



FOR RECOMMENDATION

PUBLIC

OPEN SESSION

TO: Campus Affairs Committee

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DATE: April 25, 2019 for May 2, 2019

AGENDA ITEM: 6

ITEM IDENTIFICATION:

Establishment of an Extra Departmental Unit C (EDU: C) – Centre for Medicinal Chemistry

JURISDICTIONAL INFORMATION:

Section 5.8.1 of the Campus Affairs Committee (CAC) terms of reference outlines the responsibility of the CAC in the establishment, disestablishment or restructuring of Academic Units. Proposals for Extra-Departmental Units are considered and recommended for approval, pursuant to the *Guidelines for Administrative Functions and Protocols for Extra-Departmental Units (EDU)*.

GOVERNANCE PATH:

1. **Campus Affairs Committee [For Recommendation] (May 2, 2019)**
2. Campus Council [For Approval] (May 27, 2019)
3. Executive Committee [For Confirmation] (June 13, 2019)

PREVIOUS ACTION TAKEN:

No previous action has been taken.

HIGHLIGHTS:

This is a proposal to establish an Extra-Departmental Unit (EDU):C – the Centre for Medicinal Chemistry (CMC) to be housed at the University of Toronto Mississauga (UTM), effective July 1, 2019. An EDU:C is a multi-disciplinary and/or multi-departmental research and/or academic unit with a defined research domain in a particular area of academic work. It exists to foster research and scholarly interest in the area, but does not register students.

The CMC will be a preeminent, multi-disciplinary research consortium that will advance the methodology and practical application of medicinal chemistry while offering world-class research training that will position UTM as the prime destination in Canada and a significant global competitor for students interested in pursuing a career in the pharmaceutical industry. Research will be conducted in close collaboration with clinicians and medical practitioners, allowing for more rapid advancement and translation of new and revolutionary molecular therapeutics to advanced preclinical trials and commercialization, ultimately leading to improved patient outcomes.

In its research collaborations with local community partners, the CMC will have a long-term impact on the healthcare and pharmaceutical sectors in the GTA and beyond. As such, the CMC's goals are in close alignment with President Meric S. Gertler's "Three Priorities" and U of T's "Institutional Research Strategic Plan 2018-2023." At the divisional level, the operations of the CMC align with the priorities of the Academic Plan 2017 by "establishing productive national and international partnerships" and "strengthen[ing] the university's collaborations locally and internationally with government and non-governmental organizations to the betterment of society."

By being established at UTM, the CMC will attract significant faculty membership from the Departments of Chemical and Physical Sciences and Biology. It further anticipates association from faculty with primary appointments on other campuses, including the Department of Chemistry and the Faculty of Pharmacy at UTSG. Strong involvement of faculty from the U of T research hospitals and the Faculty of Medicine will enable the translation of the drug design and development programs to examine human applications.

Planning for a formal academic unit began in 2016 with consultation between the Vice-President & Principal, the Vice-Principal Academic and Dean, the Vice-Principal Research, and the Chairs of Chemical and Physical Sciences, Biology and Computer Science. The CMC has extensively consulted with existing faculty across the Departments of Chemical and Physical Sciences and Biology. It will welcome collaborations with any future hires in these departments.

The CMC Director will report to the Vice-Principal, Academic and Dean, UTM on academic and budgetary matters. The Director, in consultation with an Advisory Board, will be responsible for overseeing all aspects of the CMC, including the direction and administration of its research programs, establishment of strategic partnerships, implementation of policies, and approval of budgets.

FINANCIAL IMPLICATIONS:

There are no net implications for the campus' operating budget.

RECOMMENDATION:

Be it Recommended,

THAT the proposed establishment of the Centre for Medicinal Chemistry (CMC) as an Extra Departmental Unit C (EDU:C), dated April 20, 2019, be approved, effective July 1, 2019.

DOCUMENTATION PROVIDED:

Item Proposal for a new EDU:C: Centre for Medicinal Chemistry

Proposal for a New EDU:C Centre for Medicinal Chemistry (CMC)

April 20, 2019

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1. Statement of Purpose

We propose the creation of a new EDU:C – the Centre for Medicinal Chemistry (CMC). The CMC will be hosted at the University of Toronto Mississauga (UTM) with tri-campus involvement by faculty, students and staff. UTM will be the lead division for the CMC and will assume administrative and budgetary responsibilities for the unit. A list of participating faculty is provided in section 5.

The proposed start date of CMC is July 1, 2019.

2. Background

Medicinal chemistry is an interdisciplinary subject covering synthetic and biophysical chemistry, cell biology, pharmacology, and computational modeling, cutting across research at UTM in the Departments of Chemical and Physical Sciences and Biology as well as overlapping with activities in the Faculty of Medicine, the Leslie Dan Faculty of Pharmacy, the Department of Chemistry, the Department of Computer Science and the Krembil Institute¹ (formerly the Toronto Western Research Institute and not part of UofT). It encompasses the design and synthesis of small organic molecules to bind biological receptors with high selectivity and potency, resulting in a change, either structurally or functionally, that elicits a beneficial biological response in the disease state.

Until recently, medicinal chemistry has primarily been the purview of pharmaceutical corporations due to the resources required to operate in the classical paradigm of drug development. The recent downsizing of pharmaceutical research and development has radically changed the scientific practices and industrial landscape. Drug discovery by intelligent design, rather than by screening compounds, and development using smaller, more efficient, multidisciplinary teams to bring new drugs to a preclinical stage is a model that has taken root in the industry, and one for exploration in medicinal chemistry that can be very effective in academia.

The CMC will be a novel integrated research unit with a program whereby molecules will be computationally designed, be efficiently synthesized, and undergo rapid assessment for therapeutic potential in extra- and intra-cellular studies. Unlike most academic drug discovery pipelines, work will extend to preliminary cost-effective pharmacokinetic screening that assesses the distribution and metabolism of the drug in the body, which is a critical decision-making step for the continuation/termination of the drug candidate development. The identification of necessary modifications to potential lead compounds is thereby determined early in the development process, and only agents with acceptable profiles are advanced to more complex preclinical models, resulting in more effective research and development.

A pilot program to determine the effectiveness of this approach has been in operation at UTM for five years and involved the collaboration of chemists, biologists, physicists, pharmacologists, and physicians. This pilot has resulted in a substantial number of publications and training for dozens of undergraduate and graduate students. It has attracted attention from the pharmaceutical industry by the development of 4 licensed lead compounds, 3 spin-out companies, and series-A funding amounting to \$22M for a class of agents (Appendix A). Such a success rate in producing lead compounds represents a per-capita productivity rate competitive with large pharma

¹ https://www.uhn.ca/Research/Research_Institutes/Krembil

companies. The CMC intends to move forward from this very successful pilot phase by establishing an interdisciplinary EDU-C based on the present faculty engagement.

3. Academic Rationale

The CMC intends to be a preeminent, multi-disciplinary research consortium that will advance the methodology and practical application of medicinal chemistry while offering world-class research training to undergraduate and graduate students at UTM. Training will also include opportunities to participate in professional development workshops as well as networking associations with the external community. Research will be conducted in close collaboration with clinicians and medical practitioners, allowing for more rapid advancement and translation of new and revolutionary molecular therapeutics to advanced preclinical trials and commercialization, ultimately leading to improved patient outcomes.

- a) **Vision Statement** – With its unique infrastructure, research strategies, and training programs, the CMC at UTM will serve as a hub for medicinal chemistry innovation and training in Canada. It has the potential to revive innovation in the pharmaceutical industry in the Greater Toronto Area (GTA) by supplying new intellectual property, training highly qualified personnel, and attracting the capital to invest in both people and technologies. Undergraduate and graduate student researchers at UTM will be given the opportunity to participate in a paradigm-shifting, collaborative training program that is uniquely geared towards industrial careers and entrepreneurship in drug discovery. CMC will pioneer innovation in modern drug discovery and empower CMC researchers and trainees to open new frontiers for the treatment of aggressive and lethal diseases.
- b) **Objectives** – In order to achieve its long-term vision, the CMC will take an interdisciplinary approach to medicinal chemistry that rests upon five specific objectives: **i) Research, ii) Partnerships, iii) Education and Training, iv) Translation, and v) Public Outreach.** An overview of each objective is described below.
 - i. **Research** – The CMC will investigate and develop innovative, small molecule therapies to deliver therapeutic solutions for diseases with highest unmet need. The core research program will focus on advancing the science of medicinal chemistry by experimenting with novel strategies for treating diseases that would not be pursued by the pharmaceutical industry. Approaches will include aspects of computational drug design, the synthesis of small molecules, biophysical/chemical assessment of the drug candidates, and the evaluation of potency and toxicity in cellular systems and in mouse models. Establishing the CMC at UTM will provide researchers with access to internal integrated physical facilities and unique interdisciplinary collaborations that will accelerate the design of new drug candidates and evaluate their clinical potential in an unprecedented timeframe, allowing for the preparation of advanced preclinical drug candidates that can be readily passed on to industry partners for further clinical development.

Undergraduate and graduate students and postdoctoral trainees will receive research training that will be unique to all of Canada in one or two sub-disciplines in drug discovery while providing exposure to the wider scope of the entire preclinical development process. Research programs will be conducted

through local, national, and international collaborations with research hospitals, academic institutions, non-for-profit organizations, and the pharmaceutical industry to enhance their quality and execution. Trainees will thereby receive a highly translational research training in drug discovery with high level of exposure to auxiliary fields, including clinical research, industrial development, and commercialization.

- ii. **Education and Training** – The CMC’s fully integrated research program will provide world-class training in modern drug design and development that will position UTM as the prime destination in Canada and a significant global competitor for students interested in pursuing a career in the pharmaceutical industry. Interdisciplinary training will be provided through internal research projects with sub-specialties in medicinal chemistry, in vitro pharmacology, pharmacokinetics and toxicology, and computationally-guided drug design. Undergraduate students will be able to participate in research projects offered through the Research Opportunity Program (ROP), independent studies, and thesis-based courses, run by a variety of academic units and co-supervised by CMC-associated faculty. Work-integrated learning programs and internship placements with partner organizations (including biotech and pharmaceutical companies) will be established with the support of the Experiential Education Unit (EEU) in the Office of the Dean to provide students with industry-relevant experiential learning. A seminar series, open to all UofT students, will focus on current trends in drug development with speakers from industry, government and academia. These programs build and expand on the strengths of our interdisciplinary undergraduate experience at UofT such as Pharmaceutical Chemistry (Department of Chemistry and Faculty of Pharmacy) to provide a unique window into both academic and industrial drug discovery platforms.

The CMC will critically provide essential training beyond research skills so that its trainees are prepared to succeed in the new pharmaceutical industry and its fast-changing landscape. We recognize that research-only positions in the pharmaceutical industry are becoming scarce and there is increased demand for scientists with broader skillsets who can succeed within smaller companies. As such, the CMC will provide its students with focused professional development training on intellectual property protection, management of drug discovery programs, modern drug discovery commercialization, and fundraising strategies. It will aim to foster an entrepreneurship spirit among its trainees through co-curricular collaborations with ICUBE, UTM’s business accelerator, and other local accelerators, including the provincial Regional Innovation Centres.

- iii. **Partnerships** – Developing and maintaining productive partnerships is central to realizing the CMC’s vision. Interdisciplinary collaborations will enhance the CMC’s research projects by fostering synergistic and complementary expertise while strengthening the translational potential of its projects and outcomes. Collaborations internal to UTM and across U of T will be encouraged between researchers interested in synthetic and biophysical chemistry, cellular biology, pharmacology, and computational modeling.

The CMC will partner with research hospitals and biology departments across the world to complement its drug design and development programs, including

institutions with expertise in treating specific diseases and the infrastructure to provide translational opportunities for performing preclinical and clinical trials (the CMC will not run the clinical trials). Particular emphasis will be placed on providing medicinal chemistry support to the numerous biology programs at local institutions, including the Princess Margaret Hospital, the Krembil Research Institute, a research institution of the Toronto Western Hospital, and the Hospital for Sick Children. Likewise, collaborations with industry partners will provide opportunities for student placements and serve as the foundation for enabling the clinical translation and commercialization of the CMC's research discoveries. The newly established UofT-National Research Council partnership in the Centre for Research and Applications in Fluidic Technologies (CRAFT) and Precision Medicine initiative will also be critical to bioanalytical collaborations in drug design.

- iv. **Translation and Commercialization** – Newly developed therapeutics only reach patients through a highly regulated clinical development process, which often requires the attraction of industrial investment to finance this expensive process. The CMC will seek to empower faculty and trainees to accelerate the translation and commercialization of their research to deliver effective drug therapies to the clinical stage. It will support faculty and students in initiating and sustaining productive collaborations with clinical researchers through extra-curricular experiential learning activities and workshops on effective collaborations and intellectual property protection, and through fundraising for trainee exchange placements (including visiting graduate students, postdoctoral fellows, and Cardiff exchange students). Commercialization of CMC technologies will be facilitated through a focused program that will assist faculty and trainees with attracting industry opportunities and maintaining strong investor relationships.

Given the translational nature of medicinal chemistry, the CMC intends to directly engage the pharmaceutical industry and has already been successful in commercializing technologies developed in the UTM research labs over the course of its pilot project. In the last two years, the CMC's labs have been visited by pharmaceutical delegations from Johnson and Johnson, Amgen, Astrazeneca, Novartis, Paraza, Trillium Therapeutics, Charles River, and Pharmaron. It has also hosted CEOs of not-for-profit organizations, including the Centre for the Commercialization of Antibodies and Biologics (CCAB), the Fight Against Cancer Innovation Trust (FACIT), the Centre for Drug Research and Development (CDRD) and Mars Innovation (MI). Industry feedback has been very positive and there is significant interest from multiple organizations for developing mutually beneficial partnerships and student internship placements within the local industry. These partnerships operate as outlined in UofT's Statement on Research Partnerships.

- v. **Community Outreach** – The pilot project has to-date been hugely interactive with non-academic communities. Numerous presentations have been given across Canada and internationally, informing various public groups about new research developments in medicinal chemistry and signaling the national significance of the CMC at UTM. Extensive multi-sector, multi-institution collaborations will attract provincial and federal cluster funding opportunities

that will enhance the international profile of UTM, further attracting top student, faculty and staff talent.

The CMC labs have been visited by representatives from the municipal (Mayor of Mississauga), provincial (Minister of Research, Innovation and Science), and federal (Minister of Science) governments; philanthropic organizations (Genome Canada, Krembil Foundation, Fidani Foundation); local charitable groups (Leukemia and Lymphoma Society Canada, Oakville Prostate Survivor Group, Jesse's Journey); local Probus clubs (Oakville, Cooksville, Port Credit, South Mississauga, Central Mississauga); and high schools (St. Thomas, Streetsville, St. Michaels). During these tours, CMC faculty members explain the drug design and development process through hands-on demonstrations of the equipment used in medicinal chemistry research. All tours finish with a visit to the Level II Cancer Cell Biology lab, where guests are invited to look at cancer cells under a microscope and see the effects of the newly developed drugs on cancer cells in comparison to normal cells.

Such efforts towards public engagement have served to inspire new interest in science, in drug development, and in the CMC research program, leading in part to the Orlando Foundation's philanthropic donation of \$7M towards a new science building at UTM. The CMC will continue to offer and expand this multi-faceted outreach program with the intention of providing the highest exposure possible for its research and training programs.

- c) University and Divisional Strategic Goals** – The CMC's research and educational goals are in close alignment with several institutional strategies that have been advanced by U of T and its campuses in recent years. President Meric S. Gertler's "Three Priorities" has issued a call for U of T to better leverage its location to "promote further success in research, teaching and learning by focusing on urban processes, dynamics and challenges, such as poverty, public health, innovation clusters, environmental and energy systems, transportation, political systems, design and planning, and more."² The CMC's research collaborations with local community partners will have a long-term impact on the healthcare and pharmaceutical sectors in the GTA and beyond. Similarly, the CMC's emphasis on improving public health is reflected in U of T's "Institutional Research Strategic Plan 2018-2023"—in particular, the theme "PROMOTE: Healthy People, Healthy Communities, Healthy World" and the subtheme "Molecular Medicine and the Biology of Disease."³ The inclusion of these themes in the university's strategic research plan signals the high level of activity and impact that medicinal chemistry has within the university and the university's commitment to supporting research in this field in the future.

At the divisional level, UTM Academic Plan 2017 has expressed a desire to demonstrate on a local and international level that "UTM is a home for world-class research" that "enriches and bridges disciplines." The operations of the CMC and its research align with the priorities of the Academic Plan by "establishing productive national and international partnerships" and "strengthen the university's collaborations locally and internationally with government and non-governmental organizations to the betterment of society."⁴

² See Gertler, "Three Priorities: A Discussion Paper." University of Toronto, 2015.

<http://threepriorities.utoronto.ca/wp-content/uploads/2015/10/Three-Priorities-Discussion-Paper.pdf>

³ <http://www.research.utoronto.ca/isrp/>

⁴ https://www.utm.utoronto.ca/dean/sites/files/dean/public/shared/UTM_AcademicPlan_V1C.pdf

UTM's confidence in the CMC is reflected in its inclusion in the campus's significant financial commitment (~\$150M) towards building a new Science Complex by 2020 (~7000 square meters of research space), which has been explicitly identified as a priority sub-objective in its Academic Plan Implementation for 2017-2021.⁵

- d) Distinctiveness** – The CMC will be an innovative research hub whose programming will encompass both world-class translational drug discovery research and professional training relevant to the current needs of local and international pharmaceutical industries. It will bring unique medicinal chemistry research infrastructure and talent to the GTA, where the field is currently underrepresented, and will supplement the vast number of biological and chemical discoveries made at the University of Toronto, the University Health Network (UHN), and other academic institutions and research hospitals.

While there are currently no comparable units at the U of T, the research and training missions of the CMC will interact with a range of science departments across the U of T tri-campus, including senior faculty members at the Faculty of Medicine and Faculty of Pharmacy, and with the Departments of Chemistry and Computer Science. The CMC will leverage the research expertise and capacity across UofT that exists in biological, synthetic and bioanalytical chemistry in parallel with the strengths of the faculty in structural biology, biophysics, cellular biology, computational modelling, proteomics and genomics. The CMC's research operations will be highly complementary to and synergistic with existing programming at UTM, including the Master of Biotechnology (MBiotech) and the Master of Science in Biomedical Communication (MScBMC) graduate programs offered by the Institute for Management and Innovation.

4. Consultation

The CMC as a concept has been in planning for almost five years. It was initially conceived as the Centre for Cancer Stem Cell Therapeutics and pilot lab operations began in March 2015 as an outcome of a \$5.9M Canada Foundation for Innovation (CFI) grant to develop small molecule therapy targeting cancer stem cells and served as the pilot project for CMC. Planning for a formal academic unit began in 2016 with consultation between the Vice-President & Principal, the Vice-Principal Academic and Dean, the Vice-Principal Research, and the Chairs of Chemical and Physical Sciences, Biology and Computer Science. The CMC has extensively consulted with existing faculty across the Departments of Chemical and Physical Sciences and Biology. It will welcome collaborations with any future hires in these departments. Principal Ulli Krull has also discussed the vision for the CMC at several town halls and department faculty meetings across UTM, recognizing it as an excellent addition to UTM whose interdisciplinary focus will provide opportunities beyond what is currently possible in a single department. Comments and feedback were engaging, positive and supportive. Consultation has also taken place with Innovation and Research.

This proposal was also discussed at the Tri-campus Deans Meeting on January 31, 2019. Suggestions and feedback have been incorporated in this proposal.

⁵ <https://www.utm.utoronto.ca/dean/sites/files/dean/public/shared/Draft%20Implementation%20Plan%20version%204.0B-without%20watermark.pdf>

5. Participation

By being established at UTM, the CMC will attract significant faculty membership from the Departments of Chemical and Physical Sciences and Biology. It further anticipates association from faculty with primary appointments on other campuses, including the Department of Chemistry and the Faculty of Pharmacy at UTSG. Strong involvement of faculty from the U of T research hospitals and the Faculty of Medicine will enable the translation of the drug design and development programs to examine human applications.

Below is a list of academic and non-academic units in affiliated hospitals on the U of T tri-campus whose Chairs or Directors have expressed support for the establishment of the CMC in terms of their faculty and researchers who may in the future be engaged in the Centre. Its is not anticipated that this support will involve or incur resource implications nor affect workload agreements.

| Unit | Chair/Director | Campus/Affiliation |
|--|-------------------|--------------------|
| Department of Chemical and Physical Sciences | Claudiu Gradinaru | UTM |
| Department of Biology | Joel Levine | UTM |
| Department of Psychology | Ashley Monks | UTM |
| Institute of Management and Innovation | Soo Min Toh | UTM |
| Faculty of Medicine | Trevor Young | UTSG |
| Leslie Dan Faculty of Pharmacy | Christine Allen | UTSG |
| Department of Chemistry | Robery Batey | UTSG |
| Department of Pharmacology and Toxicology | Ruth Ross | UTSG |
| Krembil Institute | Trevor Young | UHN |
| Princess Margaret Hospital | Trevor Young | UHN |
| Lunenfeld Research Institute | Trevor Young | UHN |

Provided below is a list of current U of T faculty who have expressed interest in engaging with the CMC at some point in the future through potential consultation and/or collaboration on research projects, the integration of the CMC's research findings into course instruction and student experience, participation at community outreach events, the routine use of lab equipment, and non-budgetary cross-appointments.

| Faculty Member | Rank | Unit of Appointment |
|-----------------------|---------------------|--|
| Andrew Beharry | Assistant Professor | Department of Chemical and Physical Sciences (UTM) |
| Sara Rauscher | Assistant Professor | Department of Chemical and Physical Sciences (UTM) |
| Ulrich Krull | Professor | Department of Chemical and Physical Sciences (UTM) |
| Scott Prosser | Professor | Department of Chemical and Physical Sciences (UTM) |
| Iva Zovkic | Assistant Professor | Department of Psychology (UTM) |
| Claudiu Gradinaru | Professor | Department of Chemical and Physical Sciences (UTM) |
| Leigh Revers | Associate Professor | Institute for Management & Innovation (UTM) |
| Loren Martin | Assistant Professor | Department of Psychology (UTM) |
| Andrew Woolley | Professor | Department of Chemistry (Faculty of Arts and Sciences) |
| Lakshmi P Kotra | Professor | Leslie Dan Faculty of Pharmacy |
| Molly S Shoichet | Professor | Department of Chemical Engineering & Applied Chemistry (Faculty of Applied Sciences & Engineering) |
| Xiao-an Zhang | Associate Professor | Department of Physical & Environmental Sciences (UTSC) |
| Aaron Schimmer | Associate Professor | Department of Medical Biophysics (Medicine) |
| Alán Aspuru-Guzik | Professor | Department of Chemistry (Faculty of Arts and Sciences) |
| Paul Piunno | Associate Professor | Department of Chemical and Physical Sciences (UTM) |
| Mark Nitz | Professor | Department of Chemistry (Faculty of Arts and Sciences) |
| Joel Levine | Professor | Department of Biology (UTM) |
| Kagan Kerman | Associate Professor | Department of Physical & Environmental Sciences (UTSC) |
| Heinz-Bernhard Kraatz | Professor | Department of Physical & Environmental Sciences (UTSC) |

6. Partnerships

The CMC has a broad and diverse research agenda, which aligns with the University of Toronto's strategic objectives to support research that facilitates interdivisional and interdisciplinary collaborations, as well as partnerships with contacts within the local and global communities. To realize its vision and meet these objectives, the CMC will form extensive, strategic collaborations at the regional, national, and international levels and which fall into the following two categories: (1) academic partnerships with research institutions; and (2) industrial partnerships with pharmaceutical companies (and hence with venture capital).

Along with a team of researchers positioned across U of T, UTM, and the UHN, the CMC will work in close collaboration with researchers from the University of Calgary and McMaster University, as well as Trillium Hospital. Strategic collaborations have already been established through the pilot phase, such as with the McMaster Children's Hospital (brain cancer), the Dana Farber Cancer Institute at the Harvard School of Medicine (blood cancers), and the Medical University of Vienna (blood cancers). The pilot program has an established student exchange program with Cardiff University (UK), where top-senior students participate in a year-long research placement in the CMC labs at UTM. Other Canadian and international institutions that have expressed interest in the CMC's research include the Structural Genomic Consortium, the Ontario Institute for Cancer Research, the Centre for Commercialization of Antibodies and Biologics, the Regional Innovation Centre, the Ludwig Cancer Institute and the Medicine by Design Initiative.

Large pharmaceutical companies (Johnson & Johnson, Boehringer Ingelheim, Amgen, Novartis, Pfizer) and smaller biotech firms (Paraza Pharma, Trillium Therapeutics) will engage the CMC in collaborative projects that will utilize their infrastructure, intellectual and financial resources, and unique perspectives on the clinical potential of the CMC's research programs. Partnerships are already under development with the Vector Institute and IBM to facilitate the integration of artificial intelligence into the drug discovery process.

7. Administration

7.1 Administrative Structure

A Director, in consultation with an Advisory Board,⁶ will lead the operations and activities of the CMC. The Director will be appointed by the Vice-Principal, Academic and Dean. The Advisory Board will be appointed by the Director and will consist of four U of T faculty members (two being external to the listing of associated faculty of the CMC), one UTM staff member, one graduate student, and three external members drawn from industry, government, and non-for-profit organizations respectively.

The proposed CMC is an EDU:C and as such, the Director is not appointed under the Policy on Academic Administrative Appointments. As a consequence, an EDU:C may not administer research funds or enter directly and on its own authority into commitments / agreements / contracts. All monies and research funding will flow through the Office of the Dean in line with

⁶ The membership and function of the Advisory Board will be consistent with the Provost's "Statement on the Role of Advisory Bodies," under which "the advice offered by advisory bodies assists the University officer who holds authority for decisions under University policy" and ensures "the University that all its teaching and research activities [are] governed by the principles of academic freedom and integrity." The full statement is available at <https://www.provost.utoronto.ca/planning-policy/advisory-bodies-role-provost-statement/>.

UTM's normal practice. Any research contracts or agreements similarly require approval and the signature of the Vice-Principal, Academic and Dean.

The Director will be responsible for overseeing, with oversight provided by the Office of the Dean, UTM, all aspects of the CMC, including the direction and administration of its research programs, establishment of strategic partnerships, implementation of policies, and approval of budgets. It is the Director's responsibility to provide annual reports on the operations of the CMC to the UTM Vice-Principal, Academic and Dean.

7.2. Review

In line with normal practice, as an EDU: C, the CMC will be subject to periodic review by the Vice-Principal Academic and Dean at UTM. The review will coincide with the appointment or re-appointment of a Director (normally every 5 years) and, where appropriate, will involve external reviewers. The review would normally assess the CMC's sustainability as an EDU and performance and achievements relative to the goals and objectives set out in section 3.

8. Resource Implications

The staff resourcing for the Centre is specifically designed to oversee, develop, and support the CMC's objectives and vision as a leader in research and education. The annual operating budget has been approved by the Office of the Vice-President and Principal UTM and Financial and Budget Services and provides funds to maintain an appropriate level of staffing to support the daily operations of the Centre. Staff positions are not only critical to the Centre's success but also provide foundational support to achieve CMC's status as an innovative leader in medicinal chemistry research in Canada.

Appendix: Select Pilot Outcomes

Publications

- Wingelhofer B., Maurer B., Heyes E.C., Cumaraswamy A.C., Berger-Becvar A., de Araujo E.D., Orlova A., Freund P., Ruge F., Park J., Tin G., Ahmar S., Lardeau C-H., Sadovnik I., Bajusz D., Keserű G.M., Grebien F., Kubicek S., Valent P., **Gunning P.T.**,* and Moriggl R.* “Pharmacologic inhibition of STAT5 in acute myeloid leukemia.” *Leukemia* **2018**, published. doi:10.1038/s41375-017-0005-9.
 - This paper describes the identification of one of the most potent and in vivo acting anti-STAT compounds.
- Shouksmith A. E., Grimard M. L., Geletu M., de Araujo E. D., Berger-Becvar A., Heaton W. L., Gawel J. L., Bakhshinyan D., Adile A. A., Venugopal C., Johns A. E., Al-Qaysi O., Lewis A. M., O’Hare T., Deininger M., Singh S. K., Luchman A., Weiss S., Fishel M. L.,* and **Gunning P. T.*** “AES-135: A Structurally Novel HDAC Inhibitor with Exceptional In Vitro Potency in Pancreatic Cancer and In Vivo Pharmacokinetics.” *J. Med. Chem.* **2019**, published. doi: 10.1021/acs.jmedchem.8b01957
 - This paper describes a potent HDAC inhibitor scaffold that has subsequently lead to several new classes of comound that will be licensed to venture capital in early 2019.
- de Araujo E.D., Erdogan F., Neubauer H., Meneksedag-Erol D., Manaswiyoungkul P., Eram M.S., Qadree A.K., Israelian J., Orlova A., Seo H-S., Suske T., Pham H., Boersma A., Tangermann S., Kenner L., Rulicke T., Dong A., Ravichandran M., Brown P., Audette G., Rauscher S., Dhe-Paganon S., Moriggl R., **Gunning P.T.*** “Structural and Functional Consequences of the STAT5B^{N642H} Driver Mutation.” *Nature Commun.* **2019**. Accepted. NCOMMS-18-27459A.
 - This paper describes the first crystal structure of mammalian STAT5B and the most frequent clinical mutant, STAT5B^{N642H}, which is an oncodriver found in leukemic patients with the worst prognosis.

Licensed Products

- 4 licensed lead compounds
 - Rexahn Pharmaceuticals: Option Agreement UT Ref 2012-1949
 - Index Ventures: \$22M licensing deal: UT Ref 2013-1585
 - Non-exclusive Patent License between the University of Central Florida Research Foundation and the Governing Council of the University of Toronto with EMD Millipore Corporation
 - DT1 class of covalent inhibitors targeting UBA5

Spin-out Companies

- **Dalriada Therapeutics** – Dalriada is an Ontario-based preclinical drug discovery and development company specializing in small molecule inhibitors. Headed by a UTM alum, Dalriada has offered to mentor CMC trainees in entrepreneurship ventures and technology commercialization, as well as provide experiential learning opportunities through course-based research opportunity projects and internship and fellowship placements.
- **Janpix Ltd.** - Janpix is a CMC spin-out company advancing one of the first small molecule STAT protein inhibitors to clinical trials for the treatment of aggressive blood and brain cancers. A unique class of molecules developed at UTM, the optimization of these lead compounds has been rapidly accelerated through the work of multiple collaborators to attract a \$19 M investment from a European Venture Captial fund: Medicxi Ventures.