

# INSPIRE: Development of an Interdisciplinary Summer Program in Research and Entrepreneurship

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## ABSTRACT

We developed the *Interdisciplinary Science Program in Research and Entrepreneurship* (INSPIRE) to address the changing career landscape that students with an interest in Physical Chemistry, Biophysics and Biochemistry face. Third and fourth-year undergraduate Chemistry and Physics students participated in a 4-week, hands-on program that introduced applications of biophysical and biochemical techniques to drug discovery, while simultaneously engaging in a crash course on entrepreneurship and pharma. The principal objective of the program was to introduce students to the interdisciplinary nature of Chemistry and Physics research in the Life Sciences while simultaneously introducing the idea of translating their future graduate work into a career in biotechnology.

## INTRODUCTION

An education within STEM associated fields such as Chemistry and Physics provides a critical advantage to students competing within a 21<sup>st</sup> century job market. According to the U.S. Bureau of Labor Statistics, STEM occupations have grown 79 percent over the past three decades and are projected to grow an additional 11 percent from 2020 to 2030 (1). Perhaps more important than the technical skills a STEM education provides are the critical thinking and innovation skills. Companies often cite these career-readiness skills as the most desirable asset in an employee, with a special emphasis on the need for employees who can work on a diverse variety of tasks. This need for graduates with an interdisciplinary skill set should be considered in contrast to most university curricula, which tend to segregate the sciences into distinct silos with labels such as Physics, Chemistry, and Biology, but fail to show the students how these disciplines inter-relate.

Another shortcoming of our modern higher education system is that research-based universities tend to train their graduate students with too much of a focus on developing the next generation of academics. This approach is getting increasingly difficult to defend as the number of PhD students who are interested in ultimately landing a faculty position decrease each year (2). A *Nature* survey of graduate students in STEM fields around the globe found that only 56% picked academia as their first choice of a career (3). This number, which has been trending downward, is still highly inflated compared to the number of those students who will actually obtain a faculty position, with an even smaller fraction achieving a tenure track appointment (4). So long as we continue to frame graduate school, primarily, as a path to the academy, it will get increasingly difficult to convince students to enroll in Chemistry and Physics graduate programs. And this challenge is only compounded by the prospect of an additional 3-5 year postdoc upon graduation with a PhD.

Recent research shows that many PhDs prefer non-academic careers upon graduation (5, 6). While many graduates may consider an industrial career, it is not clear how many have truly considered starting their own companies, perhaps through translation of technology developed during their graduate research. And

while some universities have a culture of promoting start-up companies (e.g., Stanford or MIT), most Chemistry and Physics students will attain a PhD without any training in entrepreneurship or innovation.

One area of the innovation economy where Chemistry and Physics students with a cross-disciplinary interest in the Life Sciences can uniquely contribute is within biotechnology and pharma. The primary driver of innovation and growth within the biotechnology ecosystem are start-up companies. In fact, in 2018 start-ups were responsible for some 80% of the total biopharma drug development pipeline (7).

Technologies from the physical sciences, developed by Chemists and Physicists, have had significant impact on advancing medicine. Nuclear magnetic resonance spectroscopy (NMR) and X-ray crystallography play a central role in drug discovery within many pharmaceutical companies, while advances in cryo-electron microscopy, super-resolved and single-molecule imaging are just beginning to reveal their full potential (8). As an example, the unprecedented speed at which scientists revealed the structure of the SARS-CoV-2 virus's spike protein was a major breakthrough in the COVID-19 pandemic. This structural determination was made possible by recent advances in biotechnologies, accelerated vaccine development, and enabled scientists to develop small molecules, antibodies, and other therapeutics to disrupt the proteins' function.

Quantitative chemical and physical insight enable rational, design-oriented approaches to the early phases of drug discovery. High-resolution biophysical and biochemical measurements provide detailed mechanistic, kinetic, and structural information on compound–target interactions. They may reveal binding kinetics, identify challenging targets associated with protein-protein interactions, and provide the foundation for fragment-based drug discovery. These techniques yield information on aggregation, solubility, and cell permeability and accelerate hit-to-lead drug discovery, prioritization, and optimization.

We developed the *Interdisciplinary Science Program in Research and Entrepreneurship* (INSPIRE) as an intensive, hands-on introduction to the role of interdisciplinary biophysical and biochemical techniques in drug discovery, as well as a crash-course in entrepreneurship and innovation. INSPIRE consisted of a four-week summer curriculum including modules on: bioinformatics, fragment-based drug discovery, protein expression and purification, biophysical assays, the pharmaceutical industry, and an introduction to innovation and entrepreneurship.

In this inaugural year of the program the theme was *G-protein coupled receptor (GPCR) pharmacology*. GPCRs constitute the largest family of membrane proteins in eukaryotes and are intimately involved in cellular signaling (9, 10). As such, they play a pivotal role in a variety of cellular processes from controlling neuronal and hormonal signaling to regulating cell homeostasis. Around 35% of all pharmaceuticals target GPCRs, and since only ~12% of GPCRs have been subjected to large-scale drug screens, they hold enormous potential for the development of new drugs (11). Heterotrimeric G proteins connect GPCRs to intracellular signaling networks enabling them to receive and process extracellular signals. Students focused primarily on the Go protein, which is the most abundant heterotrimeric G-protein in the central nervous system (12). As such, alterations in signaling by the Go protein is implicated in neurodegenerative conditions such as Parkinson's and Alzheimer's disease. This served as an ideal system for achieving the pedagogic goals of the *INSPIRE* program.

## SCIENTIFIC AND PEDAGOGICAL BACKGROUND

The *INSPIRE* training modules were designed to familiarize students with all the stages of drug discovery, from early research through translation. With a combination of interactive lectures and hands-on activities, students were introduced to the various available tools and methods employed at different stages of the drug discovery pipeline. The 4 key learning outcomes for this program were:

1. Students will be able to explain the various steps involved in drug discovery, from the early stages of therapeutic research through to translation of a discovery.
2. Students will be able to identify and apply a range of interdisciplinary approaches in modern medicinal/life-science research.
3. Students will be able to identify career opportunities in the life-sciences/biotechnology economy and evaluate how their skills and interests align with these potential career paths.
4. Students will leave the program with the recognition that discoveries they make in graduate school can be translated into a career path in the life-sciences / biotechnology economy.

To attain these learning outcomes students participated in a series of 4 scientific training modules and 2 industrial and entrepreneurship modules.

The scientific training modules allowed the students to develop a therapeutic strategy while exploring a biological target (see Table 1 for a summary of the tools/methods). In the *Protein Analysis* module, students learned how to make the pivotal decision of selecting a therapeutic target (e.g., protein/signaling pathways implicated in the disease, protein-protein interactions, protein structural/functional information, etc.) with the aid of online resources/open-source software. The next step was to then identify “hit” molecules capable of binding to the target protein. *Fragment-Based Drug Discovery* (FBDD), a common hit identification approach in drug discovery, was introduced as the second module. Students learned how to obtain and refine protein crystal structures, select a desired binding site on the protein, select a fragment library and use molecular docking to screen the library against the protein and identify potential hit fragments. The next step was to prepare a recombinant version of the target protein in the *Protein Expression and Purification* module. In this third module, students expressed the GPCR Go $\alpha$  in bacterial cells and purified it using immobilized metal affinity chromatography (IMAC). In the last module on *Biophysical Assays*, two assays were introduced that evaluate compound binding based on protein stability and function. The thermal shift assay (TSA) measures the change of protein stability upon binding and the GTPase Glo-sensor assay evaluates the effect of binding on GTPase activity of the protein.

The industrial and entrepreneurship modules supplemented the scientific program with the aim of introducing the students to the life-sciences / biotechnology economy. The *Innovation and Entrepreneurship* module was designed to educate science students on the translation of scientific discoveries from the lab to the marketplace through the founding of a start-up venture. Students also participated in the *From Bench to Bedside* module which led students through the initial stages of research and development at a pharmaceutical company to the launch and marketing of medicines in Canada.

**Classroom format:** Training modules were designed to be highly interactive and collaborative. The bioinformatics-based modules (i.e., Protein Analysis and FBDD modules) were held in a computer lab, while experimental modules (i.e., Protein Expression and Purification and Biophysical Assays modules) were held in chemistry teaching labs. Sessions started with a 10-min presentation by TAs to provide instructions on the module and class activities. The students were divided into groups of 4-5 and specific tasks were assigned to each group. During these sessions, students were encouraged to raise questions and problem solve for potential solutions among the group. Course instructors and TAs facilitated and directed these discussions at the tables of each group. At the end of the sessions, students recorded their data according to the instructions provided.

**Group presentations:** At the end of each module, each student group independently presented their findings to the class. The presentation materials were prepared in a separate session by all group members. For each module, student groups collaboratively prepared a presentation in a separate session. Presentations included a module introduction, learning objectives, results, and suggested modifications to improve the module. Presentations were jointly presented by all group members for 10 minutes followed by 5 minutes of questions and discussion from the rest of the cohort and instructors.

## SCIENTIFIC TRAINING MODULES

**Module #1, Protein Analysis:** The Protein Analysis module aimed to introduce students to various bioinformatics methods for identifying and analyzing disease-related target proteins using model proteins from the GPCR family. Throughout the module, students utilized a range of online tools and resources, including: DepMap (13), UniProt (<https://www.uniprot.org/>), IID (14), VMD (15), and Perseus (16) to gain hands-on experience in acquiring and analyzing protein data.

The DepMap module was designed to help students understand the role of genes in cancer progression by utilizing the database's genetic and pharmacological blueprint of over 2000 different cancer cell types. Students explored gene essentiality, target tractability, and mutation effects using GPRC5A as a model protein and analyzed correlations between specific genes and treatments across 600 cancer cell lines using the data explorer tool. Each student group was also assigned a unique protein from the GPCR family and explored its interactions with various drug molecules.

The objective of the UniProt module was to teach students how to use the UniProt database to study and extract basic information about the structure and function of proteins with a focus on protein annotations, subcellular localization, sequence search, 3D structures, mutagenesis, and disease characteristics. Students used the same protein assigned to each group in the DepMap module to now determine its functional and pathological properties.

The IID database module aimed to teach students about protein-protein interactions (PPI) and their significance in biological processes. Using two members of the GPCR family, CXCR2 and CXCR1, students learned how PPI data can be used to identify alternative pathways and to explore various search methods available in IID. The module included an exploration of interaction topology using degree and clustering coefficient concepts, and groups were assigned multiple genes and asked to map their interactions across the interactome, identifying context-specific interactions and topology.

To further enhance the students' understanding of protein structure and function, the Visual Molecular Dynamics (VMD) tool was introduced in the next module, allowing them to browse and select protein crystal structures from the Protein Database Bank (PDB) (<https://www.rcsb.org/>) and investigate their 3D properties. Using the 6KPC protein as a model for visualization, students were able to explore the protein's hydrophobic and hydrophilic surfaces and residues, its various domains, and interactions between residues that form secondary structures, ultimately applying their newfound skills to investigate key characteristics of their assigned protein.

To help students understand how to analyze and process proteomics data, the final section of the course introduced the software tool Perseus. Students used a case study of a proteomics dataset produced by Geiger et al. (17) with the Stable Isotope Labeling by Amino Acids in Cell Culture (SILAC) method. Through the module, students learned various types of proteomics data analysis using Perseus, including data filtering, normalization techniques, and intuitive representations using scatter plots, histograms, volcano plots, and intensity curves. Additionally, the module introduced Perseus-based statistical

techniques such as student t-tests, principal component analysis (PCA), hierarchical clustering, network enrichment, and correlation analysis. Students were given the freedom to explore disease biology and investigate potential drug targets. This more open-ended, exploration-focused module introduced students to the initial phase of drug discovery where you find a patient need and a druggable protein/pathway that could potentially address it. This also encouraged discussion and collaboration among students allowing them to become comfortable with each other and the instructors.

**Module #2, Fragment Based Drug Discovery (FBDD):** Fragment-Based Drug Discovery (FBDD) is a method for finding new pharmacologically active medicines and exploring potential new therapeutic targets (18). This module's objective was to inform students about the rational drug design process using FBDD and the use of several computational tools for drug screening such as Enamine (<https://enamine.net/>), ChimeraX (19), and Maestro (20). This module taught students how to use their knowledge of medicinal chemistry to develop rational drug designs and find potential hit fragments to target the heterotrimeric G protein subunit alpha ( $G\alpha$ ) protein.

A brief introduction was given at the beginning of the module to inform students about the history and evolution of FBDD, its influence on drug discovery, and its progressive departure from conventional drug research. Each group of five students was given the chance to rationally select their target binding site of interest. In this phase, students discussed in groups how they planned to target the  $G\alpha$  protein (i.e., allosterically, orthosterically, etc.). A fragment library appropriate for their suggested targeting technique was then chosen using Enamine. The fragments were then docked onto the chosen binding site on Go utilizing high throughput virtual screening (HTVS) with Maestro Schrödinger (the software licenses for Maestro were generously donated by Schrödinger). The interactive viewing and analysis of computational molecular models were made possible by the software ChimeraX. Students spoke about their protein targeting strategy, library and hit selection criteria, interpretation of the structure-activity connections of hit fragments, and their proposed hit optimization utilizing rational drug design during their final presentation.

**Module #3, Protein Expression and Purification:** After identification using FBDD, the hit compounds must be screened against a recombinant form of the target protein using a biophysical assay. In this module, students prepared recombinant  $G\alpha$  protein with an N-terminal 6xHis and Maltose Binding Protein (MBP) tag with a Tobacco Etch Virus (TEV) cleavage site, which was overexpressed in *E. coli* BL21 (DE3) cells. The *E. coli* cultures were harvested the following day after sufficient growth and induction with isopropyl-D-1-thiogalactopyranoside (IPTG).

Students prepared 1 L bacterial cultures to overexpress recombinant  $G\alpha$  protein, induced the cultures with IPTG, and harvested the cells the following day. Protein purification was performed in pairs, with students given 20 mL of lysed cells to filter and load in a Ni-NTA column. They purified His-MBP- $G\alpha$  and subsequently removed the tag to isolate  $G\alpha$ . Quality was assessed by electrophoresis and intact mass analysis. At the end of the module, students learned to perform a protein concentration assay, analyze data, and create figures in Microsoft Excel. They also analyzed gels on Image Lab (<https://www.bio-rad.com/fr-ca/product/image-lab-software>). At the end of the purification module, a discussion was held to reinforce concepts and foster a collaborative workspace. Students presented their purification results and discussed pitfalls during expression and/or purification. Instructors presented potential scenarios and questions on protein expression and purification to assess students' ability to catch mistakes and to suggest viable solutions. This allowed students to communicate and apply the materials they learned.

**Module #4, Biophysical Assays:** The final training module aimed to provide students with a hands-on experience in evaluating the impact of compound binding on the stability and functional attributes of target proteins. To achieve this, two biophysical assays were included in the module. The first was the

thermal shift assay (TSA), which measures changes in the thermal denaturation temperature (melting temperature) of a protein to determine its stability, a property that is often altered by drug binding. The second assay was the GTPase Glo-Sensor Assay, a bioluminescent assay that monitors the activities of GTPases and their immediate regulators. This assay was used to track the effect of compound binding on the GTPase activity of the G $\alpha$  protein.

To ensure that students had a firm grasp of the background theory and experimental procedures, these were thoroughly explained and reviewed prior to conducting the assays. This approach proved effective in providing students with direction and confidence as they performed the assays. The class was divided into five groups, each investigating the effects of different regulators or components of the reaction. This encouraged meaningful discussions among students about the numerous factors affecting the signaling pathway and how to activate or inhibit certain effects. The students presented their findings and faced questions from their instructors and peers. Communication between and amongst groups was critical to their teamwork development and successful experimentation. The students learned how to operate instruments, collect raw data, and process it through Excel to create figures for their final presentation.

In addition to the hands-on component of the module, a series of lectures were delivered by expert faculty members introducing students to modern biophysical techniques with concrete examples of how the techniques can be used to further a drug discovery program. Students were encouraged to ask questions and engage in discussions during the lectures. Often, the 1-hour sessions concluded with students following the professor to their next appointment to continue their discussions. To allow for an extended and complete discussion of the matter at hand, it may be beneficial to shorten the lecture and leave more time for questions or extend the sessions by 15-30 minutes. Table 2 provides a list of the lecture titles and their relevance to drug discovery.

## INDUSTRIAL AND ENTREPRENEURSHIP MODULES

**Module #1, Innovation and Entrepreneurship:** The Innovation and Entrepreneurship module was intended for students in the physical, chemical, and life sciences, and served as an overview of the process of translating scientific research into practical applications with societal impact. This module aimed to educate science students on the transition from science to the marketplace and direct those who express an interest in entrepreneurship to further resources. The format consisted mainly of lectures with integrated short activities and real-world examples drawn from scientific research and technology.

The following topics were covered during the module:

- Introduction to the course and overview of innovation within the context of university research, including a case study.
- Exploration of the sources of ideas, the origins of companies, the innovation gap, and the distinction between invention and innovation, followed by a brainstorming session using design thinking.
- Overview of intellectual property and strategy, including record keeping.
- Introduction to value propositions and business models, including a case study of science-based companies.
- Overview of business communications and networking, with a practical component.
- Discussion of the steps to be taken when one has an invention, including working with the university, co-inventors, and supervisor.

In addition to the lectures, a networking lunch was held featuring invited guests from newly founded life-science companies, industry, and academic research groups. This event provided students with an

opportunity to apply the skills acquired during the module and foster connections among peers and with the invited guests.

**Module #2, From Bench to Bedside:** The objective of this module was to provide an overall understanding of the entire drug discovery process, from the initial stage of research and development to the launch and marketing of medicines in Canada (See Table 3). The module was provided in an interactive lecture format.

The module covered topics such as:

- Transforming medicine from the laboratory to large-scale production.
- Navigating the global and Canadian regulatory approval processes.
- Career opportunities in regulatory affairs, market access, and best practices for launching a medicine in Canada.
- How to effectively negotiate and manage relationships with stakeholders.
- How to make informed decisions when launching, marketing, and selling medicines.

In addition, two guest speakers from pharmaceutical companies within the Greater Toronto Area visited, participated in presenting the material, and interacted with students after the class lecture.

## DISCUSSION

On the last day of the program, we surveyed participants asking for both feedback on what they found most useful/informative and on areas in which they felt the program could improve. Overall, we received positive and reassuring feedback from this first cohort of students (See Table 4 for a summary of responses. For access to the full survey responses see *Supporting Information*.).

Many students said the program gave them the chance to learn about novel biophysical techniques while also improving their awareness of the academic and corporate world of drug development. The program's value in terms of networking with other students and professors was also noted. Many students stressed the value of the hands-on experience the curriculum offered, both in the lab and in computational contexts, facilitated by the absence of pressure to produce results. Additionally, several students pointed out that the lab experience was particularly beneficial because it was uncommon for undergraduate programs to offer something similar. The program received praise for its balance of computational and wet lab experience, as well as for providing students with a chance to collaborate and work with students from different backgrounds. Students were particularly excited about the many conversations they had with professors and graduate students.

While participants had a mostly favorable impression of the program, we received a number of suggestions for how to improve the program moving forward. For instance, some students felt that the step-by-step, guided instruction we provided on computational tools such as Maestro and VMD would have benefitted from more of an overview of the algorithms. This was a balance we had to navigate throughout development of the program, that is, weighing the need to provide background content with the desire to get the students working with the tools. Similarly, a few students commented that some modules were a bit rushed and suggested that we lengthen the duration of the program. Some students felt that since activities in the computer lab and the wet lab could only be done by one person at a time, due to limited materials and bench space, this restricted the learning opportunities. Again, here we are balancing two needs, one is the cost of running the program, in terms of hardware and consumables, and the other is a desire to provide each student with a sufficient level of hands-on experience. Finally, we noted a mix of responses in regard to the translational biotech modules. Many of the students really

appreciated being exposed to this aspect of the science, while many others were uninterested and would have preferred more talks on the actual science. These responses reveal a challenge faced by any program of this nature, that is, pitting a desire to expose students to the practical/pragmatic aspects of a career in science, against the pure enthusiasm most young scientists have at such an early stage of their career.

We next relate information gained through the survey responses directly to the primary learning outcomes for the program:

1. *Students will be able to explain the various steps involved in drug discovery, from the early stages of therapeutic research through to translation of a discovery.*

Students got hands-on experience with early stage in-silico docking, bioinformatics, and biochemical research. Several students reported a more nuanced understanding of the drug discovery process beyond just learning individual concepts in their coursework. One student identified “the practical experience to be the most valuable aspect” of the program. Students also noted that the entrepreneurial and translational aspects were mostly consumed via lecture. In future years, an interactive case study focused around strategic translational and business decisions could provide students with a more concrete grasp on later-stage drug discovery. We are also planning to enable students to spend one day with a start-up company housed within an incubator space on campus.

2. *Students will be able to identify and apply a range of interdisciplinary approaches in modern medicinal/life-science research.*

Between the diverse entourage of instructors, faculty lecturers, university leadership, and industrial partners, the inter-disciplinary nature of drug discovery was on full display. Several students identified the lecture series on biophysical techniques to be “highly valuable”. However, some students felt overwhelmed by the breadth of material or felt more enthusiastic about some modules/topics while less so about others. In future years, we are planning on allowing students to enroll in a subset of modules that most pique their interest. This will enable us to develop longer modules of more depth while better tailoring the program to the varied academic backgrounds of the students.

3. *Students will be able to identify career opportunities in the life-sciences/biotechnology economy and evaluate how their skills and interests align with these potential career paths.*

Driven by speakers largely from outside of academia, entrepreneurship focused modules provided students with an entry-level understanding of the life-sciences / biotechnology economy. Several students identified the “networking opportunities in the program to be highly valuable” but they reported less enthusiasm about the business aspect of the program and were significantly more excited about the science or career aspects. This might be partially rectified by better motivating these sessions, perhaps, by providing statistics on the actual career paths of PhDs and inviting recent graduates who found employment within industry and/or at a start-up.

4. *Students will leave the program with the recognition that discoveries they make in graduate school can be translated into a career path in the life-sciences / biotechnology economy.*

Students were introduced to a diverse network of future academic collaborators, industrial partners, entrepreneurial mentors, and fellow entrepreneurs. This network will likely have a far greater impact on their success than any one individual technique ever could. Still, overall, the students reported less satisfaction, or perceived personal relevance, with the translational discussions. To connect better



with the participants, we intend to invite to speak, and/or hold a round table with, actual graduates who went on to translate their research into a business.

We hope that the lessons learned through development of this program will inform the creation of similar programs at other institutions. With the changing landscape of a career in Chemistry and Physics, it is becoming increasingly important to help students chart their future course. By exposing students early on to the idea that options exist beyond academia, and that the research they undertake may one day translate into a company or business of their own design, programs like the INSPIRE program described here are better preparing our students for the challenging and exciting road ahead.

USE OF HUMAN SUBJECTS (if relevant): A Human Participants Ethics Protocol was approved by the University of Toronto (RIS Human Protocol Number 42854).

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#### REFERENCES

1. Watson, S.F., Alan Lacey, and Audrey. Science, technology, engineering, and mathematics (STEM) occupations: past, present, and future : Spotlight on Statistics: U.S. Bureau of Labor Statistics. .
2. Sherman, D.K., L. Ortosky, S. Leong, C. Kello, and M. Hegarty. 2021. The Changing Landscape of Doctoral Education in Science, Technology, Engineering, and Mathematics: PhD Students, Faculty Advisors, and Preferences for Varied Career Options. *Front Psychol.* 12:711615.
3. Woolston, C. 2019. PhDs: the tortuous truth. *Nature.* 575:403–406.
4. 2016. Higher Education at a Crossroads: The Annual Report on the Economic Status of the Profession, 2015-16. *AAUP.*
5. Fuhrmann, C.N., D.G. Halme, P.S. O’Sullivan, and B. Lindstaedt. 2011. Improving Graduate Education to Support a Branching Career Pipeline: Recommendations Based on a Survey of Doctoral Students in the Basic Biomedical Sciences. *LSE.* 10:239–249.
6. Roach, M., and H. Sauermann. 2017. The declining interest in an academic career. *PLOS ONE.* 12:e0184130.

7. 2022. Emerging Biopharma's Contribution to Innovation. *IQVIA Institute for Human Data Science*.
8. Renaud, J.-P., C. Chung, U.H. Danielson, U. Egner, M. Hennig, R.E. Hubbard, and H. Nar. 2016. Biophysics in drug discovery: impact, challenges and opportunities. *Nat Rev Drug Discov.* 15:679–698.
9. Katritch, V., V. Cherezov, and R.C. Stevens. 2012. Diversity and Modularity of G Protein-Coupled Receptor Structures. *Trends Pharmacol Sci.* 33:17–27.
10. Odoemelam, C.S., B. Percival, H. Wallis, M.-W. Chang, Z. Ahmad, D. Scholey, E. Burton, I.H. Williams, C.L. Kamerlin, and P.B. Wilson. 2020. G-Protein coupled receptors: structure and function in drug discovery. *RSC Adv.* 10:36337–36348.
11. Sriram, K., and P.A. Insel. 2018. G Protein-Coupled Receptors as Targets for Approved Drugs: How Many Targets and How Many Drugs? *Mol Pharmacol.* 93:251–258.
12. de Oliveira, P.G., M.L.S. Ramos, A.J. Amaro, R.A. Dias, and S.I. Vieira. 2019. Gi/o-Protein Coupled Receptors in the Aging Brain. *Frontiers in Aging Neuroscience.* 11.
13. Tsherniak, A., F. Vazquez, P.G. Montgomery, B.A. Weir, G. Kryukov, G.S. Cowley, S. Gill, W.F. Harrington, S. Pantel, J.M. Krill-Burger, R.M. Meyers, L. Ali, A. Goodale, Y. Lee, G. Jiang, J. Hsiao, W.F.J. Gerath, S. Howell, E. Merkel, M. Ghandi, L.A. Garraway, D.E. Root, T.R. Golub, J.S. Boehm, and W.C. Hahn. 2017. Defining a Cancer Dependency Map. *Cell.* 170:564-576.e16.
14. Kotlyar, M., C. Pastrello, Z. Malik, and I. Jurisica. 2019. IID 2018 update: context-specific physical protein-protein interactions in human, model organisms and domesticated species. *Nucleic Acids Res.* 47:D581–D589.
15. Humphrey, W., A. Dalke, and K. Schulten. 1996. VMD: visual molecular dynamics. *J Mol Graph.* 14:33–38, 27–28.
16. Tyanova, S., T. Temu, P. Sinitcyn, A. Carlson, M.Y. Hein, T. Geiger, M. Mann, and J. Cox. 2016. The Perseus computational platform for comprehensive analysis of (prote)omics data. *Nat Methods.* 13:731–740.
17. Geiger, T., A. Velic, B. Macek, E. Lundberg, C. Kampf, N. Nagaraj, M. Uhlen, J. Cox, and M. Mann. 2013. Initial quantitative proteomic map of 28 mouse tissues using the SILAC mouse. *Mol Cell Proteomics.* 12:1709–1722.
18. Rees, D.C., Congreve, C.W. Murray, and R. Carr. 2004. Fragment-based lead discovery. *Nat Rev Drug Discov.* 3:660–672.
19. Pettersen, E.F., T.D. Goddard, C.C. Huang, E.C. Meng, G.S. Couch, T.I. Croll, J.H. Morris, and T.E. Ferrin. 2021. UCSF ChimeraX: Structure visualization for researchers, educators, and developers. *Protein Sci.* 30:70–82.

20. Laimer, J., J. Hiebl-Flach, D. Lengauer, and P. Lackner. 2016. MAESTROweb: a web server for structure-based protein stability prediction. *Bioinformatics*. 32:1414–1416.

SUPPLEMENTAL INFORMATION (movies, database files, etc. may be uploaded as separate files).

**Table 1:** Summary of tools/methods in the research training modules.

Module	Tools/Methods	Description	Application
Protein Analysis	DepMap	Free online database	Selection of protein target and the model cell line.
	Perseus	Open-source software	Analysis of proteomics data to explore biological processes and pathways implicated in diseases.
	Uniprot	Free online database	Obtaining information about protein sequence, structure and function.
	IID	Free online tool/database	Obtaining protein-protein interaction (PPI) information.
Fragment Based Drug Discovery (FBDD)	Enamine	Free online tool	Selection and filtering of compound libraries.
	Chimera X	Open-source software	Interactive visualization and analysis of molecular models.
	Maestro	Commercial software (Free for educational purposes)	Molecular docking and high-throughput library screening.
Protein Expression and Purification	GenSmart™ Design	Free online tool	Design of DNA plasmid for bacterial transfection.
	Bacterial transformation	Biochemical method	For protein expression.
	Protein extraction	Biochemical method	For protein extraction.
	Affinity Chromatography	Biochemical method	For protein purification.
	SDS-PAGE	Biochemical method	For protein quantification.
Biophysical Assays	GTPase Glo-Sensor Assay	Biophysical assay	Evaluation of protein function.
	Thermal shift analysis	Biophysical assay	Evaluation of protein stability and binding.

**Table 2.** Biophysical lectures

Lecture Topic	Drug Discovery Relevance
Single-Molecule Imaging	Quantify GPCR oligomerization, interactions, and spatial organization.
NMR I	Combinatorial screening to quickly generate a high affinity regio-specific hit molecule.
Molecular Dynamics	Predict drug-induced protein conformational changes.
Ultrasensitive Protein Detection	Detect low abundance biomarkers in patients in response to drug treatment.
NMR II	Identification of druggable allosteric pathways.
Single-Molecule Spectroscopy	Investigate dynamics induced by the local environment or structural orientation that may be hidden within ensemble averages.
Intrinsically Disordered Proteins	Improve rational drug design on novel molecular targets.
Crystallography	Observe Angstrom level protein-drug interactions to guide compound development.
EPR	Observe of drug-induced dynamic re-arrangements within a protein.

**Table 3:** From Bench to Bedside Sessions

Session title	Topics
Introduction to Pharma R&D: Clinical trials and manufacturing	<ul style="list-style-type: none"> <li>• An overview of the global drug discovery process</li> <li>• Transforming the medicine from lab to factory-scale</li> <li>• Navigating the global and Canadian regulatory approval processes</li> </ul>
Regulatory Affairs: Getting the drug approved	<ul style="list-style-type: none"> <li>• Overview of the Canadian healthcare system</li> <li>• Summary of Canada's pharmaceutical environment</li> <li>• Effectively navigating the systems How to effectively negotiate and manage relationships with stakeholders</li> <li>• Career opportunities in Regulatory Affairs</li> </ul>
Market Access: Getting medicines reimbursed	<ul style="list-style-type: none"> <li>• Best practices for launching a medicine in Canada</li> <li>• Understanding the market access processes and stakeholders</li> <li>• The importance of multichannel promotion</li> <li>• Introduction to Pharmaceutical Sales</li> <li>• Changing behavior through persuasion and influence</li> </ul>
Launching, Marketing and Selling Medicines in Canada	<ul style="list-style-type: none"> <li>• Introduction to the Canadian life sciences ecosystem</li> <li>• An overview of the generic and biosimilars industry in Canada</li> <li>• An overview of vaccines</li> <li>• The emergence and importance of biologics</li> </ul>

**Table 4:** Participant survey responses (1, Strongly Disagree; 2, Disagree; 3, Somewhat Disagree; 4, Neither Agree nor Disagree; 5, Somewhat Agree; 6, Agree; 7, Strongly Agree).

<b>Survey Statements</b>	<b>Avg. Score</b>	<b>Std. Dev.</b>
What was your level of interest in the lab portion of the program ( <i>i.e.</i> , <i>When you first learned about it</i> )?	6.6	0.7
The laboratory manual provided information required to conduct the experiments effectively.	5.9	1.1
The laboratory module activities stimulated my interest in the subjects.	6.4	0.8
The difficulty level of the laboratory modules was appropriate.	6.1	0.5
The pace of the program was appropriate.	5.7	1.2
I have more of an understanding of how interdisciplinary science promotes drug discovery.	6.7	0.5
I feel more confident in my understanding of modern biophysical techniques.	6.3	0.6
I encountered new concepts I had not been exposed to during my formal academic courses.	6.6	0.6
The instructors were helpful.	6.9	0.3
The instructors were well prepared.	6.9	0.4
The teaching assistants were helpful.	6.7	0.5
The teaching assistants were well prepared.	6.6	0.5
I feel more confident in my ability to perform biophysical assays.	6.2	0.7
I feel more confident in my ability to find the disease relevance of a protein.	6.4	0.5
I feel more confident in my ability to dock fragments to a protein.	6.2	1.1
I feel more confident in my ability to visualize proteins.	6.1	0.9
I feel more confident in my ability to express and purify proteins	6.1	0.9
I acquired a better understanding of how innovation happens in a university research context.	6.5	0.5
I better understand the various aspects of the pharma industry.	6.4	0.6
I would recommend this program to other undergraduate students.	6.9	0.3