**Biomarker Discovery, Validation, & Implementation**

**The university of Toledo**

**(BRIM program in Bioinformatics)**

**Alexi Fedorov & Kathryn Eisenmann CRN 15316 BRIM 6200-001**

**Term**: Spring  
**Class Location**: 127HEB  
**Class Day/Time**: Mon/Thu, 11:15 am -12:45 pm

**Instructors**: **Unit 1**: Dr. Alexei Fedorov, PhD; **Unit2**: Dr. Kathryn Eisenmann, PhD  
**Email**: [alexei.fedorov@utoledo.edu](mailto:alexei.fedorov@utoledo.edu) and [kathryn.eisenmann@utoledo.edu](mailto:kathryn.eisenmann@utoledo.edu)   
**UNIT1: Office Hours**: Mon/Wed 2-3pm at 308 BHS Building. For other time please request an appointment via email ([alexei.fedorov@utoledo.edu](mailto:alexei.fedorov@utoledo.edu)) at least one day in advance. **Office Phone**: 419-383-5270

**UNIT2: Office Hours**: Please request an appointment with session facilitator via UT-email at least one day in advance.

**Delivery:** Conventional lecture in classroom (unless online delivery is noted) will be recorded with Echo 360 and uploaded on Blackboard by next day.

All procedures related to current COVID-19 requirements will be engaged. For the first two weeks of Spring semester, no conventional seminars/lectures are allowed by UT Administration. Thus, all teaching activities during this period will be provided via online Blackboard web site and Collaborate Ultra facilities. Online lectures/seminars will be every Monday and Thursday from 11:15 am till 12:45 pm.

When possible, conventional face-to-face lecture/labs will take place in our computer room (rm 127 HEB, Medical campus). All traditional lectures will be also recorded and posted on blackboard next morning.

**SPECIAL COURSE EXPECTATIONS DURING COVID-19**

Maintaining a safe campus during the ongoing COVID-19 pandemic remains a top priority. UToledo continues to follow the guidance of the U.S. Centers for Disease Control and Prevention and Ohio Department of Health to keep our campus safe.   
   
**ATTENDANCE**   
The University of Toledo has a missed class policy. It is important that students and instructors discuss attendance requirements for the course. Before coming to campus each day, students should take their temperature and complete a self-assessment for symptoms of COVID-19, such as cough, chills, fatigue or shortness of breath. Anyone with a temperature at or above 100.0 degrees Fahrenheit or who is experiencing symptoms consistent with COVID-19 should not come to campus and contact their primary care physician or the University Health Center at 419.530.5549. For more information on the symptoms of COVID-19, please go to <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>

COVID-19 testing for sick students is available on both Main Campus and Health Science Campus. Call 419.383.4545 for an appointment. Absences due to COVID-19 quarantine or isolation requirements **are** considered excused absences. Students should notify their instructors and follow the protocols summarized in this document on [Navigating COVID-Related Course Concerns](https://www.utoledo.edu/offices/provost/docs/covid-19/COVID%20student%20flow%20chart.pdf).

In the event that you have tested positive for COVID-19 or have been diagnosed as a probable case, please review the [CDC guidance](https://nam04.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fif-you-are-sick%2Findex.html&data=04%7C01%7CDenise.Bartell%40UToledo.Edu%7Cc3ecf55590d548a6006a08d95c3b8e19%7C1d6b1707baa94a3da8f8deabfb3d467b%7C0%7C0%7C637642233117266556%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=8jvRsGSu5bu%2BPHxfo75XszlKKqTfQig3w8ecZQR863w%3D&reserved=0) on self-isolation and symptom monitoring, and report the disclosure to the Division of Student Affairs by emailing [StudentAffairs@utoledo.edu](mailto:StudentAffairs@utoledo.edu) or by connecting with their on-call representative at 419.343.9946. Disclosure is voluntary and will only be shared on a need to know basis with staff such as in the Office of Student Advocacy and Support, The Office of Residence Life, and/or the Office of Accessibility and Disability Resources to coordinate supportive measures and meet contact tracing requirements.

**FACE COVERINGS**   
Face coverings are required while on campus, except while eating, alone in an enclosed space, or outdoors practicing social distancing. Students will not be permitted in class without a face covering. If you have a medical reason preventing you from wearing a face covering due to a health condition deemed high-risk by the CDC, submit an [online application](https://teton.accessiblelearning.com/Toledo/) to request an accommodation through the Office of Accessibility and Disability Resources. Students will need to provide documentation that verifies their health condition or disability and supports the need for accommodations. Students already affiliated with the Office of Accessibility and Disability Resources who would like to request additional accommodations due to the impact of COVID-19, should contact their accessibility specialist to discuss their specific needs. You may connect with the office by calling 419.530.4981 or sending an email to [StudentDisability@utoledo.edu](mailto:StudentDisability@utoledo.edu).

**VACCINATION**   
Doctors and other health care professionals agree that the best way to protect ourselves and each other is to get vaccinated. Case data clearly show that vaccines remain highly effective at preventing serious illness from COVID, including the highly contagious delta variant. If you have not yet received your COVID vaccine, the University encourages you do so as soon as possible. No appointment is needed to get the shot at the UTMC Outpatient Pharmacy, University Health Clinic or Main Campus Pharmacy. Once you receive the COVID vaccination, please register on the COVID Vaccine Registry site at: <https://utvaccinereg.utoledo.edu/>.

**SPECIAL NOTES**   
It’s important to note, that based on the unpredictability of the COVID-19 virus, things can change at any time. So please be patient and understanding as we move through the semester. I also ask that you keep me informed of concerns you may have about class, completing course work/assignments timely and/or health concerns related to COVID.

**COURSE OVERVIEW**

**Unit 1 Biomarker Research**

* Students are expected to attend in class lectures. In class lectures are Echo-recorded and posted on Blackboard. Class times: Mondays and Thursdays; 11:15 am -12:45 pm.
* Assignment and/or quiz will be given after each session. Students will have one week to complete an assignment and upload it into Blackboard. At the end of Unit-1 there will be a mid-term take-home exam. Assignments are equally weighted and averaged for Unit 1 grade.
* Grading principles: Homework/projects and quizzes= 65%; Mid-term exam = 30%; Class activity = 5%.
* Office hours will be held every Monday and Wednesday from 2:00-3:00 PM in Dr. Fedorov’s office, room 308, Health Science Building.

Description of Unit-1 lectures:

1. Thursday, January 20th Human Genome Introduction (Alexei Fedorov)
2. Monday, January 24th, Human SNPs Part 1 (Dr. John Gray)
3. Thursday, January 27th, Human SNPs Part 2 (Dr. John Gray)
4. Monday, January 31st, The Human Microbiome in the Context of Biomarker Research & Individualized Medicine (Dr. Robert Blumenthal)
5. Thursday, February 3rd, EXOME PROJECT (beginning): raw FASTQ data; introduction to SAM, BAM, and VCF files (Dr. Alexei Fedorov)
6. Monday, February 7th,EXOME PROJECT (continuation). LAB: From FASTQ to SAM, BAM, and VCF files using GATK program package. (Dr. Alexei Fedorov)
7. Thursday, February 10th, EXOME PROJECT (end). Visualization of BAM files with IGV program. Complex patterns of SNP arrangements (haplotypes, haplogroups, SNP flip-over) (Dr. Alexei Fedorov)
8. Monday, February 14th, GWAS and Identification of disease-susceptibility genes (Dr. George Cicila)
9. Thursday, February 17th, Human population genetics intricacies (Dr. Alexei Fedorov)
10. Monday, February 21st, Epigenomics (Dr. Ivana de la Serna)
11. Thursday, February 24th, Exam for Unit-1 (Dr. Alexei Fedorov)
12. Monday, February 28th GALAXY web tools (Beginning) (Dr. Robert Trumbly)
13. Thursday, March 3th GALAXY web tools (End) (Dr. Robert Trumbly)

**Unit 2 Individualized Medicine**

**Director – Dr. Kathryn Eisenmann, PhD**

Department of Cancer Biology, UT-HSC

E-mail: kathryn.eisenmann@utoledo.edu

Delivery: Online lectures posted on blackboard *unless in class lecture is indicated*. Students are expected to attend in class lectures. In class lectures are Echo-recorded and posted on Blackboard. Class times: Mondays and Thursdays; 10am -12pm

Exam: Short take home assignment after each session. Students will have one week to complete assignments and submit to instructor by email, unless indicated otherwise.

Grading Strategy: Take home assignments are equally weighted and averaged for Unit 2 grade.

Work days: Students are given periodic assignment work days to complete assignments in a timely and thorough fashion. Students may work on assignments on work day sessions in the location of their choice.

1) March 16 (M): Biomarkers identification and validation

(S. Khuder, PhD – Dept. Medicine)

2) March 19 (Th): Development of genome-based biomarkers of hypertension

(S. Kumarasamy, PhD - Dept. Physiology and Pharmacology)

3) March 23 (M): DNA damage response biomarkers of cancer **(In class)**

(K. Williams, PhD - Dept. Cancer Biology,

D. Allison, MD – Dept. Surgery)

4) March 26 (Th): Biomarkers of cancer cell motility **(In class)**

(K. Eisenmann, PhD – Dept. Cancer Biology)

5) March 30 (M): *Unit 2 take-home assignment work day*

6) April 2 (Th): Salivary Biomarkers and Sjogren's Syndrome Diagnosis **(In class)**

(D. Giovannucci – Dept. Neurosciences)

6) April 6 (M): Individualized immunotherapy **(Online only)**

(L. Wuescher, PhD – Dept. Microbiology and Immunology)

7) April 9 (Th): Targeted transplant, donor-recipient matching

(S. Stepkowski, PhD – Dept. Microbiology and Immunology)

8) April 13 (M): Validation - Design and conduct of trials - Patient selection

(J. Willey, MD – Dept. Medicine)

9) April 16 (Th): *Unit 2 take-home assignment work day*

10) April 20 (Th): TBD **(online only)**

(Caitlyn Baum, Ph.D., Dept. Pathology)

11) April 23 (M): TBD

(Alexzander Asea, Ph.D., MBA, Dept of Medicine)

12) April 27 (Th): TBD

(Punit Kaur, Ph.D., Dept of Medicine)

1. April 30 (M): TBD

1. 14) May 4 (Th): TBD

15) May 7 (Th): *Final Unit 2 homework assignments due.*

**STUDENT LEARNING OUTCOMES**

Successful students will be able to:

1. understand and perform RNAseq gene expression investigation starting from raw Fastq datafiles to the expression matrixes.
2. be able to perform large-scale SNP analysis of individual human genome based on initial SNP microarray chip or Next Generation Sequencing datasets.
3. Recognize quality and level of predictability of whole-genome SNP datasets. Appreciate power and limitations of Genome Wide Association Studies.
4. Manage data from different genomics and transcriptomics studies.
5. Comprehend importance of SNP biomarkers for modern medicine and learn pipelines for bioinformatics analysis of genomic polymorphism.
6. Recognize functional regions in the human genome and learn how to interpret GWAS studies.
7. Grasp insights into epigenetic control of activation and silencing genes.
8. Describe mammalian and nonmammalian genome structure and function. Discuss the processes of genome evolution, including mutation dynamics and consequences and exploitation of SNPs.
9. Apply bioinformatic methods to clinical problems, by demonstrating understanding of:  
   a.  Biomarker discovery and validation and b.  Molecular bases for major diseases such as cancer, diabetes, and autoimmunity.
10. Explain how DNA repair mechanisms may be targeted for drug development/used in personalized medicine approaches. Give examples of drugs developed that target DNA repair mechanisms in clinic.
11. Define critical characteristics and adhesion receptors that underlie cancer cell migration and how their expression levels can be used to stage cancer progression.
12. Explain how mutational profiling of cell-free tumor DNA can inform oncologists’ selection of drug therapy for their patients.
13. Discuss potential biomarkers of hypertension and describe the evidence for their clinical utility.
14. Summarize various tests and approaches for determining the validity and reliability of proposed biomarkers.
15. Generalize how understanding molecular mechanisms of disease (for example, cancer, organ transplant/rejection) combined with proteogenomics approaches can drive biomarker development in the clinic.
16. Communicate competently both in writing and orally.

**PREREQUISITES AND COREQUISITES**

None. However, previous completion of BIPG5100 (Fundamentals of BPG) is suggested.

**REQUIRED TEXTS AND ANCILLARY MATERIALS**

No textbooks are required. Students will work with the information/instructions provided online.

All assignments, quizzes, video-lectures, and supporting materials will be available through UT Blackboard portal.

**TECHNOLOGY REQUIREMENTS**

None. Computers will be provided in the computer lab.

**UNIVERSITY POLICIES**

Policy Statement on Non-Discrimination on the basis of Disability (ADA)  
The University is an equal opportunity educational institution. Please read The University’s Policy Statement on Nondiscrimination on the Basis of Disability Americans with Disability Act Compliance*.*

**ACADEMIC ACCOMMODATIONS**

The University of Toledo is committed to providing equal access to education for all students. If you have a documented disability or you believe you have a disability and would like information regarding academic accommodations/adjustments in this course, please contact the Student Disability Services Office*.*

**ACADEMIC POLICIES**

This course follows the main UT policies.

**GRADING**

Final grade will be an average of Unit-1 and Unit-2 grades.

**STUDENT SUPPORT SERVICES**

Student Support Services can help students succeed in this course by providing academic services when needed in the areas of, advising, tutoring, financial resources, self-directed learning, and by directing students to other specific resources, as needed. Students can access these services by calling Student Services at, 419-383-6286.