The Ohio State University College of Pharmacy
Center of RNA Nanotechnology and Nanomedicine
November 2016

Introduction

In 2016's College of Pharmacy External Review, it was reported that COP has strong international recognition due to its achievements in innovative research and educational practices. Yet, in order to grow, it must address some of the weaknesses mentioned in 2016's College of Pharmacy Program Review, including the need to enhance cutting-edge research groups, to encourage collaborations with OSUWMC, and to develop key domestic and international partnerships to further research and outreach missions.

The Center of RNA Nanotechnology and Nanomedicine (referred herein as 'Center') endeavors to confront some of these challenges by providing students the opportunity to further their education with world-class research teams, enhancing communications among scientists throughout the university, and bringing economic growth to the university and Columbus as a whole, both building upon and enhancing Ohio State's reputation for excellence in the pharmaceutical sciences. Recently, OSU has signed an agreement to accept $1,4 million, $400,000 as donation, and $1,000,000 as sponsored research to initiate the setup of this center. Additional funding to this center in under discussion.

Strategic Environmental Scan

The concept of the Center is based on a number of key themes that are rooted in its primary objectives:

1) Create the next generation of scientists who are armed with skills in innovative treatment options based in the growing field of RNA nanotechnology and nanomedicine.
2) Further enhance the visibility of the COP on a national and global scale
3) Promote collaborations between researchers at OSU across a variety of disciplines
4) Provide a platform for students to enhance their training and research with leading experts
5) Attract funding opportunities and create jobs.

Organization of the Strategic Plan

The purpose of this document is to outline and highlight the high level goals that the Center intends to address over the next one to five years. Following it are letters of support from notable individuals who support the establishment and growth of the Center.

Vision

The Center will serve as a platform for collaboration among the many investigators in the College of Pharmacy and existing centers across the OSU campus with research efforts in RNA nanotechnology and nanomedicine.

Mission

The Center's cross-disciplinary research will achieve novel materials and innovative therapeutic strategies to treat indications with few effective treatment options such as cancer, obesity, diabetes, cardiovascular disease, lung disease, and drug abuse. The Center intends to transform basic science research in RNA nanotechnology and nanomedicine through innovative approaches to disease treatment and diagnostics, creating the next generation scientific workforce and launching small agile spin-off companies to pursue Center breakthroughs. The mission is well aligned with COP's strategic plans to enhance visibility, to continue to build on drug discovery research, and to move new drugs to the clinic.

Goals

Long term goals:

(1) Engage in fundamental research or applied research to create intellectual properties, high impact publications, and valuable patents.
(2) Successfully pursue the translation of fundamental research from the lab bench to the clinic and the market, using the created intellectual property to launch spin-off companies and attract high technology companies to the region.
(3) Generate royalty income to continue growth of the Center.
(4) Secure extramural funding to continue to support the Center's research efforts and allow the foundation to successfully compete for major extramural funding.

Short term goals:

(1) Establish a platform for exchange of ideas and develop a research plan based on the expertise of OSU members.
(2) Enhance communication and collaborative activity among OSU faculty interested in RNA nanotechnology and nanomedicine with the goal of building fruitful new relationships across disciplines.
(3) Enhance the training of graduate and postdoctoral students by in-reach and out-reach mechanisms for communicating OSU's growing nanobiotechnology research, such as organizing symposia in the individual relevant areas and establishing a seminar series. Lab training programs consisting of a mix of lectures, conception/design of research projects, and hands-on lab training designed to introduce participants to the working framework of nanobiotechnology will be offered, supported by tuition collected from the trainees and funding agencies, with the goal of promoting the fields pioneered by members of the Center.
(4) Build an infrastructure necessary for national and international recognition as a leading research center in nanobiotechnology by accepting international institution membership.
(5) Exchange graduate students, postdocs, and faculties (visiting scholars) among member institutes to help trainees rapidly advance their research projects, providing them with an opportunity to work with leading scientists and become part of an international network. The host institute will provide facilities and equipment, while the visiting institute will provide travel and support for room and board.

Rationale

Nanobiotechnology seeks to exploit recent advances in nanotechnology to address critical needs in medicine and the biological sciences. In particular, RNA nanotechnology has demonstrated significant potentials for developing RNA nanoparticles for *in vivo* drug delivery. To advance the field, these complex, large-scale scientific opportunities require cutting-edge interdisciplinary work by teams of researchers drawn from multiple disciplines. Important examples include, but are not limited to, more effective therapies for cancer, obesity, and drug abuse and innovative diagnostics for early detection of diseases.

These opportunities can be seized by world-class research teams when the challenges of assembling and fielding interdisciplinary teams are successfully met. These challenges include connecting and integrating researchers in teams across many different disciplines; enabling communication between the different cultures of medicine, natural science and biomedical engineering; building relationships to establish the essential trust at the basis of all collaboration; and managing effectively without creating bureaucratic obstacles that slow activity. All of these call for innovative approaches.

Responding to the opportunity and addressing these challenges, the OSU Center of RNA Nanotechnology and Nanomedicine will be established as an innovative platform for a flexible and agile center providing unique contributions, functioning as a node linking many researchers across multiple networks and as a matrix from which to create both new interdisciplinary research collaborations and the next generation scientific workforce in nanoscience and technology. The proposed center will leverage already established but dispersed OSU biomedical research efforts, using nanotechnology as a multidisciplinary focal point to integrate these efforts for maximum impact. The proposed Center will build upon effective collaborations located within the campus including the James Comprehensive Cancer Center, Center for RNA Biology, Center for Brain and Spinal Cord Repair, Center for Clinical and Translational Science, and Center for Retrovirus Research. Given how quickly science and technology are moving, timing for the new Center is critical and speed is of the essence.

<u>Projected benefits to OSU:</u>

(1) The Center would enable substantial return on a minimal start-up investment by enabling OSU to compete successfully for large-scale, long-term extramural funding from NIH, NSF and DOD, which would not only strengthen OSU research over the near term but also attract high caliber faculty and graduate students for long term sustained OSU growth in interdisciplinary research.
(2) The Center would impact Ohio economic development by enhancing the knowledge economy of the region, generating intellectual property and spin-off companies, attracting technology and life sciences firms to the area, and creating jobs.

Administration

<u>Advisory Board</u>

This advisory group would be composed of senior representatives from several key research focus areas that will meet quarterly or biannually. Composition of this advisory board will be determined as the Center gets established based on specific needs. Key focus of this board will be to provide input to the Center committee on meeting the key objectives and address potential challenges.

(1) Dean Henry Mann (COP)
(2) Dr. Cynthia Carnes (COP)

(3) Dr. Peter Mohler (COM)

Oversight Committee

Committee members would initially meet every 1-2 months then less frequently as warranted by the Center. Key focus of this committee is to provide overall guidance and direction for the Center with regards to coordination and execution of project plans, review of milestones, educational outreach, research and development, strategic outreach and professional relationships.

Executive committee:

Committee members will be selected from Center members based on their stature and extensive experience in (1) RNA nanotechnology, nanobiotechnology, patient care, and clinical and translational research; (2) research project management; regulatory, legal, and technology transfer compliance; and senior administration. These qualities will position them well as scientific advisors to Center leadership.

Meetings will be held every quarter to ensure consistent and direct communication between members. Plenary meetings will be held every year to encourage the flow of new ideas within the university and instigate collaborations between other departments. Individuals from various backgrounds will be periodically invited to attend closed sessions with the intent of strengthening and advancing the Center.

(1) Peixuan Guo
(2) Yizhou Dong
(3) Alex Sparreboom
(4) Jack Yalowich
(5) Rajgopal Govindarajan
(6) Carlo Croce
(7) Peter Shields
(8) Raj Muthusamy

Director

The Director will oversee the day-to-day operations across all contributing components to provide support for all research, administrative, budgetary and operational aspects of the Center. The founding director will be Peixuan Guo, PhD., who is the Sylvan G. Frank Endowed Chair in Pharmaceutics and Drug Delivery at The Ohio State University College of Pharmacy and professor of the Division of Pharmaceutics and Pharmaceutical Chemistry; and College of Medicine/Department of Physiology & Cell Biology/ Dorothy M. Davis Heart and Lung Research Institute.

Staff

The Center would require two half-time staff positions to begin operations. The center manager and administrative assistant positions might be combined into one full-time position if the appropriate candidate is identified.

(1) *Center Manager* - one half-time Center manager at the Ph.D. level will oversee the daily scientific operations of the Center and assist in the preparation of grant proposals and publications ($50,000 for a 100% position plus fringe benefits and office supplies).

Administrative Structure:

(1) The Center Director will report to the Dean and Vice President for Research.
(2) The Center members will report to the Director.
(3) The Center will be monitored by the Oversight Committee.

Faculty Membership

Application Procedure

To apply for membership, faculty must submit a completed application form and a current CV. Two levels of membership will be offered

(1) Full Membership: Faculties (a) with active federal/state grants or publications supporting research related to nanobiotechnology, such as nanoscale biomaterials, nanomedicine, nanobiomechanics, nanophotonics, biomolecular imaging, etc.; and (b) that currently have graduate and/or postdoctoral students.
(2) Associate Membership: No specific requirements, but a strong interest to engage in nanobiotechnology research and nanomedicine involving RNA.

Membership is free. The only stipulation is that the PI must have sufficient resources (funding support, physical lab space, facilities, equipment, and research staff) to conduct projects related to nanobiotechnology. Other criteria for selection are to be determined by the Oversight Committee.

Description of Faculty Involvement

OSU faculty will be involved in Center activities in numerous ways:

(1) Faculty will be critical knowledge experts in diverse research areas, including but not limited to: (1) RNA nanotechnology; (2) Nanopore sensing and early disease diagnosis; (3) Drug transporters and Nanotechnology; (4) Cancer Nanotechnology; (5) Liposomes as a nanodelivery system; (6) Micelles as nanodrugs; (7) Nanosynthetic chemistry; (8) Synthetic Biology; (9) Nanoimmunology; (10) Single molecule instrumentation; (11) Nanotechnology for therapy of viral diseases; and (12) Drug development.
(2) Investigators in research to foster sustainable development of the Center through research grants and outreach efforts.
(3) Collaborators with partners to transform research from the bench to the clinic/industry.

Tentative list of Faculty and research staff to join the Center:

(1) Dr. Peixuan Guo, Division of Pharmaceutics & Pharmaceutical Chemistry, COP
(2) Dr. Henry Mann, Division of Pharmacy Practice & Science, COP
(3) Dr. Michael Caliguiri, Division of Hematology, COM
(4) Dr. Cynthia Carnes, Division of Pharmacy Practice & Science, COP
(5) Dr. Sharyn Baker, Division of Pharmaceutics & Pharmaceutical Chemistry, COP
(6) Dr. Carlo Croce, Department of Cancer Biology & Genetics, COM
(7) Dr. William Carson, Division of Surgical Oncology, COM
(8) Dr. Peter Shields, Division of Cancer Prevention & Control, COM
(9) Dr. Jack Yalowich, Division of Pharmacology, COP
(10) Dr. Yizhou Dong, Division of Pharmaceutics & Pharmaceutical Chemistry, COP
(11) Dr. Alex Sparreboom, Division of Pharmaceutics & Pharmaceutical Chemistry, COP
(12) Dr. Dan Shu, Division of Pharmaceutics & Pharmaceutical Chemistry, COP
(13) Dr. Mamuka Kvaratskhelia, Division of Pharmaceutics & Pharmaceutical Chemistry, COP
(14) Dr. Jianhua Yu, Department of Internal Medicine, COM
(15) Dr. Richard Fishel, Department of Cancer Biology & Genetics, COM
(16) Dr. Jianjie Ma, Department of Surgery, COM
(17) Dr. Sylvan G. Frank, Division of Pharmaceutics & Pharmaceutical Chemistry, COP
(18) Dr. Robert Lee, Division of Pharmaceutics & Pharmaceutical Chemistry, COP
(19) Dr. Tae Jin Lee, Comprehensive Cancer Center, COM
(20) Dr. Hui Zhang, Division of Pharmaceutics & Pharmaceutical Chemistry, COP
(21) Dr. Xiaoming He, Department of Biomedical Engineering, College of Engineering

(22) Dr. Deliang Guo, Department of Radiation Oncology, COM
(23) Dr. XueFeng Bai, Department of Pathology, COM
(24) Dr. Noah Weisleder, Department of Physiology & Cell Biology, COM
(25) Dr. Chad Bennett, Comprehensive Cancer Center, COM
(26) Dr. Dasheng Wang, College of Pharmacy
(27) Dr. Dennis Bong, Department of Chemistry & Biochemistry, College of Arts & Sciences
(28) Dr. Rajgopal Govindarajan, Division of Pharmaceutics & Pharmaceutical Chemistry, COP
(29) Dr. Charles Bell, Department of Biological Chemistry & Pharmacology, COM
(30) Dr. Qi-en Wang, Department of Radiology, COM
(31) Dr. Hua Zhu, Division of Cardiac Surgery, COM
(32) Dr. Emanuele Cocucci, Comprehensive Cancer Center, COM
(33) Dr. Vicki Wysocki, Department of Chemistry & Biochemistry, COM
(34) Dr. Krishan Kumar, Department of Radiology, COM
(35) Dr. Renzhi Han, Division of Cardiac Surgery, Wexner Medical Center
(36) Dr. Mitch Phelps, Director of Pharmacoanalytical Shared Resource, Pharmaceutics and Pharmaceutical Chemistry, COP

Affiliated International Institutes Outside OSU:
More than 10 universities have expressed their interest to join the Center pending administrative paperwork.

Description of Student Involvement
Students at the College of Pharmacy will be exposed to Center activities through a variety of ways. Students will use the Center for growth in nanobiotechnology knowledge and practice development skills and information. They can utilize Center mentors and participants as a networking resource as they progress through their own development. By building a community of learners, the students can continue to view and use the Center as an important resource throughout their careers.

Budget and Funding

Dr. Peixuan Guo has acquired $1.4 million over five years to support the center, provided by RNA Nanobio Ltd USA, established in Columbus.

Equipment and Instrumentation: No new equipment is requested for Center start-up. State-of-the-art equipment is available and more will be acquired through federal grants as needed. Institutional support for this equipment will be requested at a later date.

Projected Operating Costs: To be determined. Tentative costs include:

(1) *Seminar series*
10 total seminars per academic year (5 per semester) featuring eminent researchers from outside OSU. $10,000 per year/$1,000 per seminar

(2) *One day symposium/research day*
Initially, the annual center symposium (featuring two invited speakers from outside OSU) will be coupled with another event (e.g. OSU Cancer Center Research Day or COP Research Day) to build interest in the new Center and to reduce costs, as compared to a stand-alone event. $5,000 per year)

(3) *Intramural research seed funding*
The Center will offer two seed grants annually to fund pilot research projects in nanobiotechnology and nanomedicine (@$50,000 each) and to initiate cross-disciplinary interactions among OSU faculty.

Estimated costs per year:

(1) Manager: $67,700
(2) Seminar: $10,000
(3) Symposium: $5,000
(4) Seed Funding: $100,000.

Subtotal: $182,700 per year

Participants in continuing professional development programs and other educational programming will pay a fee to access course materials or attend programs. The Center will also seek contracted services for programming to industry partners.

The Center will seek grant funding and collaborative partnerships for research projects and practice development tools. Additionally, CAPP will partner with the College of Pharmacy Development Office to seek financial support through endowments and sponsorships. The Center plans to be self-sustaining within five years of establishment.

Evaluative Criteria and Benchmarks

In general, measurable outcomes to be assessed will include extramural funding, peer-reviewed publications, patent disclosures and technology commercialization, technologies brought to clinical trials, educational and outreach programs, and effectiveness of the collaborative research development model.

Overall Significance: The Center must address important biomedical problems with the application of an innovative nanotechnology-based solution. Center research projects must be able to ultimately lead to the development of translational, clinically worthy solutions to prevention, diagnosis, or therapy of diseases.

Overall Approach: The Center must take advantage of multidisciplinary approaches to promote and advance both the discovery and application of innovative nanotechnology solutions to important disease-related problems. Accordingly, overall research goals, experimental design, methods, and capabilities must be sound and well developed. Effective mechanisms must be in place to foster strong collaborative interactions and promote “cross-fertilization” among investigators (and participating institutions) representing both biology and applied nanotechnology/engineering/physical sciences. Efforts should be made to involve clinicians in preclinical studies to support the development of nanotechnology-based solutions to the point where rapid translation into clinical trials is achievable. If applicable, goals should be advanced through the meaningful participation of a commercial entity.

Leadership and Organizational Framework: There must be adequate evidence for the managerial and collaborative capabilities of proposed Center leadership. The backgrounds, expertise, and commitments of the Director and other key personnel must meet the requirements for the proposed scope of activities and be in line with the overall goals for the Center. There must be evidence of sufficient institutional support for proposed Center activities.

Supporting materials

Appendix A: Agreement of Sponsored Research

Appendix B: Letters of support from relevant division chairs and directors within the college, interested parties outside the college, and entities with similar emphases at other universities.

(1) Sharyn Baker, Head of the Division of Pharmaceutics & Pharmaceutical Chemistry, COP
(2) Cynthia Carnes, Associate Dean, COP
(3) Henry Mann, Dean, COP
(4) Michael Caligiuri, Director, CCC.

APPENDIX A

AGREEMENT FOR SPONSORED PROGRAM

THE OHIO STATE UNIVERSITY

THIS AGREEMENT**,** made effective this 15th day of November, 2016 by and among The Ohio State University, located at 1960 Kenny Road, Columbus, Ohio 43210 (hereinafter called the UNIVERSITY), Nanobio Delivery Pharmaceutical Co. Ltd., whose address is 1275 Kinnear Road, SciTech Campus OSU, Columbus, OH, 43212, United States (“Nanobio”) (Nanobio collectively referred to herein as "Sponsor").

WHEREAS, the UNIVERSITY has valuable experience, skill, and ability in the research described in Appendix A and Article 2 (the “PROJECT”), which is incorporated and made part of this Agreement,

WHEREAS, UNIVERSITY and SPONSOR share a common interest in seeing nanobiotechnology and nanomedicine technology developed and commercialized for the benefit of the public,

WHEREAS, UNIVERSITY intends to form a college center within its College of Pharmacy named “Center of RNA Nanotechnology and Nanomedicine” ("the Center") to promote research, training, and international collaborations on RNA nanotechnology and nanomedicine directed by Peixuan Guo (where “RNA nanotechnology” refers to nanometer scale RNA architectures with its major frame composed mainly of RNA.),

WHEREAS, UNIVERSITY has offered to provide SPONSOR the first option to negotiate an exclusive license to intellectual property generated through the PROJECT supported by SPONSOR,

WHEREAS, the performance of the PROJECT is of mutual interest to SPONSOR and UNIVERSITY, and is consistent with the instructional and research objectives of The Ohio State University and with its status as a public educational Institution, and

WHEREAS, the UNIVERSITY will use reasonable efforts to perform the PROJECT.

NOW THEREFORE, the parties mutually agree as follows:

1. Principal Investigator: Peixuan Guo

The Principal Investigator (“PI”) shall be responsible for the conduct, supervision and management of the PROJECT and the Center.