Center for Integrative Chemical Biology and Drug Discovery: Business Plan (non-financial)

OUTLINE

- ***Why Academic Drug Discovery?***
- ***Executive Summary & Center Overview***
- ***Center Design***
- ***Execution***
- ***Appendices***

Why Academic Drug Discovery?

Scientific progress in the biomedical sciences has accelerated enormously over the last 2-3 decades. The cellular signal transduction processes and biochemical pathways that enable life are increasingly understood at the molecular level and the aberrations that result in disease can be defined within this rational context. Additionally, with the sequencing of the human and other genomes, the identity of the cast in this drama of life is known with ever greater certainty. Technology to enable discovery of ligands for molecular targets has also advanced such that many complementary approaches exist for creating small molecule tools to interrogate biological processes.

However, even as basic science and technology seem poised to create a revolution in the availability of potent, selective and safe small molecule drugs, the pharmaceutical industry, where >90% of drugs have historically been discovered, is struggling for survival. While industry investment in R&D has grown exponentially, approval of new medicines has stagnated and pricing pressures and litigation have further eroded profitability. These conditions have resulted in frequent mergers, reorganizations and reductions in scientific staff across the industry. Given the rate of organizational change in the industry, it is increasingly difficult for a research project or strategy to bear fruit before it is abandoned. As a result, there is a growing trend for larger pharmaceutical companies to outsource and externalize the early phases of drug discovery via either active partnerships or opportunistic in-licensing of novel compounds.

In this context, there is a clear societal need for enhanced innovation and productivity in drug discovery in order for advances in biomedical research to result in new medicines. Bringing a variety of scientific approaches and sponsors to the early stages of drug discovery will result in greater technological innovation; exploration of higher risk targets; and more balance between the dominant pharmaceutical focus on the diseases of affluent societies and less prevalent diseases and the diseases of the developing world. Exclusive reliance on large pharmaceutical companies for drug discovery will not achieve either the innovation or the balanced perspective that a broader-based effort can contribute. Academia is a critical area where relatively small additional investments can enable the translational research which will contribute directly to meeting this challenge.

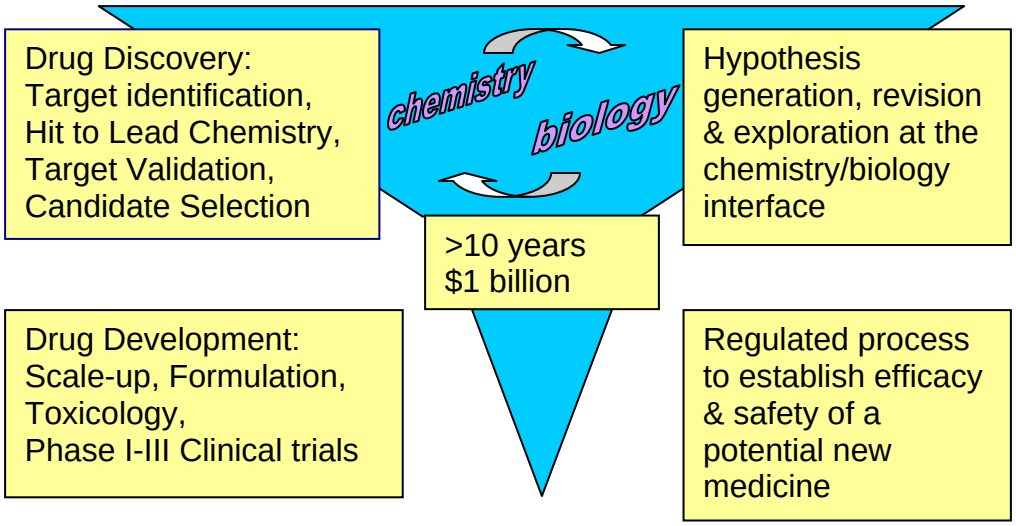


Figure 1. Drug discovery & development are both lengthy and expensive but differ markedly in the cost per opportunity and the related risk of each decision. The interface between chemistry and biology is the crucible for drug discovery.

UNC possesses the scientific and medical talent to contribute substantially to the discovery of small molecule drugs; however, each new insight into human biology with potential therapeutic relevance faces similar challenges in translation: limited alignment, resources and experience. Although academic biology excels in the identification and characterization of potential targets, there is rarely collaboration between biological sciences and synthetic and medicinal chemistry to advance into the hit generation and lead discovery phase. In addition, the frequency of drug discovery in academia is so low that very few academic investigators have the opportunity to gain experience in this highly complex arena where decision-making and prioritization are so important. The creation of the CICBDD will fill this key gap in expertise and resources at UNC and enable translation of basic scientific discoveries into potential human therapeutics.

Importantly, the research culture of the University, which is based upon fostering innovation and nurturing new ideas, is fertile ground for the hypothesis generation, revision & exploration that characterize drug discovery (Fig.1). This aspect of academia is distinct from the current short-term, bottom-line and conformity driven culture in many corporations. As discussed above, creating multiple approaches to the relatively low cost, high risk and innovation driven early phase of drug discovery is essential to continued progress in healthcare. By contrast (Fig. 1), the development phase of drug discovery has a very high cost per opportunity, is highly regulated and is an appropriate arena for centralized control of decision-making – a good match for the culture of large pharmaceutical companies.

An explicit benefit to the University in creating the CICBDD is the enhanced ability to recruit, retain and secure funding for scientific & biomedical faculty who are motivated to have their discoveries improve healthcare. By supplying a dedicated assay development and medicinal chemistry resource in the CICBDD that is devoted to the progression of hypotheses generated by UNC faculty, the University has positioned itself to have a competitive advantage in attracting and retaining talented investigators. Additionally, researchers in the CICBDD will be able to act as co-investigators and/or provide letters of support for grant applications focused on translational research. With the increasing emphasis from the National Institutes of Health on the impact on healthcare of the research supported by their grants, the CICBDD will positively influence the overall fundability of such research at UNC.

UNC is not alone in recognizing the need to enhance translational research effectiveness in biomedicine and a number of other academic centers have been created to address this challenge. While each effort is unique, these centers can be roughly divided into two groups – those that place an emphasis on recruitment of experienced drug discoverers from industry with strong focus on delivery and those where the emphasis is on raising funds for 'drug discovery' to support the basic research of well-recognized scientists who do not have experience in the pharmaceutical industry. It will be important to the effectiveness of the CICBDD to actively assess the approaches taken at other institutions and seek out collaborations that can enhance the impact of UNC's investment on drug discovery. A listing of other academic drug discovery Centers is provided in Appendix 1.

Center Overview

Mission

The Center for Integrative Chemical Biology and Drug Discovery (CICBDD) was created with the mission of bringing dedicated medicinal chemistry expertise to bear on biological targets of therapeutic relevance under investigation by UNC faculty. Synthetic chemists and assay development and compound profiling scientists will work in the Center and create dedicated, multidisciplinary project teams with other groups on campus in order to progress targets through the drug discovery and pre-clinical development process. In addition to this collaborative mission to support UNC investigators, the CICBDD will initiate a self-sustaining academic program in chemical biology & molecular tool discovery. A strong synergy is anticipated between the drug & tool discovery activities.

Translational Research

Academic laboratories have traditionally provided an environment for deep expertise and curiosity-driven research to flourish. While these characteristics are still essential to innovation, there is an increasing opportunity and need for better translation of academic discoveries to provide tangible products to benefit society. This is particularly true in the biomedical sciences where progress in understanding basic biology and the biological causes of disease can immediately suggest therapeutic interventions. To enable translational research there must be a mechanism to align interests, expertise and resources toward the goal of producing a therapeutic outcome. One area where this alignment could be enhanced in academia is at the interface of chemistry and biology. The CICBDD will focus on creating expertise and providing resources at this key interface.

Faculty Retention, Recruitment and Funding

An explicit benefit to the University in creating the CICBDD is the enhanced ability to recruit, retain and secure funding for scientific & biomedical faculty who are motivated to have their discoveries improve healthcare. By supplying a dedicated assay development and medicinal chemistry resource in the CICBDD that is devoted to the progression of hypotheses generated by UNC faculty, the University has positioned itself to have a competitive advantage in attracting and retaining talented faculty. Additionally, the CICBDD researchers will be able to act as co-investigators and/or provide letters of support for grant applications focused on translational research. With the increasing emphasis from the National Institutes of Health on the potential healthcare impact of the research supported by their grants, the CICBDD will positively influence the overall fundability of this research at UNC.

Increasing Licensing and Start-up activity

Center projects are expected to produce a combination of mechanistic data; chemical series with well-defined structure-activity relationships; preliminary toxicity and animal efficacy data; and corresponding intellectual property. Possession of data packages such as this will significantly enhance the number and value of licenses (as compared to the value of licensing target identification IP), sponsored research and startup companies based on Center projects, all of which further the Center's broader mission. (See Appendix 3 for the invention income policy of the Center.)

Measures of success

The CICBDD will have tangible short, medium and long-term goals in order to create the value that is expected by the University and to secure additional sources of funding to support its activities beyond the initial start-up phase of its operation. These goals fall into three categories: 1) collaborative goals where the benefits include tangible monetary and academic objectives achieved in concert with UNC investigators and; 2) 'pipeline' progress goals which demonstrate the viability of the Center's process; 3) identification and successful pursuit of funding from government, foundation and private sector sources to support sustainability and growth.

Collaborations & Opportunities Beyond 2010

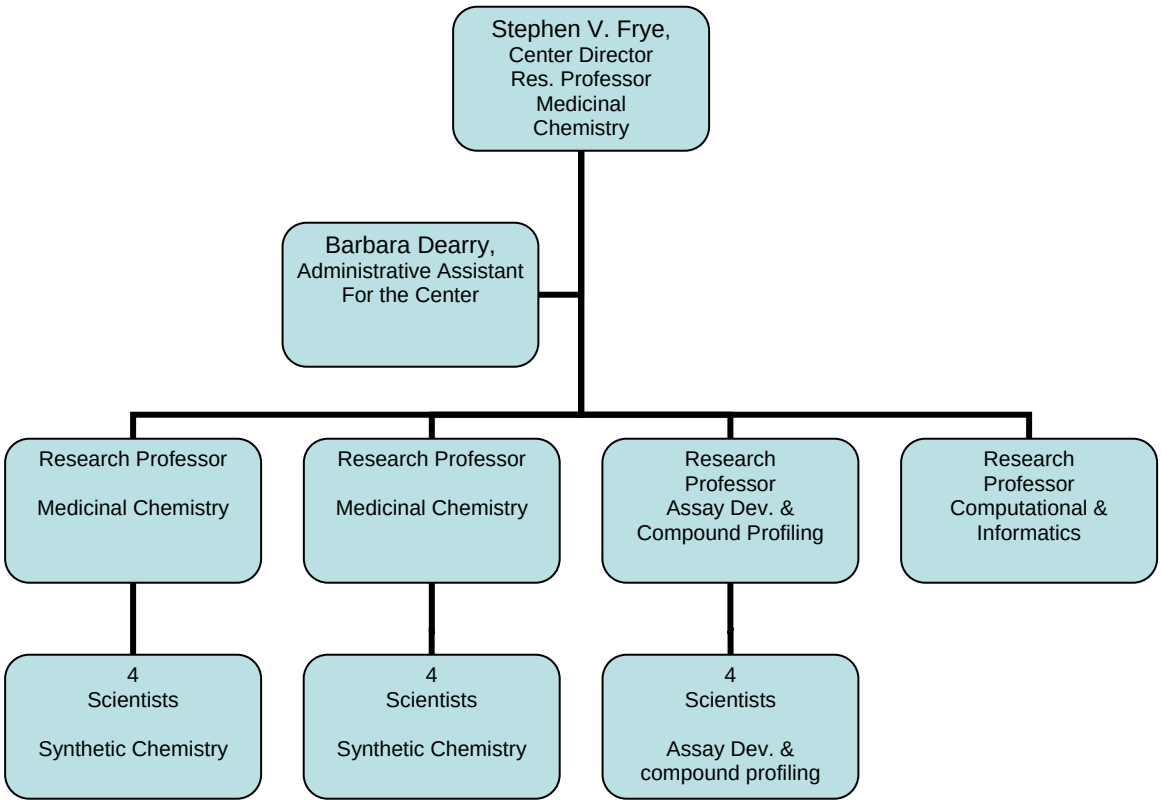
The strategic theme for the Center beyond 2010 will be exploration of means to increase the impact of the CICBDD to an extent greater than the growth in fixed costs (facilities & staff). Opportunities to leverage the impact of the Center via collaborations with other academic drug discovery centers will be vigorously pursued and the possibility of creating a NC or Southeast regional effort based upon complementary expertise & infrastructure is a serious possibility. However, some growth at UNC will be required and includes: relocation of the Center to the new Imaging Research Center; creation of an additional 5 person chemistry team; and procurement of increased external synthetic chemistry resource. In addition, the critical mass within the Center can be expanded via realization of another Center objective: the creation of an extramurally funded program in chemical biology and molecular tool discovery.

Center Design

Resources:
The Center has been initiated with funding from across the University and a significant contribution from the Cancer Research Fund (recently created by the State legislature). This initial funding and the facilities devoted to the Center will provide the majority of the investment needed through June, 2010 for:

- 10 medicinal/synthetic chemists – including two research professor positions
- 5 assay development & compound profiling scientists – one research professor
- 1 computational/informatics research professor
- Creation of a UNC compound collection to be held & assayed at the Biomanufacturing Research Institute and Technology Enterprise (BRITE) at NC Central University – a key collaborator for high throughput screening
- Capability to procure external synthetic chemistry to enhance productivity
- Laboratory equipment and supplies for staff

Organization Structure: (reporting to Dean Blouin, School of Pharmacy)



Scientific Advisory Board:

The scientific advisory board (initially comprised of UNC faculty) for the Center has been created to provide scientific input and advice to the director. Domains for SAB input include:

- review of proposals
- identification of funding/grant opportunities for the center
- project review & consultation
- review of contract research opportunities
- review of specific technical/strategic decisions

The scientific advisory board:

- Alex Tropsha, Chair, Medicinal Chemistry
- Bryan Roth, NIMH Screening Program Director, Pharmacology & Medchem
- Gary Johnson, Chair, Pharmacology
- Matt Redinbo, Chemistry & Biochem
- David Lawrence, Chemistry & Medchem
- Ned Sharpless, Cancer center
- Russ Mumper, Director, Nanotechnology & Drug Delivery
- Howard Mcleod, Pharmacogenomics (IPIT)
- Scott Forrest, Tech transfer office

The director remains accountable for all decisions undertaken based on the advice of the SAB. The addition of external scientists to the SAB will explored in the future.

Board of Directors:

The director of the CICBDD will report to a Board who will review, support and advance the strategic mission of the Center. Additionally, the Board will provide oversight of the activities and performance of the Center director.

- Bob Blouin (Chair), Dean, School of Pharmacy
- Etta Pisano, Dean, School of Medicine
- Holden Thorpe, Dean, College of Arts & Sciences
- Shelton Earp, Director, Lineberger Cancer Center
- Tony Waldrop, Vice-Chancellor for Research and Economic Development
- Gary Johnson, Chair of Pharmacology
- External advisor – TBD

Execution

Portfolio creation:

The Center for Integrative Chemical Biology and Drug Discovery (CICBDD) was created with the mission of bringing dedicated medicinal chemistry expertise to bear on biological targets of therapeutic relevance under investigation by UNC faculty. Therefore the primary focus of work in the Center will be progression of targets proposed by UNC investigators through the drug discovery process. Proposals from faculty will be solicited by the director and reviewed by the SAB (see Appendix 2 for proposal format & contents). As the CICBDD resource will only support progression of 3-5 targets at steady-state with a projected turnover of 2-3 targets per year, prioritization of opportunities will be critical to the Center's success. Criteria for target evaluation include: disease relevance of target/pathway; potential scientific impact of small molecule tools; tractability of assay development and ligand discovery; portfolio balance; and fit with Center expertise.

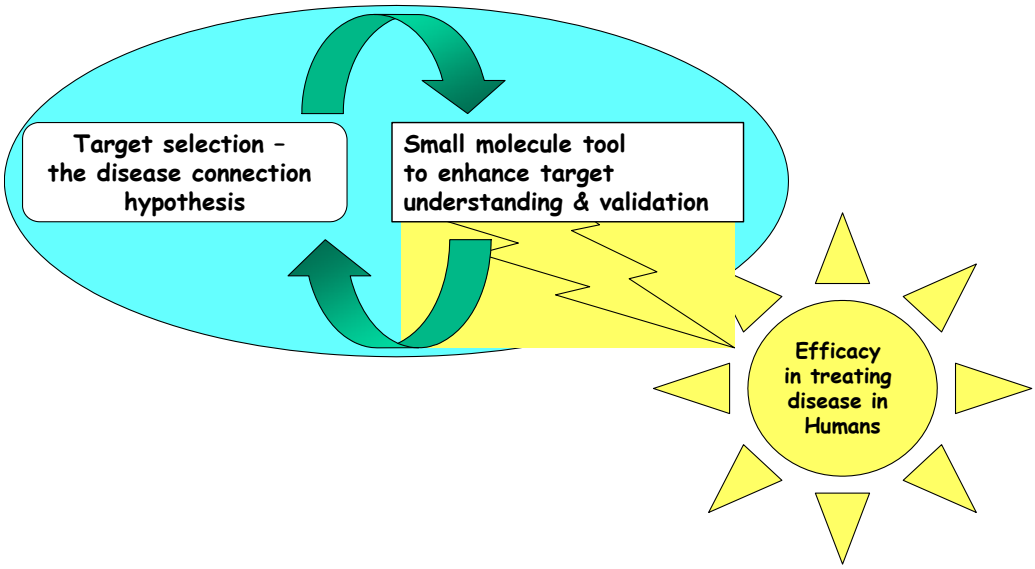


Figure 2. The iterative testing of therapeutic hypotheses with small molecules designed and synthesized in the CICBDD.

Figure 2 illustrates the basic paradigm for the work in the center and indicates where academia can add unique value: UNC can excel at small molecule driven elucidation of biology relevant to drug discovery.

Technology and Strategies:

Modern drug discovery is dependent on numerous complementary technologies to advance through the hurdles of target identification, hit generation, hit to lead optimization and selection of a pre-clinical candidate. Figure 3 below depicts the

flow of projects in the center and the associated technologies appropriate to each stage in the process.

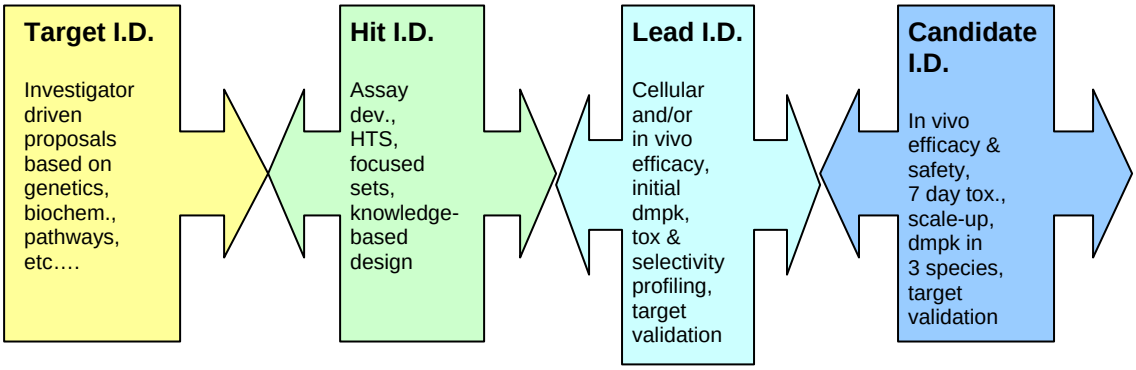


Figure 3. Process flow & associated technologies within the Center and in collaboration with UNC Investigators and other Centers on campus & in RTP. Activities beyond candidate identification will typically require partnership with the private sector or creation of a new venture funded corporation.

Hit generation & identification:

- Assay development & high throughput screening with a diverse, developable compound collection. HTS will be done in collaboration with existing screening centers (BRITE-NCCU and NIH NCGC)
- Knowledge-based focused screening sets built on target-class, structural and computational models
- Target specific mechanism and/or pharmacophore based design

Hit to lead & pre-candidate selection:

- Parallel solution-phase synthesis of designed arrays (20-50 compounds) to pursue 2-3 series per target applying multiple objective optimization
- Post synthesis automated purification, isolation & registration
- Structure-driven design where feasible
- Compound profiling for efficacy & selectivity (NIMH-PDS)
- Early dmpk and physical property assessments (CNDD)
- Early focus on enabling translational medicine to verify mechanistic hypothesis – animal studies enabled with pharmacodynamic read-out of effect on target (IPIT, Genome Sciences)

In addition to the expertise in basic biological sciences present in Pharmacology, Biochemistry, the Cancer Center and the Medical School, the School of Pharmacy has several initiatives that will strongly synergize with the drug discovery focus of the CICBDD: The Center for Nanotechnology in Drug Delivery (CNDD), the Institute for Pharmacogenomics and Individualized Therapy (IPIT) and the National Institute of Mental Health Psychoactive Drug Screening program (NIMH-PDS). State of the art drug delivery systems developed in the

CNDD will permit rapid progression of small molecules into a broad and genetically characterized set of animal models, provided by the IPIT, Genome Sciences & the NIMH-PDS, which will create an enormously powerful mechanism for rapid target validation & compound profiling. UNC's strengths in transgenic and 'knock-out' technologies (e.g. – leading to specific mouse models of disease) are globally recognized as reflected in the recent award of the Nobel prize in Medicine to Oliver Smithies. The Center will take advantage of these capabilities for characterization of small molecules in vivo. The co-location of these efforts will greatly enhance successful translation of projects through the discovery and early development stages.

In addition to studies to determine in vivo efficacy & mechanism of action, the CICBDD will collaborate with the Hamner Institutes for Health Sciences to explore preclinical toxicology via their innovative platforms that integrate genomic & metabolomic data with traditional histological determinations of toxicity.

Timelines:

Initial proposals to the center from faculty will be reviewed with target and project selections made by the end of 2007. Outsourcing of synthetic chemistry can commence in February/March coincident with the anticipated starting date of the first recruits to the Center. Laboratories for the Center will be in the Genetics Medicine building and will be occupied upon its completion (Aug/Sept '08). The Center will be fully staffed by 4th quarter, 2008. It is anticipated that the CICBDD will occupy space in the new Imaging Research Center to be completed by 2011/12 and any growth in resources could take place at that time if warranted based upon success.

Measures of Success:

The CICBDD will have tangible short, medium and long-term goals in order to create the value that is expected by the University and to secure additional sources of funding to support its activities beyond the initial start-up phase of its operation. These goals fall into three categories: 1) collaborative goals where the benefits include tangible monetary and academic objectives achieved in concert with UNC investigators and; 2) 'pipeline' progress goals which demonstrate the viability of the Center's process; 3) identification and successful pursuit of funding from government, foundation and private sector sources to support sustainability and growth.

<u>Collaborative Academic Goals</u>:

- Enable interrogation of biology with small molecules by hit generation and optimization resulting in enhanced funding of new UNC grant proposals beginning in 2008
- Create strong academic program within the Center that competes effectively for external funding in a defined area of chemical biology by 2010

- Create mechanisms for student and faculty training and enrichment in the areas of expertise within the Center by 2010
- Establish external collaborations and funding base such that the Center is sustained & can grow beyond 2010

Pipeline & Infrastructure Progress Goals:

- Generation of UNC composition of matter intellectual property on 2-3 chemical series per year with potential utility in treating disease beginning in 2009
- Deliver 1 or more small molecule pre-clinical candidates with in vitro & in vivo profiling data consistent with target validity and 'drug-like' characteristics per year beginning in 2010
- Out license one project and/or create one 'spin-out' company per year beginning in 2010
- Partner with other existing UNC and RTP Centers/organizations (Hamner Institutes for Health Sciences *[toxicology]*, Center for Nanotechnology in Drug Delivery, Institute for Pharmacogenomics and Individualized Therapy, National Institute of Mental Health – Center for Psychoactive Drug Screening *[compound profiling]*, Biomanufacturing Research Institute and Technology Enterprise – NC Central University *[high throughput screening]*, Carolina Center for Genome Sciences *[in vivo profiling]*) to accelerate pre-clinical development of New Chemical Entities (NCEs) and to enable an effective project flow
- Create a flexible laboratory facility in the new Imaging Research building that will accommodate the CICBDD and enable a resilient infrastructure that adapts to the changing scientific/technological environment for drug discovery.

Appendix 1. Selected Academic Drug Discovery Centers

University of Kansas Center for Drug Discovery (http://www.cdd.ku.edu/)
University of Kansas Office of Therapeutics, Discovery and Development.
Center for Drug Discovery at the University of Connecticut (http://www.centerdrugdiscovery.org/)
City of Hope/Beckman Research Institute Center for Gene Regulation and Drug Discovery (http://www.cityofhope.org/gerdd/)
The University of Georgia Center for Drug Discovery (http://www.uga-cdd.org/)
Northeastern University Center for Drug Discovery (http://www.pharmsci.neu.edu/researchcenters/center_drugdiscovery.html)
Baylor University Center for Drug Discovery (http://www.baylor.edu/drug_discovery/index.php?id=21636)
Northwestern University Center for Drug Discovery and Chemical Biology (http://www.research.northwestern.edu/research/cddcb/)
University of Minnesota Center for Drug Design (http://www.ahc.umn.edu/cdd/about/home.html)
University of Tennessee Center for Drug Discovery
USCF Center for Chemical Diversity (http://pharmacy.ucsf.edu/ccd/about/)
The Center for Drug Discovery at Duke University Medical Center
Dana-Farber Center for Drug Discovery and Development
Harvard Center for Applied Cancer Science
Harvard Center for Neurodegeneration & Repair Laboratory for Drug Discovery in Neurodegeneration (LDDN)
Penn Center for Molecular Discovery (http://www.seas.upenn.edu/~pcmd/)
University of New Mexico Health Sciences Center and Chemical Diversity Labs
University of Virginia Burger Drug Discovery Center
The Bioinformatics Center at Rensselaer and Wadsworth: Drug Design and Discovery to Fight Substance Abuse (http://www.bioinfo.rpi.edu/research/drug_design.html)
Purdue Cancer Center – Drug Discovery (http://www.cancer.purdue.edu/discovery.php)
Dana-Farber Cancer Institute Center for Applied Cancer Science
Yale Cancer Center Signal Transduction and Drug Discovery
Georgetown University Medical Center's Drug Discovery Program
Fox Chase Cancer Center – Drug Discovery
The Center for Drug Discovery at Duke University Medical Center
Virginia Commonwealth University Center for Structural Biology and Drug Discovery
University of Buffalo Center for Drug Discovery and Experimental Therapeutics (http://cddet.buffalo.edu/)
LSUHSC Neuroscience Center of Excellence
National Cooperative Drug Discovery Groups (NCDDGs) – Funded U19s (2005-2010)
- University of CA - Santa Cruz
- University of Utah
- Johns Hopkins University
- University of California-Davis
- Arizona Cancer Center
- Burnham Institute
- H. Lee Moffitt Cancer Center Dept. of Drug Discovery Program
- University of Wisconsin
- University of Michigan Center for Chemical Genomics

University of Alabama-Birmingham Center for AIDS Research Drug Discovery/Development Program
Sloan-Kettering Experimental Therapeutics Center
Molecular Libraries Screening Centers Network – Funded NIH Centers
- Universities of New Mexico
- University of Pennsylvania
- University of Pittsburgh
- Vanderbilt University

- Columbia University Health Sciences
- Southern Research Institute
- The Burnham Institute
- The Scripps Research Institute
- Emory Center for Drug Discovery

University of Mississipi National Center for Natural Products Research
USC/MUSC Center for Drug Discovery
University of Alabama-Birmingham Center for Biophysical Sciences and Engineering (CBSE)
Georgetown University Drug Discovery Program
The University of Texas Medical Branch at Galveston (UTMB) Drug Discovery and Development Program
Tufts University Center for Drug Discovery
Cleveland Clinic Taussig Cancer Center Experimental Drug Discovery and Development
Georgia State University Center for Biotechnology and Drug Design
University of Florida Center for Drug Discovery

Appendix 2. Proposals to the Center

Center for Integrative Chemical Biology and Drug Discovery
School of Pharmacy, UNC Chapel Hill
Proposal for Collaboration

Thanks for your interest in submitting a proposal for small molecule hit/lead/tool discovery in the CICBDD. Successful proposals will result in the formation of a project team and development of a plan for creating the small molecule needed to advance your research. The Center will provide assay development, screening and medicinal chemistry resource to achieve the project objectives. Investigators will typically be expected to serve as a member of the project team and must provide resource from their laboratory to advance the project within their field of expertise. Existing funding must be sufficient to obtain preliminary data to support the pursuit of further joint funding for projects. **Data created as a result of the collaboration may be used by the Center and the sponsoring investigator(s) who will also cooperate with one another regarding publications/presentations. Any inventions resulting from the collaboration will be managed by the University's Office of Technology Development, which will consult with the Center and the sponsoring investigator(s) in accordance with its usual practices.** More background on the Center can be found at http://www.pharmacy.unc.edu/labs/center-for-integrative-chemical-biology-and-drug-discovery. Please complete each section below and submit a maximum of 4 pages to: Stephen Frye (*svfrye@email.unc.edu*) by <DATE> consideration. Proposals will be reviewed by the Scientific Advisory Board for the Center. You should expect feedback on your proposal by <DATE>. In addition to the information below, the fit of your proposal with expertise and resources in the Center will be considered in reaching a decision.

Principal Investigator(s):
Affiliation(s): (sponsoring department)
Contact Info: (name, phone, e-mail, website)
Molecular Target, Pathway or Cell-based system for which a small molecule 'interrogator' is desired: (please include known acronyms & alternative names)

A successful collaboration would result in: (brief statement of your aspirations – e.g. - 'a compound active in cells'; 'a compound for in vivo profiling'; how do you envision collaborating with the Center? etc…)

How will this small molecule aid your future funding? (What specific grants will this tool enable? What is your current funding status for the work proposed? Is it envisioned that the CICBDD could facilitate and/or have a part in your grant proposals – such as a core resource or co-investigator?)

Disease relevance of target/pathway: (summarize genetic, biochemical, pharmacological or clinical data – be specific about species and emphasize current state of small molecule interrogators if known)

Potential scientific impact of small molecule tools: (in addition to potential therapeutic application, what are the basic science questions that a small molecule will enable? How significant are these to the field of research? Are there alternative methods? si-RNA, antisense, KO's etc…? Have they been employed & what were the results?)

Tractability of assay development: (What is the status of biological reagents for the target? (protein supply, characterization & purification, cell lines available, in vitro/in vivo readouts) How will you assess the activity of potential hit compounds – what is the assay format? What throughput and signal to noise does your assay achieve? What selectivity readouts are important from a mechanistic perspective? …from a therapeutic perspective?)

Tractability of ligand discovery: (Is there precedent for discovery of small molecule interrogators of this target? …..of homologues or related targets? Does this target or pathway possess known binding sites for a small molecule? If unprecedented for small molecule discovery, what evidence is there of tractability? – i.e. – biochemical mechanism, x-ray structural evidence)

Selected References: (please briefly annotate your references to indicate their relevance to the questions above – PDF files of the 3 most relevant references should be attached)

Appendix 3. Intellectual Property Policy & Invention Income Distribution Plan

Proposed Invention Income Distribution Plan

Center for Integrative Chemical Biology and Drug Discovery (CICBDD)

Background:

The CICBDD was created to enable the translation of UNC biomedical research further toward the discovery of new small-molecule medicines. In general this will be based upon proposals from UNC faculty to collaborate with the Center on progression of a biological target hypothesis through the hit generation, lead discovery and candidate selection phase (see: http://www.pharmacy.unc.edu/labs/center-for-integrative-chemical-biology-and-drug-discovery). The Center will generally provide assay development, screening and medicinal chemistry resource to achieve the project objectives. Investigators will typically be expected to serve as a member of the project team and to provide support for activities in the project plan that are within their area of expertise. Regular collaborative project team meetings will be held where data will be reviewed and next steps for the project proposed and agreed. **Data created as a result of the collaboration may be used by the Center and the sponsoring investigator(s) who will also cooperate with one another regarding publications/presentations. Any inventions resulting from the collaboration will be managed by the University's Office of Technology Development, which will consult with the Center and the sponsoring investigator(s) in accordance with its usual practices.**

The Center is critically dependent upon sponsorship of targets by biologically oriented UNC faculty to achieve its mission. In order to encourage collaboration and ensure that all contributing investigators and the Center share in revenue from IP resulting from collaborations with the Center, the following Income distribution plan has been created (Mark Crowell, Tech Transfer & Dhiren Thakker, School of Pharmacy) and approved by the Board of Directors for the Center (Chair: Bob Blouin, Dean of Pharmacy; Etta Pisano, Dean of Medical School; Tony Waldrop, Vice-Chancellor for Research & Economic Development; Shelley Earp, Director of the Lineberger Cancer Center; Holden Thorp, Dean of Arts & Sciences; Gary Johnson, Chair of Pharmacology).

A. Current formula and procedures for determining inventorship and distributing invention income:

The following is a summary of the University's Patent and Copyright Policies (as amended 2001) and its Patent and Copyright Procedures (1994). If there is any conflict between the summary and the then-current policies and procedures, the latter will take priority.

Procedure for Inventorship determination – Strictly legal, objective determination of inventorship based on legal criteria for determining inventors; under this approach, all legal inventors must be named, and no one may be named who is not an inventor.

1. 20% of invention income is distributed to the Invention Management Fund in the Office of Technology Development.

2. 40% of invention income is distributed to the inventor(s) (the "inventor share"). When there is more than one inventor, the presumption is that the inventor share of income will be distributed in equal portions to each inventor, provided that the University may

adjust distribution among inventors (e.g., the University will typically honor an agreement of all inventors to distribute income in other than equal shares).

3. 40% of invention income is distributed to the department(s) of the inventor(s). When there is more than one inventor, the department share of income is distributed to each inventor's department in the same relative proportion as the share received by the inventor in such department.

B. Proposed formula and procedures for determining inventorship and "Contributing Innovator" status and distributing invention income for CICBDD:

As a condition of CICBDD's participation in a project, University personnel involved in the project and their departments agree to the following:

Procedure for "Contributing Innovator" determination – "Contributing Innovator(s)" will be determined at the time a target is referred to and accepted for development within CICBDD. In general this designation will apply to the UNC faculty member(s) who proposed the target and/or other individuals who played a critical, creative role in establishing the therapeutic/biological hypothesis and who will be fully engaged in the collaboration with the Center. Department heads of those identified as Contributing Innovators will review and approve the designation of Contributing Innovators. The Board of Directors of the CICBDD will serve as a dispute review and resolution body for addressing concerns, questions, or disagreements about the designation of Contributing Innovator status. The intention of this provision is to fairly reward target sponsors for their role in the collaboration.

Procedure for Inventorship determination (same as used under current approach) – Strictly legal, objective determination of inventorship based on legal criteria for determining inventors; under this approach, all legal inventors must be named, and no one may be named who is not an inventor.

Designation of "Inventors" for purposes of distribution of invention income – Contributing Innovator(s) may become legal inventors on patents. Any Contributing Innovator who is not a legal inventor will be administratively considered an inventor for the purposes of calculating the distribution of the inventor share of invention income and department share of invention income.

1. 20% of invention income is distributed to the Invention Management Fund in the Office of Technology Development.

2. 40% of invention income is distributed to the inventor(s) and the Contributing Innovator(s) (the "inventor share"). When there is more than one inventor and/or Contributing Innovator, the presumption is that the inventor share of income will be distributed in equal portions to each inventor and Contributing Innovator, provided that the University may adjust such distribution (e.g., the University will typically honor an agreement of all inventors and Contributing Innovators to distribute income in other than equal shares).

3. 20% of invention income is distributed to the department(s) of the inventor(s) and Contributing Innovator(s). When there is more than one inventor and/or Contributing Innovator, the department share of income is distributed to each inventor's and Contributing Innovator's department in the same relative proportion as the share received by the inventor or Contributing Innovator in such department.

4. 20% of the invention income is distributed to CICBDD to support research.

Signatures signifying agreement with Plan:

Target:

Target sponsor(s)/Contributing Innovators:
Date:

Department Chair of target sponsor(s):
Date: