD Assistant Professor of Computer Science	Classification and clustering algorithms, protein motif recognition, datamining methodologies.
Fred Wright, PhD (co-program leader) Associate Professor of Biostatistics	Statistical methods for gene mapping and gene expression analysis, computational tools for genome annotation.
Fei Zou, PhD Assistant Professor of Biostatistics	Statistical and theoretical analysis of quantitative traits, association data, and gene-expression profiling, statistical tools for comparative genomics.

- **Mammalian Genomics -** The completion of the human and mouse genomes has stimulated a growing interest in understanding the often complex relationship between mammalian gene function and disease. All of the faculty in the Mammalian Genomics group share interests in elucidating the genetic basis of human disease; each provides unique perspective and expertise in areas like human genetics, mouse models, epidemiology, and statistics. Maximizing the interplay among these highly complementary approaches is critical to success and will provide unprecedented opportunities to advance human health.

Mammalian Genomics Group

Name	Research Interests
Eric Everett, PhD Associate Professor of Pediatric Dentistry	Genetics of craniofacial and dental development, mouse models of palatogenesis and dental fluorosis.
Ethan Lange, PhD Assistant Professor of Genetics	Development and application of statistical genetic methodologies, human disease gene mapping, prostate cancer susceptibility.
Leslie Lange, PhD Research Assistant Professor of Genetics	Genetic epidemiology of cardiovascular disease, chronic inflammation, prostate lanceer, asthma.
Terry Magnuson, PhD Professor of Genetics	Genomic imprinting, X-chromosome inactivation, epigenetics, genome-wide functional analysis in mouse.
Bob Millikan, PhD Associate Professor of Epidemiology	Genetics and epidemiology of breast cancer and melanoma, gene-environment interactions.
Karen Mohlke, PhD Assistant Professor of Genetics	Genetic analysis of complex traits, type-2 diabetes susceptibility.
Kari North, PhD Assistant Professor of Epidemiology	Genetic and environmental etiology of cardiovascular disease.
Fernando Pardo Manuel de Villena, PhD Assistant Professor of Genetics	Non-random segregation of chromosomes in mammals, asymmetrical cell division and polarity.
Charles Perou, PhD Assistant Professor of Genetics	Breast cancer genetics and toxicogenomics, microarray-based classification of tumor subtypes.
Daniel Pomp, PhD Professor of Nutrition	Genetic architecture of complex traits, metabolomics, obesity, livestock improvement.
Ivan Rusyn, PhD Assistant Professor of Environ. Sci. & Engineering	Molecular, biochemical and genomic approaches for elucidating the mechanisms of chemical-induced carcinogenesis.
Pat Sullivan, MD Professor of Genetics	Etiology of psychiatric and behavioral disorders: schizophrenia, smoking behavior, chronic fatigue syndrome.
David Threadgill, PhD (program leader) Assistant Professor of Genetics	Genetic and environmental factors contributing to cancer susceptibility, individual variation, mouse models.
Kirk Wilhelmsen, MD, PhD Associate Professor of Genetics	Genetic mapping of susceptibility loci for complex neurological diseases, high-throughput genotyping and data processing.

- **Translational Genomics -** Virtually all human diseases have a significant genetic component. The deluge of information resulting from the new science of genomics will shed light on the underpinnings of human disease and will define the individual genetic differences that determine susceptibility to those diseases. This emerging information will have an enormous impact on both the research and healthcare communities, necessitating an effective interface between them. Our burgeoning knowledge of genomics will change medicine in many ways and will influence issues such as confidentiality, informed consent, and discrimination. Thus, they require specific considerations in the context of a genomics research center's objectives. Gene-based approaches expand the language of "probability" and "susceptibility" to medical care, and have far-reaching implications that affect not only patients, but families, governments, insurers, law enforcement agencies and scientific researchers. The CCGS has incorporated a translational component within its mission to investigate the impact of basic scientific discoveries on society and public policy as well as 'translating' them directly into useful clinical tools.

Translational Genomics Group

Name	Research Interests
Art Aylsworth, MD Professor of Pediatrics	Medical genetics and dysmorphology, congenital malformations, bone dysplasias.
Don Bailey, PhD Professor, School of Education	Newborn screening, Fragile X syndrome, ELSI research on large-scale gene discovery and disclosure.
Giselle Corbie-Smith, MD Associate Professor of Social Medicine	Influence of culture, race, ethnicity, and social class on health and healthcare.
Jim Evans, MD, PhD (co-program leader) Associate Professor of Genetics	Clinical cancer genetics, breast cancer susceptibility.
Gail Henderson, PhD Professor of Social Medicine	Global health inequality and genetics research ethics.
Tony Johnson, DO Professor of Obstetrics & Gynecology	Fetal diagnosis and therapy, *in utero* interventions and screening for major fetal malformations.
Nancy King, JD Professor of Social Medicine	Bioethics and health law, human subjects research ethics and policy, informed consent
Joe Muenzer, MD, PhD Associate Professor of Pediatrics	Inborn errors of metabolism including mucopolysaccharidosis, lysosomal and glycogen storage disorders.
Dan Nelson, MS Associate Professor of Social Medicine	Director of Office of Human Research Ethics (UNC), ethical and policy issues surrounding human subjects research.
Cindy Powell, MD Associate Professor of Pediatrics	Cytogenetics, dysmorphology, genetic counseling.
Kathleen Rao, PhD Professor of Pediatrics	Director of Cytogenetics Laboratory, clinical genetics.
Marcia Van Riper, PhD (co-program leader) Associate Professor, School of Nursing	Social and ethical implications of genetic testing.

IV. Department of Genetics Organization & Research Programs

With the sequencing of the genome, human genetics has rapidly moved toward functional and computational analyses of genes and gene variation among different patient populations, families, etc. This vast and rich dataset is essential for understanding the detailed molecular pathogenesis of human disease. Since this new knowledge will form the basis for novel, individualized treatment, prevention, and intervention strategies, it will result in a profound transformation in the practice of medicine. The Genetics Department embraces a unified program devoted to outstanding research, clinical care and teaching in all areas of genetics with a particular emphasis on the relationship of genomics to animal models, human genetics and clinical genetics.

Organization: The Chair meets with the Internal Advisory Committee (IAC) twice a month (and more often on an informal basis) to discuss aspects pertaining to Department recruitment, policies and operations. Department-wide faculty meetings are conducted once per month and consist of business followed by a research presentation from one faculty member.

Genetics Department Internal Advisory Committee

Position	Name
Chair	**Terry Magnuson, PhD** - Professor
IAC members	**Shawn Ahmed, PhD -** Assistant Professor **Karen Mohlke, PhD** - Assistant Professor **Fernando Pardo Manuel de Villena, PhD -** Assistant Professor **Pat Sullivan, MD** - Professor **Terry Van Dyke, PhD -** Professor

Junior Faculty Mentoring: The academic home department is responsible for the mentoring of junior faculty. For CCGS faculty, the Director has input into this process. For the Genetics Department, mentoring committees have been arranged. The committees consist of the Chair and three other senior faculty members picked according to expertise. A faculty report (Appendix 3.5) is filed with the Chair and the committee in June. A meeting of the mentoring committee is held June/July to discuss progress. The goal is to provide guidance for building a strong portfolio for the tenure decision. In addition, committee members serve as readers for grant applications and manuscripts. The program has been extremely well received by the junior faculty.

Genetics Faculty Mentoring Committees

Junior Faculty	Mentoring Committee
Shawn Ahmed	T. Magnuson, B. Marzluff, J. Griffith, S. Matson
Frank Conlon	T. Magnuson, S. Milgram, J. Dangl, C. Patterson
Fernando Pardo Manuel de Villena	T. Magnuson, D. O'Brien, B. Weissman, R. Farber
Mark Heise	T. Magnuson, R. Swanstrom, N. Raab-Traub, B. Johnston
Ethan Lange	T. Magnuson, P. Sulllivan, M. Knowles, D. Lin
Leslie Lange	T. Magnuson, P. Sullivan, G. Heiss, K. Wilhelmsen
Karen Mohlke	T. Magnuson, M. Knowles, N. Maeda, P. Sullivan
Chuck Perou	T. Magnuson, S. Earp, A. Baldwin, C. Derr
Larysa Pevny	T. Magnuson, B. Snider, S. Crews, T. Van Dyke
Debbie Threadgill	T. Magnuson, T. Van Dyke, R. Farber, V. Bautch

Basic Research: The conceptual framework for the Department's basic research program is that individuals differ in disease susceptibility based upon either the inheritance of mutant genes in defined molecular pathways, or more commonly, polymorphic differences in low-penetrance susceptibility genes. Based on this framework we have emphasized a spectrum of research approaches based on model organisms, populations, and genomes.

Genetics Department Basic Research Faculty

Name and Rank	Research Interests
Shawn Ahmed, PhD Assistant Professor	*C. elegans* telomere replication, DNA damage response, germline immortality.
Scott Bultman, PhD Research Assistant Professor	Mammalian chromatin remodeling.
Kathleen Caron, PhD Assistant Professor	Genetics of reproduction, adrenomedullin, RAMPs, mouse models, pre-eclampsia, hypertension.
Frank Conlon, PhD Assistant Professor	Amphibian heart development and mesoderm patterning.
Rosann Farber, PhD Professor	Human molecular genetics, somatic cell genetics, genome instability.
Marc Heise, PhD Assistant Professor	Viral pathogenesis, virus-host interactions, genetics of virulence.
Beverly Koller, PhD Associate Professor	Models of inflammatory diseases.
Ethan Lange, PhD Assistant Professor	Statistical genetic methodologies, human disease gene mapping, prostate cancer susceptibility.
Leslie Lange, PhD Research Assistant Professor	Genetic epidemiology of cardiovascular disease, chronic inflammation, prostate cancer, asthma.
Terry Magnuson, PhD Professor	Chromatin remodeling, epigenetics, mammalian development.
Mark Majesky, PhD Professor	Coronary development, vascular stem cells, angiogenesis.
Karen Mohlke, PhD Assistant Professor	Human complex traits, genetics of type-2 diabetes.
Fernando Pardo Manuel de Villena, PhD Assistant Professor	Non-Mendelian genetics, chromosome segregation, chromosome evolution.
Charles Perou, PhD Assistant Professor	Breast cancer, genomics, microarrays, tumor classification, drug resistance.
Larysa Pevny, PhD Assistant Professor	Genetics of neural induction, *Sox* genes, stem cells.
Ned Sharpless, MD Assistant Professor	Cancer genetics, tumor suppressor genes, mouse tumor models, cell cycle and senescence.
Pat Sullivan, MD Professor	Complex traits in humans, psychiatric genetics, twin studies, schizophrenia, major depression, nicotine dependence.
David Threadgill, PhD Assistant Professor	Disease susceptibility, complex traits/QTLs, gastrointestinal biology, microarrays.
Deborah Threadgill, PhD Research Assistant Professor	*C. jejuni,* glycobiology, genetics of glycosylation.
Terry Van Dyke, PhD Professor	Cancer genetics, molecular carcinogenesis.
Kirk Wilhelmsen, MD, PhD Associate Professor	Genetic mapping of human susceptibility loci for complex traits, neurodegenerative disorders.

Clinical Activities & Research: An opportunity to expand the clinical human genetics efforts at UNC was created by a gift from Vaughn and Nancy Bryson. The Bryson Program in Human Genetics was officially established in July 2003 and is directed by Dr. Jim Evans, an integral faculty member in both Genetics and the CCGS. The vision for the program is based on facilitating and harnessing our burgeoning understanding of the genetic basis of common diseases. Such advances promise to have a profound impact on the practice of medicine in areas ranging from prevention to diagnosis and therapeutics. The field of medical genetics, which has historically been focused on a small number of rare diseases, faces a serious challenge: How do we expand our emphasis to encompass common diseases and provide useful advice and service to patients? Moreover, how can we help other physicians who will increasingly be called upon to incorporate genetics into their practices? If medical genetics does not successfully rise to this challenge it will fail to live up to the promise of the "genomic revolution." A three-pronged approach is being developed in the Department to accomplish widespread integration of adult genetics into medicine. Key features of this effort include:

(i) Receptive clinicians in several specialty areas have been identified who perceive the need for more advanced genetic analysis of their patients (e.g., Ron Falk-renal, Ric Boucher-pulmonary, Balfour Sartor-inflammatory bowel disease, Gene Orringer/Stephan Mohl-hematology, Cam Patterson-cardiovascular among others). A genetics team (clinical geneticist and genetic counselor) will participate in existing clinical conferences in order to identify and further refine precisely what the needs and opportunities are with respect to genetics.

(ii) A DNA bank has been established to provide easy and efficient collection of samples. Engagement with clinicians, access to patients and routine collection/processing of DNA samples will provide the infrastructure for important studies of genotype-phenotype relationships and pharmacogenomics.

(iii) A CLIA-approved laboratory will be established to carry out genetic testing that is clinically useful but not adequately available at present. A search is underway for a genotyping core director and for a bioinformatics team.

The challenges of integrating genetics into clinical medicine are most formidable in the realm of adult medicine. Unlike its counterparts in the pediatrics and prenatal arenas, genetics is a relative newcomer to adult medicine. However, in order to achieve true integration across disciplines and reap the benefits of our emerging knowledge for the institution as a whole, it is critical that our clinical efforts be integrated with existing efforts in pediatrics and obstetrics/gynecology (OB/GYN). Towards this end the clinical geneticists in both of these departments have secondary appointments in the Department of Genetics. Weekly meetings are held during which members of each department (Genetics, Pediatrics and OB/GYN) discuss clinical cases, research ideas and advances recently reported in the literature. These meetings are also attended by basic scientists, offering a rare example of true cross-disciplinary activity. Finally, the Bryson DNA processing facility and CLIA-approved laboratory described above will be of great benefit to pediatric genetics and counterparts in OB/GYN, facilitating clinical diagnosis of cases as well as enabling sophisticated and methodical investigation into phenomena identified in the clinic.

Genetics Department Clinical Research Faculty

Name and Rank	Clinical Interests
Art Aylsworth, MD Professor of Pediatrics	Pediatric medical genetics, phenotype delineation
Jim Evans, MD, PhD Associate Professor of Genetics Director of Bryson Program	Adult medical genetics, clinical cancer genetics
Tony Johnson, DO Professor of Obstetrics & Gynecology	Maternal-fetal medicine
Kathy Kaiser-Rogers, PhD Clinical Assistant Professor	Human chromosomal abnormalities
Joe Muenzer, MD, PhD Associate Professor of Pediatrics	Inborn errors of metabolism
Cynthia Powell, MD Associate Professor of Pediatrics	Dysmorphology and birth defects
Kathleen Rao, PhD Professor of Pediatrics	Clinical cytogenetics

V. Other CCGS & Genetics Initiatives

In addition to the major impact that modern genetics and genomics are having on biomedical research and scientific training, healthcare and public policy will be profoundly affected. It is important that we integrate these aspects to stay competitive and make the most of what genomics has to offer. In recent years, many funding agencies, most notably the NIH, have placed a greater emphasis on multi-investigator, interdisciplinary research. The CCGS and the Department of Genetics are well positioned to respond to this growing emphasis because we have established the necessary infrastructure, both scientifically and administratively to respond to these requests.

Carolina Center for Exploratory Genetic Analysis: The CCGS and the Department of Genetics partnered with the Renaissance Computing Institute (RENCI), led by Prof. Dan Reed (Dept. of Computer Science), to establish the Carolina Center for Exploratory Genetic Analysis (CCEGA). The purpose of the Center is to promote multidisciplinary, institutional collaboration amongst researchers in the biomedical and computing disciplines. Kirk Wilhelmsen (CCGS and Department of Genetics) and Alan Blatecky (RENCI) are coordinating this effort. The Center was recently funded by an NIH Roadmap P20 planning grant with the goal of establishing an interdisciplinary infrastructure for efficient identification of complex genetic traits underlying human diseases. The collaboration is based on the quantitative analysis of relationships among genotypes and clinical/experimental phenotypes in the context of three interrelated components: family linkage studies, expression profile studies, and public health studies. Three distinct, but highly complementary groups of UNC scientists have established programs in high-performance computing, applied biomedical computing, and experimental genetics, statistics, genomics and proteomics. This planning grant will build a collaborative, interdisciplinary community as a prototypical infrastructure that will ultimately support an extended, national and international community of users with diverse projects. Strategies for handling genotyping data generated from clinical, population, and experimental studies, as well as phenotyping data from molecular, cellular, organismal, and clinical research are being developed. These strategies will be explored and refined via case studies in UNC areas of national research strength (e.g., cancer genetics, cystic fibrosis, addiction, and mental illness). This effort stems from the rapidly emerging and urgent need to integrate experimental genetics research with computational science.

Ethical, Legal, and Social Implications of Genetic Screening and Disclosure: One of our missions is to investigate the impact of basic scientific discoveries on society and public policy. The CCGS organized a one-day cross-campus retreat on March 1, 2002 that eventually led to submission of an NIH P20 planning grant application focused on ethical, legal and social issues surrounding genetic screening and disclosure. Fourteen UNC-CH investigators from multiple disciplines including education, public health, medicine, social medicine, bioethics, pediatrics, genetics, anthropology, law, and nursing, form the core group for the project. Don Bailey serves as the PI. The work focuses on three major efforts at UNC-CH involving large samples for gene discovery and disclosure: (i) plans to screen 1,000,000 newborns for fragile X syndrome, the most common inherited cause of mental retardation; (ii) a study of more than 20,000 individuals in their late 20s who have been followed since adolescence, and for whom collection of DNA for gene exploration is now proposed; and (iii) a campus-wide DNA banking initiative, with a goal of collecting, tracking, and sharing more than 100,000 DNA samples. These three projects all involve a wide range of issues regarding the 'ownership', disclosure and dissemination of genetic information. The goals of the project are to identify critical issues and collect sufficient pilot data that would allow us to submit a P50 center grant to create a fully integrated Center of Excellence in ELSI Research (CEER) in which ELSI research would be conducted to inform public policy.

Science, Health and the Courts: As our knowledge of genomics and its power to transform society grow, education must broaden beyond the scientific community and embrace the general population as well as those who influence public policy. The law is increasingly called upon to mediate disputes that hinge on emerging genetic technology. This is true not only in the forensic realm but in civic, patent and social arenas as well. However, in spite of the growing importance of genetics in legal deliberations, judges, by their own admission, are often ill equipped to deal with such questions due primarily to their lack of training in the sciences. The Carolina Center for Genome Sciences has been intimately involved with the EINSHAC consortium (Einstein Institute for Science, Health and the Courts) in judicial education at the state and federal supreme court level in the US and at the Federal Supreme Court level internationally. Currently plans are in place for the CCGS to co-sponsor an ambitious program for national judicial education throughout the US. In cooperation with the Supreme Courts of California, Ohio and Maryland, a series of judicial workshops are to be held throughout the US which will result in the certification of high-court justices as Scientific Resource Judges. These efforts are to be anchored by two major "Judges Science Schools", the first in October of 2005 at the Salk Institute in La Jolla, California, and the second at UNC in March of 2006 under the auspices of the CCGS and the North Carolina Supreme Court.

Mutant Mouse Regional Resource Center (MMRRC): Due to the recent completion of the human and mouse genomes as well as advances in mouse technologies, there has been an enormous increase in the number of mouse mutants and models for human disease. Maintaining and distributing pathogen-free mouse strains is both labor-intensive and costly for individual investigators to sustain long term. The NIH/NCRR recognized the need for a common repository and distribution center for genetically modified mice and in 1999 they responded by funding the MMRRC. UNC-Chapel Hill (PI: T. Magnuson) is one of four MMRRC centers that are developing this resource for the benefit of the entire biomedical community. Since the initial funding, a significant amount of effort has been invested in creating the organizational infrastructure and establishing standard operating procedures for importation, rederivation, phenotyping, cryopreservation and distribution of mutant mouse strains. The MMRRC-UNC was recently refunded for another five-year period. In parallel with these efforts, the MMRRC has also taken advantage of the expertise available at UNC to bring new technologies and resources to the community such as mutant ES-cell lines, gnotobiotic (defined gut microbial flora) strains (a collaboration with Balfour Sartor in Medicine who was able to build upon this to obtain NIH funding for a gnotobiotic center), and improved in vitro fertilization methods. More recently the MMRRC-UNC participated in a meeting of various resource centers from around the world. The outcome of that meeting was the establishment of an International Federation of Mouse Resources. The mission of the Federation is to

ensure the quality, preservation and availability of genetically defined mice. Our mission also includes dissemination of information and the promotion of sharing of mouse strains as well as technical expertise within the global biomedical research community.

Mouse Models of Human Cancer NCI Consortium: David Threadgill (CCGS and Genetics) and Terry Van Dyke (Genetics) are PIs on two separate projects of this NCI-sponsored consortium. These projects represent an example of collaboration between the Genetics Department and the Lineberger Comprehensive Cancer Center. David Threadgill is conducting a new systems biology approach to discover biological signatures of cancer susceptibility using mouse models. Building upon recent successes in defining complex genetic networks, his team is extending their approach to include metabolic, physiologic, endocrine, immunologic, and proteomic analyses to define a cancer susceptibility state. They will also begin to describe the mechanisms by which an individual's genetic makeup, age, and environmental exposures are translated into altered cancer susceptibility and, eventually, differential response to therapy. Terry Van Dyke's initial findings in efforts to model astrocytomas in mice, together with longstanding observations of human tumors, have highlighted basic mechanistic associations between genetic lesions observed in the human disease and the resulting cellular and tissue responses. Ongoing studies are focusing on the target cell type and the role of the microenvironment in tumor development. These studies involve mouse models generated to develop low and high-grade astrocytomas. A sophisticated series of imaging technologies are being used to define cellular and tissue abnormalities resulting from specific manipulations of the mouse brain and then they are correlated with expression analyses.

VI. Research Initiatives Under Development

Systems Biology of Chromosomes: The CCGS Basic Process Genomics program organized a group of UNC chromosome biologists and they began meeting regularly to identify collaborative research opportunities. This effort first included CCGS faculty, but as expected, it has grown to encompass many different faculty outside the Center as well. Although most of this research at UNC is based on standard experimental methodologies (e.g., cell biology, biochemistry, genetics), we are incorporating computational and theoretical tools to create a true modeling approach. This is now possible because of new faculty hires with expertise in computational genomics, mathematical modeling and biostatistics, whose methodologies and tools are essential for systems biology. The CCGS sponsored a summit on January 6, 2005 to bring together the chromosome biologists and computational and theoretical scientists to brainstorm new research ideas that take advantage of their combined expertise. The summit began with talks by Kerry Bloom (chromosome biologist), David Odde (molecular modeler) and Rich Superfine (physicist), who discussed their existing collaboration on the mechanics of chromosome segregation. Other scientists, some of whom have collaborated for years, and others who met each other for the first time, gave additional talks. We decided to leverage our strengths in chromosome biology to create a Center for Systems Biology of Chromosomes under the auspices of the CCGS. Specific areas of interest that emerged from the summit include chromosome movement, genetic variation, information access and utilization. The CCGS will be working with these investigators to put forward a NIH proposal for support.

Environmental Bioinformatics: CCGS members F. Wright, A. Tropsha, D. Threadgill, and I. Rusyn are submitting a proposal to the Environmental Protection Agency to create an Environmental Bioinformatics Research Center (EBRC) at UNC. If funded, this 5-year project will create a bioinformatics infrastructure for the EPA's Computational Toxicology program to elucidate the genomic effects and signatures of environmental toxicant exposure, and will provide the foundation for genomics-based quantitative risk assessment. The goals as outlined by the EPA include (i) improving the "linkages in the source-to-outcome continuum," i.e., establishing relationships at levels from environmental release

to downstream adverse effects on humans and other organisms; (ii) producing predictive models for hazard identification through chemoinformatics; (iii) providing enhanced quantitative risk assessment, so that the findings can be applied to make regulatory decisions. The investigators have proposed an interdisciplinary approach that will unite biostatistics, chemoinformatics, and comparative genomics in pursuit of these goals. The proposal will create an enhanced informatics infrastructure that will benefit all of the CCGS, and the new informatics approaches will provide further leverage to the UNC Center for Environmental Health Susceptibility and the Toxicogenomics Research Consortium. The proposal draws on heavily on CCGS faculty and programs as well as the historical strengths of the UNC School of Public Health in Environmental Sciences. The CCGS is the sponsoring unit for this proposal.

UNC Protein Design and Simulations Portal: CCGS researchers A. Tropsha, N. Dokholyan, B. Kuhlman have submitted a CCGS-sponsored proposal to the National Science Foundation to acquire a cluster of computer workstations designated for the development, testing, porting, and dissemination of specialized structural bioinformatics software developed by UNC researchers. If funded the proposed acquisition will help to integrate research computational tools under development in UNC labs and to translate these tools into professional web-accessible software available to scholars at UNC and elsewhere for research, education, and training in the area of protein structural family annotation, design and simulation. The proposed specialized cluster will be integrated within the existing infrastructure of the Information Technology Services at UNC-CH and it will host the UNC Protein Design and Simulations Portal.

Mammalian Genotyping Core (MGC): The genetic dissection of complex traits requires access to large-scale resources and equipment that are often beyond the reach of individual investigators. To facilitate and streamline the efforts of both human and mouse geneticists, two key resources will be made accessible through the MGC: (i) high-throughput genotyping and (ii) murine colony management. Our goal is to establish a centralized core facility that is designed to provide efficient, high-quality and cost-effective service. We anticipate that when the Bryson Program becomes fully operational, many researchers will require these services. Because genotyping platforms and cost structures are constantly evolving, there is generally no single "best" approach but rather a dynamic answer that depends on the number of samples, the number of genetic markers (generally SNPs), and cost. With these ideas in mind we have established the following plan for the core facility's infrastructure and goals:

MGC Organization and Goals

Contributing Units	CCGS, Genetics, Lineberger Comprehensive Cancer Center, Program in Molecular Biology & Biotechnology
Faculty Oversight Committee	Pat Sullivan (Chair), Karen Mohlke, Fernando Pardo Manuel, David Threadgill, Terry Van Dyke, Kirk Wilhelmsen
Core Director	Search underway.
Goal 1	Human studies: implement a workable, verifiable, and functional moderate-throughput genotyping pipeline based on ABI TaqMan Assays-on-Demand/Assays-by-Design.
Goal 2	Mouse studies: deliver robust, accurate, and fast genotyping to assist in colony management.
Goal 3	Develop capacity to conduct whole-genome association studies. Implement, test, and integrate technologies.

VII. Education & Training

Our mission is to become a major center for training graduate students, postdoctoral fellows and physicians to become the new leaders in the rapidly evolving world of genomics and its integration into many fields of knowledge. There are four training programs administered by the CCGS. Many different departments across campus are represented by the training faculty in these programs since genetics/genomics is a significant element in many biomedical disciplines. The Department of Genetics actively participates and helps support these training programs, particularly in the areas of experimental, clinical and medical genetics. A brief description of each program and the faculty involved is provided below.

The Curriculum in Genetics & Molecular Biology: This program (Appendix 4.3) is a long-standing interdepartmental graduate program training students for careers in academic, government or commercial positions. There are 87 faculty (Appendix 4.1) associated with the program from multiple departments in the Schools of Medicine, Public Health and the College of Arts and Sciences. A faculty member qualifies as a preceptor if their research incorporates classical and/or molecular genetics approaches. This program now also serves as the main graduate program for the Department of Genetics. There are currently 75 graduate students enrolled in the program (Appendix 4.2). The Curriculum is in its 30th year of NIH support (8 slots). The training grant was recently renewed for another five years of support. The Curriculum receives additional support from the Dean's Office, the Department of Genetics, the CCGS, and the Program in Molecular Biology and Biotechnology (PMBB). The Curriculum has matriculated an average of 10 students per year for the last five years. Dr. Bob Duronio is the Director and also the PI of the training grant. He is an Associate Professor in the Department of Biology, a member of LCCC, PMBB and CCGS.

Proposed changes: The explosion of information based on the human genomic sequences and that of all major experimental organisms has changed the very nature of biological research, especially genetic research. There is an expanding need to merge quantitative disciplines with biology. This is especially true for the analysis of complex human traits, which requires the modern geneticist to use many quantitative and computational skills that are not provided by the current training program. We therefore are proposing a reorganization of the Genetics Curriculum such that all graduate students receive some computational and quantitative training. In addition, we intend to implement a new track structure to provide flexibility in the training program and to relieve some of the first year course burden.

The proposed tracks are:

- Track 1: Genetics
- Track 2: Molecular Biology
- Track 3: Developmental Biology
- Track 4: Bioinformatics/Computational Genetics

The choice of these tracks is dictated by the research interests of Curriculum faculty and the commonly recognized need to provide some bioinformatics/quantitative training to ALL of our Genetics students. The proposed changes (Appendix 4.4) will be discussed by the Curriculum leadership and the faculty with the goal of finalizing the changes for implementation beginning in the 2006-2007 academic year.

Bioinformatics & Computational Biology (BCB) Training Program: This new graduate program was established within the CCGS in 2002, with the first ten students recruited into the program in the fall of 2002. The BCB mission is to train a new generation of biomedical researchers specializing in the development and application of innovative mathematical, computational, and statistical tools to important biomedical problems. The training program is directed by Dr. Alex Tropsha, Professor of Medicinal Chemistry and a CCGS program leader for computational genomics. The 39 faculty members (Appendix

4.5) involved in BCB are distributed across more than a dozen departments at UNC-CH, yet they have many common research interests, and equally important, a strong commitment to training students in the broadly defined areas of bioinformatics and computational biology. Most of these faculty are also members of the CCGS**.** The training program does not grant degrees, but does offer a Certificate in Bioinformatics and Computational Biology, which complements the PhD degrees received from participating graduate curricula/departments. However, we envision that as both the program and the fields of bioinformatics and computational biology mature, we will transition into a stand-alone PhD-granting curriculum within the next five years. The program was initiated with an award from the UNC General Administration for three years (beginning in the 2002-2003 academic year). We recently applied for an NIH training grant (PI: A. Tropsha) and were subsequently site-visited. NIH program staff have recommended to NIGMS council that the BCB program be funded at 8 slots per year. We have also reapplied to the UNC General Administration for continuation of their support. A list of current students and a description of program details can be found in Appendices 4.6 and 4.7, respectively.

Developmental Biology Training Program: Training in developmental biology has historically been strong at UNC-CH, and the number and breadth of scientists in this area has increased consistently over the last 20 years. However, in the last 5 years there has been an incredible surge in the number of new faculty in developmental biology, including those from the CCGS and the Department of Genetics. This recruitment has spurred efforts to focus and consolidate these interests into a training program for both pre-doctoral students and post-doctoral fellows. Building on existing strengths in plant, invertebrate, and vertebrate developmental biology, we have begun to provide students with training opportunities through courses, journal clubs, and research symposia and seminars (Appendix 4.10). We already have a solid base of trainees in developmental biology, and we anticipate that our efforts will only increase the attraction of UNC-CH to students and post-doctoral fellows who wish to train in this area. We believe that our faculty represents a breadth of approaches and uses of model systems in developmental biology that is seldom seen on one campus. The program now includes 34 training faculty (Appendix 4.8) and it is in its first year of operation with 9 pre- and 4 postdoctoral trainees (Appendix 4.9). We submitted an NIH training grant (PI: T. Magnuson) and it received an outstanding score. NIH program staff has recommended to NICHD council that it be funded with six pre- and two postdoctoral slots. We anticipate funding to begin in July, 2005. The program director is Dr. Victoria Bautch, who is currently a Professor in the Department of Biology. Dr. Bautch has a distinguished record of achievement in developmental biology and has significant experience in mentoring graduate students and post-doctoral fellows.

Postgraduate Medical Genetics Residency Training: We offer a new, fully ACGME-accredited clinical two-year medical genetics residency program to prepare physicians for board certification in medical genetics (Appendix 4.11). This program is directed by Dr. Cindy Powell who is also Division Director for Pediatric Genetics. It is designed to prepare physicians to be independent clinical geneticists, proficient in providing comprehensive medical genetics services, capable of initiating and collaborating in basic and applied research activities, and effective in teaching and communicating their expertise to others. These goals are achieved through in-depth clinical experience with adult and pediatric patients who have cytogenetic, biochemical, single-gene and complex multifactorial genetic conditions. Candidates for the Medical Genetics Residency Program apply after completing two or more years of primary specialty training. Most applicants will have completed an ACGME-accredited residency in Pediatrics, Internal Medicine, Family Medicine, or Obstetrics-Gynecology. The Genetics Department funded the first fellow for two years. Currently the UNC Health Care System and the Bryson Program for Human Genetics each fund one fellow.

Basic Genetics for Year 1 Medical Students: The Genetics Department combined efforts with the Biochemistry Department to offer a new course for year I medical students entitled, “Molecular Biology and Genetics” (Appendix 4.12). Jim Evans from Genetics is the course director. The rationale for the course is that medicine is advancing rapidly as a result of our increased understanding of the molecular

basis of human disease and that the pace of progress will accelerate. A clear understanding of molecular biology and genetics has become a necessary framework for understanding human health and disease, and will be increasingly critical for the practicing physician. In addition, solid training in molecular biology and genetics will be critical for proficiency in the basic science courses, during clinical rotations in years 3 and 4, and for successful completion of National Board exams. The course is divided into two parts: the first half focuses on basic molecular biology and is taught by Biochemistry faculty (Marzluff, Ramsden, Lee); whereas the second half focuses on genetics and is taught by the Genetics faculty (Evans, Magnuson, Threadgill). The institutional commitment to the importance of this subject in medical education is attested to by the fact that it is the first course which students take as they enter medical school. Student evaluations are very positive overall as illustrated by the following comment from one of the students: "Learning objectives were as well defined in this course as any that I have ever taken. The professors are to be commended for doing a fantastic job stressing what was most important to learn."

VIII. Seminars and Colloquia

Friday Noon Seminar Series: The CCGS organizes a seminar series (Appendix 5.1) during the academic year that is held on Fridays at noon. Speakers are, for the most part, external to the University. A small number of internal faculty are invited to speak and these are usually new faculty petitioning to join the Curriculum in Genetics & Molecular Biology. Curriculum students host one speaker per semester and Developmental Biology Program students also host one speaker per semester. CCGS faculty invite one speaker per month (9 total per year) and the Curriculum faculty, which includes the Genetics Department, invite the remaining speakers.

Genetics Department Research Colloquium: The Department holds a weekly research conference (Appendix 5.2), the goal of which is to provide a venue for Department graduate students (including students from several different graduate programs) and postdoctoral fellows to gain experience in presenting formal seminars. The colloquium is held every Wednesday at noon and a pizza lunch is provided. The series is considered to be important for the professional development of students and postdocs and it is well attended by Department faculty and lab members. On average, two outside speakers are invited each semester. These are usually faculty from other departments within UNC that are conducting genetics-related research. Occasionally a speaker from outside UNC is invited to present but only if a Friday noon slot is not available.

Curriculum in Genetics & Molecular Biology Student Research Seminar: A seminar series (Appendix 5.3) is held each week in which students during their third year and beyond present their research to first- and second-year students. The goal is to provide a forum for Curriculum students to present their data and to foster scientific interchange among them. Third-year students present a 25-minute talk, and fourth-year students (and beyond) present a 50-minute seminar. Attendance is required for first- and second-year students, and they receive course credit and a grade based on attendance and participation. The Curriculum Director attends all seminars to evaluate participation and to provide feedback to the presenter.

Bioinformatics & Computational Biology Research Colloquium: The BCB colloquium meets weekly (Appendix 5.4). It is a mix of journal club discussions, student research presentations, and faculty research presentations. Participation is mandatory for first- and second-year graduate students and all senior students are required to present their work. The Program Director organizes the fall series to increase contact time with new students. The spring series is organized by rotating BCB faculty.

Developmental Biology Research Colloquium: All trainees are required to participate in the Developmental Biology Journal Club (Appendix 5.5) where students and post-docs from developmental biology labs present current literature or their own work. This journal club meets twice per month. Trainees are required to present their work at least once per year in this forum. This provides trainees with an excellent opportunity to give and receive scientific input from their peers. It also provides trainees with public-speaking opportunities, which is a critical aspect of the training experience.

Genetic Epidemiology Journal Club: Members of CCGS in the Departments of Genetics and Epidemiology organize a journal club (Appendix 5.6) to promote interaction and exchange of ideas between groups interested in the genetics of complex traits, especially as they relate to humans. The journal club meets once or twice per month. Discussion is usually led by a faculty member or postdoctoral fellow using current literature or their own work. Regular attendees include faculty, postdoctoral fellows, and students in the Departments of Genetics, Epidemiology, Biostatistics, Medicine, and Endodontics, as well as NIEHS.

IX. Research Symposia

Genetics Department: As described above, we have established various seminar series that feature students, postdoctoral fellows and outside speakers but no forum existed that featured our own faculty. Having the faculty give presentations increases their internal visibility to both students and the University as a whole and fosters collaboration. We therefore decided to create a one-day symposium that would feature two outside keynote speakers along with talks from our own faculty. We also felt that this venue would be good for highlighting genetics-related work by faculty in other departments. The decision was made to partner with another department to sponsor the symposium, and our first faculty symposium was held on December 1, 2004, with the Departments of Genetics and of Medicine as co-hosts (Appendix 5.7). The title of the symposium was "Frontiers in Medicine and Genetics". Our keynote speakers were Drs. Mary-Claire King (University of Washington) and Oliver Smithies (UNC-Chapel Hill). The symposium was a success and was very well attended. We have decided to continue this series with the next symposium being in the fall of 2005. The Department of Biology has agreed to co-sponsor the symposium with us and the focus will be "Model Systems and Human Disease."

Bioinformatics and Computational Biology: The BCB program organizes a half-day symposium every fall consisting of platform and poster presentations followed by a social hour (Appendix 5.8). The goal is to introduce new students to the rest of the program members. The platform presentations are a mix of faculty and student talks. The posters are presented by students.

Developmental Biology: The Developmental Biology Program will be holding its inaugural one-day symposium on April 8, 2005. Dr. Gail Martin from UCSF will be the keynote speaker. Drs. Mark Peifer, Sarah Liljegren, Anthony LaMantia and Larysa Pevny are the internal faculty speakers and four student/postdoc speakers will be selected from submitted abstracts. In addition, there will be two poster sessions for students/postdocs to present their work. This symposium will be held each year in the spring.

X. Scientific Retreats

Curriculum in Genetics & Molecular Biology: The Curriculum has, in the past, sponsored an annual retreat at a nearby conference center. It consisted of lunch, a student poster presentation, and three short (20 minute) talks by Curriculum faculty. This event was held at the beginning of each school year, and it provided an introduction to the program for new students as well as an opportunity for all of the Curriculum faculty and students to interact both socially and scientifically. Poster presentations were required of all third-year and above students. Poster presentations were optional, but encouraged, for

second-year students, and the decision of whether or not to present a poster was made at the discretion of the thesis advisor. As described below, we have decided to expand this retreat into a 2.5-day off-site meeting.

Department of Genetics: Since 2003, the Genetics Department has sponsored an off-site annual scientific retreat. All lab personnel including faculty, postdocs, graduate students, and technicians are invited. The goal is to promote both scientific and social interactions. The first two retreats were held jointly with Duke University's Cell Biology Department. This was done to promote closer ties between the two institutions. The retreat was held over a weekend beginning on Friday afternoon and finishing on Sunday at noon. The first retreat was held at the Southern Pines resort (Oct 10-12, 2003). The second retreat was held at the Blockade Runner Hotel in Wrightsville Beach (Sept 10-12, 2004). Each lab selects one representative (faculty, students or postdocs) to speak during the platform session. All other students and postdocs present their work at the poster sessions. Cash awards are given to the best presentations from students and postdocs from each institution.

Combined Curriculum and Department Retreat: A retreat for 2005 has been set for September 16-18 at Wrightsville Beach. However, this year we decided to combine the Department and Curriculum retreat and not to include the Duke University Cell Biology department. The faculty felt that this would promote a more cohesive genetics graduate program. The organizers are Mark Heise, Kirk Wilhelmsen and Bob Duronio. All Genetics Curriculum graduate students will be required to attend and the Department/Curriculum will cover their costs. Other lab members are also invited and the format will be similar to that followed during the last two retreats.

XI. Administrative Support

To maximize operational and financial efficiency, the CCGS and the Department of Genetics share administrative support. This unit has been organized with the intent to serve the faculty as best as possible within the rules of University/State system.

CCGS and Genetics Department Administrative Organization

Position	Name	Function
Chair & Director	Terry Magnuson	Oversees all aspects of the CCGS and the Genetics Department.
Associate Director	Mary Sym	Facilitates research organization and proposals for the CCGS.
Business Manager	Geri Osborn	Oversees departmental finances and administration.
Student Services	Cara Marlow C. Hawkins	Administers four training programs.
HR Facilitator	Linette Tyson	Responsible for all EPA and SPA personnel actions, HR postings, advertisements and payroll.
Grants Management	Brandon Leonard	Responsible for all grant submissions and renewals.
Accounting	Dana Xiao Robin Ward Carolyn Holland Jessica Nation (50%)	Management of all accounts.
Administrative Assistance	Louisa Baroudi Kathleen Hanlon (50%) Phil Lee Gita Maden (50%) Erin West Erricca Williams	Office support for Genetics Department faculty.
Web site	Clint Osborn	Part-time web developer.
Program Development	Amy Perou	Program specialist for the Bryson Program.

XII. Programmatic Areas for Future Growth

The CCGS and the Department of Genetics have undergone phenomenal growth and productivity since their inception 4.5 years ago. Nonetheless, in this rapidly evolving arena additional areas of expertise critical to the success of the program are required as we look to the future. The following represent areas that need strengthening during the next five years.

Quantitative & Systems Biology Faculty: The CCGS lacks critical faculty who are able to link proteomic, genetic, gene expression and genome sequence data into a single unified infrastructure so that higher-level discoveries that bridge these datasets can occur. Our biomedical computing effort has made us keenly aware that we need to focus recruits in this area. Another programmatic area that needs strengthening is systems biology. We need to recruit more individuals who create computational models of complex biological systems and then are able to collaboratively test these models experimentally. Although we have recruited Tim Elston in this area, it is clear that modeling for experimental design and interpretation requires varied expertise and training that is rarely found in most applicants. Individuals that understand the nature of biological information transfer, and also have a deep understanding of pattern detection (or extracting useful information from noise) and the computational methods used for that purpose would be ideal. They should have experience doing experiments, and therefore an appreciation for the limitations and potential errors associated with current experimental techniques. We envision these recruits to be joint with Computer Science, Applied Math and the new College of Arts & Sciences initiative focused on Quantitative Biology. Following along this theme, we also need to expand our faculty experienced with modern algorithm design and their genomic applications to the analysis of massive data sets, thereby allowing dissection of the genetic basis of complex traits, comparative genomics, candidate gene prioritization and data curation. We envision these recruits to be joint with Health Affairs departments such as Biostatistics, Epidemiology, Genetics, and College Departments such as Statistics and Operations Research.

Clinical Human Genetics Faculty: We have presented a forward-thinking plan for the Department to integrate genetics into various clinical settings across campus. We have obtained external advice from Drs. Robert Nussbaum (outgoing President of the American Society of Human Genetics-ASHG) and Peter Byers (incoming President of ASHG) and both have indicated that our plan would without a doubt facilitate the widely sought but seldom realized goal of relevant integration of genetics into the clinical world (a keen desire of the Genetics Department). Accomplishing this goal would serve as a national model for how such integration can be achieved. However, to achieve this goal, our external advisors recommend (and we agree) that recruitment of two additional MD clinical geneticists and a similar number of genetic counselors are required.

Center for Human Disease Models: The complexity of most human diseases dictates that a full understanding can only be accomplished with the aid of *in vivo* studies. Fortunately, sophisticated technologies for manipulating both invertebrate and vertebrate experimental systems in meaningful ways have been developed and continue to expand at a rapid pace. Over the past decade, advances in genomic and computational technologies have increased both the power and complexity of analyses in such systems. Although the capabilities to model human disease are enormous, it is clear that in most cases, no single model can fully recapitulate the human state. Thus, there is an equally great challenge to developing, interpreting, and utilizing disease models and understanding their limitations. The CCGS is proposing to establish under its umbrella a Center for Human Disease Models (CHDM) as a conduit for UNC physician scientists to advance the understanding of human disease through the use of experimental animal model systems.

The Center would be led by Dr. Terry Van Dyke (a leading mouse models geneticist), and would be comprised of existing faculty with significant expertise in human disease models as well as recruitment

of new investigators of human disease that utilize animal models as a component of their research. Initial areas to be targeted include those areas on campus that are missing or are weak such as zebrafish studies and translational research/technology development (e.g., drug discovery and pre-clinical testing). A primary goal would be to partner with clinical departments for recruitment of physician scientists. The CHDM would provide an intellectual focal point for translating work from model systems into the clinical arena. In addition, the CHDM would be responsible for ensuring that appropriate core facilities and infrastructure are established and maintained to facilitate state-of-the-art capabilities. For some facilities this would be accomplished in collaboration with other relevant centers or departments. Examples of cores existing or under development that would benefit from CHDM input or oversight include (i) the Animal Models Core, (ii) the Small Animal Imaging Core, and (iii) the Mammalian Genotyping Core. The CHDM will work to expand mouse phenotyping methods in general and will implement and maintain a directory of accessible capabilities, both on and off campus.

A longer-term objective would be to establish the infrastructure and expertise for pre-clinical testing in the mouse. Such an effort would dovetail with drug-discovery and diagnostic screening efforts on and off campus. It is envisioned that such a facility could potentially support itself by "hosting" or partnering with projects from other institutions, including biotechnology and pharmaceutical companies. The CHDM expertise could include not only the management of relevant mouse strains during experimentation, but also the monitoring and development of "read-outs" including, but not limited to, molecular and physiological animal imaging, proteomics and genomics technologies.

XIII. Space

One of the main struggles for the CCGS is that it is a virtual center. Center faculty are housed all over campus with no central home or designated CCGS space. One advantage to this arrangement, however, is that the CCGS faculty are able to act as a true liaison between their home departments and the CCGS. This has proven beneficial in that many of our efforts include faculty not formally associated with the Center. However, the downside is the lack of day-to-day contact and a loss of funds from indirect costs to the CCGS. Recovery of indirect cost flow goes primarily to the unit supplying lab space. If the Center has no assigned space, it is not compensated for its efforts in recruitment and program development. In an attempt to rectify the problem, the University is re-examining how indirect cost recovery is assigned. To remedy some of these problems with a virtual center, the Provost and the Dean of the College have assigned the CCGS a floor in the new Genome Science Building that will be designated as the home for CCGS faculty with primary appointments in the College. This building is currently in the planning phase and has been identified as the number one priority for UNC infrastructure needs; however, completion is expected to be 4-5 years away. Each floor in this building is designed to hold 9 PIs conducting wet-lab work and 3 PIs for computational work. This space would be the home for new CCGS/College recruits, which would include scientists working with invertebrate systems as well as those recruited for computational genomics.

The Department of Genetics is scheduled to move into the new Genetic Medicine Building when it opens in 2.5 years (groundbreaking scheduled for February 2005). The major benefit of this move is the opportunity to design an ideal floor plan, including a 37,000-cage mouse facility. The Department has been allotted one floor in this building. To provide the CCGS a home within the health affairs side of campus, we propose that our current wet lab space on the 4th floor of the MBRB building be designated as CCGS space to house the Center for Human Disease Models described above. Faculty housed in this space would be CCGS members with academic homes in clinical departments. We also propose that the dry space we currently occupy in the 4200 suite of the MBRB be retained as the home of our Bryson Program in Human Genetics. We have remodeled the space to include six offices and several cubicles. It would be ideal space for the clinical geneticists, the genetic counselors and the medical residents.

XIV. External Advisory Committee

A far-reaching bench-to-bedside program in genomics has been established, with the CCGS and the Department having distinct but important overlapping and synergistic missions. Now that a program is in place, an External Advisory Committee (EAC) has been formed to offer ongoing advice as to what we have done and also to provide input on plans for future growth. The EAC is appointed for a three-year, one-time renewable term, and consists of six internationally recognized experts in the area of human, mouse, invertebrate and computational genomics. The EAC will meet for the first time on campus on September 19, 2005 to review progress and to make recommendations for future operations. All subsequent meetings will occur on a yearly basis at the beginning of the academic year.

External Advisory Committee

Name	Expertise
Joe Ecker, PhD - Professor of Plant Biology The Salk Institute for Biological Studies	Plant genomics and molecular biology.
Evan Eichler, PhD - Associate Professor of Genome Sciences, University of Washington	Human genome structure and evolution; bioinformatics.
Skip Garner, PhD - Philip O'Bryan Montgomery, Jr., MD Distinguished Chair, Bioinformatics Center, UT Southwestern	Applied computational biology, genomics, proteomics.
Robert Nussbaum, MD - Senior Investigator and Chief, Genetic Disease Research Branch, National Human Genome Research Institute	Human disease, clinical genetics.
Dagmar Ringe, PhD - Professor of Biochemistry and Chemistry, Rosenstiel Basic Medical Sciences Research Center, Brandeis University	Protein crystallography, structural enzymology.
Richard Woychik, PhD - Director of the Jackson Laboratory	Mouse genomics, disease models.