# Biomarkers Discovery Validation & Implementation

**The University of Toledo**

**BRIM Program in Bioinformatics & Proteomics/Genomics**

**BRIM6200 Biomarker Discovery Validation & Implementation, Section 001, CRN #15444**

**Instructors**: Unit 1: Alexei Fedorov, PhD

Unit 2: Kathryn Eisenmann, PhD

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**Office Hours**: Unit1: M/W 2-3P. Unit2: Request an appointment with session facilitator via UT-email at least one day in advance.

**Office Location**: Unit1: BHS 308/Unit2: As arranged.

**Instructor Phone**: 419-383-5270 / 419-383-4101

**Offered**: Spring, even-numbered years

**Course Website**: [Blackboard Learn](https://blackboard.utdl.edu/) (if applicable)

**Class Location**: HEB 127   
**Class Day/Time**: Mon./Thurs., 11:15am-12:45pm

**Lab Location**: HEB 127

**Lab Day/Time**: Mon./Thurs., 11:15am-12:45pm

**Credit Hours**: 3

CATALOG/COURSE DESCRIPTION

Unit 1 of this survey course will explore the clinical need and methodologic approaches to biomarker development and validation. Unit 2 will consider biomarker use in individualized medicine.

STUDENT LEARNING OUTCOMES

Successful students will be able to:

L1. Understand and perform RNAseq gene expression investigation starting from raw Fastq datafiles to the expression matrices.

L2. Perform large-scale SNP analysis of individual human genome based on initial SNP microarray chip or Next Generation Sequencing datasets.

L3. Recognize quality and level of predictability of whole-genome SNP datasets, and appreciate power and limitations of Genome Wide Association Studies.

L4. Manage data from different genomics and transcriptomics studies.

L5. Comprehend importance of SNP biomarkers for modern medicine and learn pipelines for bioinformatics analysis of genomic polymorphism.

L6. Recognize functional regions in the human genome and learn how to interpret GWAS studies.

L7. Grasp insights into epigenetic control of activation and silencing genes.

L8. Describe mammalian and nonmammalian genome structure and function. Discuss the processes of genome evolution, including mutation dynamics and consequences and exploitation of SNPs.

L9. 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.

L10. 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.

L11. Define critical characteristics and adhesion receptors that underlie cancer cell migration and how their expression levels can be used to stage cancer progression.

L12. Explain how mutational profiling of cell-free tumor DNA can inform oncologists’ selection of drug therapy for their patients.

L13. Discuss potential biomarkers of hypertension and describe the evidence for their clinical utility.

L14. Summarize various tests and approaches for determining the validity and reliability of proposed biomarkers.

L15. Generalize how understanding molecular mechanisms of disease (for example, cancer, organ transplant/rejection) combined with proteogenomics approaches can drive biomarker development in the clinic.

L16. Communicate competently both in writing and orally.

TEACHING METHODOLOGY

The course is team-taught by faculty from The University of Toledo Health Science and Main Campuses. The course is blended, with both face-to-face and pre-recorded online lectures. Online lectures are posted on Blackboard *unless in-class lecture is indicated*. Students are expected to attend in-class lectures. However in-class lectures are Echo-recorded and posted on Blackboard.

PREREQUISITES AND COREQUISITES None, however previous completion of BIPG5100 (Fundamentals of BPG) is suggested, particularly for students who do not have a good background in molecular biology.

## TEXTS AND ANCILLARY MATERIALS

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

TECHNOLOGY REQUIREMENTS   
Blackboard access

ACADEMIC POLICIES   
[Graduate Policies](file:///C:\Users\hbuska\Desktop\Graduate%20Policies): <http://www.utoledo.edu/policies/academic/graduate/>

COURSE EXPECTATIONS

**Homework:** Each homework assignment must be returned in ten days by noon. (For example, for a Tuesday class this homework must be returned via e-mail by the next Friday at 1 pm.) Absolutely NO late homework will be accepted. A majority of online lectures/labs will be available on the web in advance for at least one day. Several EXTRA assignments will be available through the course, designed to help students improve grades. Accordingly, special assignments must be returned in two weeks. Take home assignments are equally weighted and averaged

OVERVIEW OF COURSE GRADE ASSIGNMENT

The course is team-taught by faculty from The University of Toledo and Bowling Green State University. The grade will be determined entirely by performance on projects assigned and graded by each instructor. Final grade will be an average of Unit-1 and Unit-2 grades.

**Grading principles:**

• Homework 30%

• LABs + activity 10%

• Mid-term Exam 30%

• Final Exam 30%

• Extra points may be earned for outstanding homework and SPECIAL ASSIGNMENTS, given at the discretion of the faculty.

## 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.](http://www.utoledo.edu/policies/administration/diversity/pdfs/3364_50_03_Nondiscrimination_o.pdf)   
Students can find this policy along with other university policies listed by audience on the [University Policy webpage](http://www.utoledo.edu/policies/audience.html/#students) (http://www.utoledo.edu/policies/audience.html/#students).

<https://www.utoledo.edu/title-ix/policies.html> <https://www.utoledo.edu/policies/administration/diversity/pdfs/3364_50_01.pdf>

<https://www.utoledo.edu/policies/main_campus/student_life/pdfs/3364_30_04_Student_code_of_conduct.pdf>

### Academic Accommodations

(Include the following, verbatim; please refer to the face-to-face syllabus guidelines for more guidance/details.)

The University of Toledo embraces the inclusion of students with disabilities. We are committed to ensuring equal opportunity and seamless access for full participation in all courses. For students who have an accommodations memo from Student Disability Services, I invite you to correspond with me as soon as possible so that we can communicate confidentially about implementing accommodations in this course. For students who have not established affiliation with Student Disability Services and are experiencing disability access barriers or are interested in a referral to healthcare resources for a potential disability or would like information regarding eligibility for academic accommodations, please contact the [Student Disability Services Office](http://www.utoledo.edu/offices/student-disability-services/index.html) (http://www.utoledo.edu/offices/student-disability-services/) by calling 419.530.4981 or sending an email to [StudentDisability@utoledo.edu](mailto:StudentDisability@utoledo.edu).

## ACADEMIC AND SUPPORT SERVICES

Please follow this link to view a comprehensive list of [Student Academic and Support Services](http://www.utoledo.edu/studentaffairs/departments.html) (http://www.utoledo.edu/studentaffairs/departments.html) available to you as a student.

## SAFETY AND HEALTH SERVICES FOR UT STUDENTS

Please use the following link to view a comprehensive list [Campus Health and Safety Services](http://www.utoledo.edu/offices/provost/utc/docs/CampusHealthSafetyContacts.pdf) available to you as a student.

INCLUSIVE CLASSROOM STATEMENT

In this class, we will work together to develop a learning community that is inclusive and respectful. Our diversity may be reflected by differences in race, culture, age, religion, sexual orientation, gender identity/expression, socioeconomic background, and a myriad of other social identities and life experiences. We will encourage and appreciate expressions of different ideas, opinions, and beliefs so that conversations and interactions that could potentially be divisive turn, instead, into opportunities for intellectual and personal development.

COURSE SCHEDULE

| WEEK | DATES | TOPIC | FACILITATOR | LEARNING OUTCOME(S) | ASSIGNMENTS DUE |
| --- | --- | --- | --- | --- | --- |
| 1 | Jan 20 | The Human Microbiome in the context of Biomarker Research | Fedorov | L4, L15 | TBD |
| 2 | Jan 24, 27 | Human SNPs Parts 1 & 2 | Gray | L2, L5, L8 | TBD |
| 3 | Jan 31 | The Human Microbiome in the Context of Biomarker Research and Individualized Medicine | Blumenthal | L2, L5, L8 | TBD |
|  | Feb 3 | EXOME PROJECT (beginning):raw FASTQ data; introduction to SAM, BAM, and VCF files | Fedorov |  | TBD |
| 4 | Feb 7 | EXOME PROJECT (continuation) LAB from FASTQ to SAM, BAM and VCF files using GATK program package | Fedorov | L2, L5, L8 | TBD |
|  |  | EXOME PROJECT (end) Visualization of BAM files with IGV program. Complex patterns of SNP arrangements (haplotypes, haplogroups, SNP flip-over | Fedorov |  | TBD |
| 5 | Feb 14 | GWAS and Identification of disease-susceptibility genes/ Human population genetics intricacies | Cicila | L3, L6 | TBD |
|  | Feb 17 | Human population genetics intricacies | Fedorov |  | TBD |
| 6 | Feb 21 | Epigenomics | de la Serna/  Fedorov | L7, L8 | TBD |
|  | Feb 24 | Exam for Unit 1 | Fedorov |  | TBD |
| 7 | Feb 28 | Galaxy web tools (beginning) | Trumbly | L1 | TBD |
|  | Mar 3 | Galaxy web tools (end) | Trumbly |  | TBD |
| 8 | Mar 7, 10 | **SPRING BREAK** | – | – | – |
| 9 | Mar 14, 17 | Biomarker identification, development, and validation/Microbiota as biomarkers of hypertension and other pathologies | Khuder/ Tummala | L3, L9, L13, L14 | TBD |
| 10 | Mar 21, 24 | DNA damage response biomarkers in cancer / Biomarkers of cancer cell motility | Williams & Allison / Eisenmann | L10, L11 | TBD |
| 11 | Mar 28, 31 | [Mar 31 free to work on take-home assignment] / Salivary biomarkers and Sjögren’s syndrome | [None] /  Giovannucci | [L16], L9 | TBD |
| 12 | Apr 4, 7 | Individualized immuno-therapy / Targeted transplant donor-recipient matching | Wuescher / Stepkowski | L9, L15 | TBD |
| 13 | Apr 11, 14 | Validation: design & conduct of trials; patient selection /  [Apr 14 for take-home assignment] | Willey /  [None] | L14, L15, [L16] | TBD |
| 14 | Apr 18, 21 | Designing an Assay in the Middle of a Pandemic / Using proteomics to define biomarkers | Baum /  O’Donovan | L12 | TBD |
| 15 | Apr 25, 28 | Using kinome arrays to define biomarkers / | McCullumsmith / TBD | L15 | TBD |

[Final exam during week of May 02]