PubH 6162
Biomarkers
Fall/2015

Credits: 2
Meeting Days: Monday
Meeting Time: 5:45 pm to 7:40 pm
Meeting Place: Mayo 1250
Instructor: Irina Stepanov, Ph.D.
Assistant Professor, Division of Environmental Health Sciences, U of M
Office Address: 2-140 CCRB
Office Phone: 612-624-4998
Fax: 612-624-3869
E-mail: stepa011@umn.edu
Office Hours: e-mail to make an appointment

I. Course Description
Biomarkers are invaluable tools in identifying and preventing human disease. Due to significant concerns over the risk of human exposure to airborne pollutants, persistent organic pollutants, heavy metals, and other environmental agents, the potential of molecular markers is especially high in identifying susceptible individuals and preventing environmentally-induced disease. This course will introduce current status of molecular biomarker research, including biomarkers of chemical exposures, genetic toxicity markers, genomics-based biomarkers of susceptibility, and organ and systems biomarkers. The progression of biomarker development and application from the laboratory environment to the clinical or population-based settings and to the development of public health policies and interventions will be discussed. The course will include a collaborative project.

II. Course Prerequisites
Introductory courses in toxicology and exposure analysis recommended (PubH 6103, PubH 6104 or equivalent) or instructor consent.
III. Course Goals and Objectives

**General goal.** The goal of this course is to introduce students to the value and challenges of using biomarker applications in research and intervention activities pertinent to environmental health, and to provide a view of emerging trends and technologies in the evolving field of biomarker discovery.

**Specific objectives.** Upon completion of this course students should be able to:

- Recognize the diversity of biomarker types and applications, as well as the variety of cutting-edge analytical techniques used for their identification and measurement.
- Describe the biological meaning of various types of biomarkers and their utility in addressing specific environmental health issues.
- Design a biomarker-based study that coherently incorporates methodological, ethical, and communication considerations.
- Analyze biomarker data and interpret their meaning to public health on population and individual levels.
- Communicate the results and the meaning of biomarker measurements to various audiences.

IV. Methods of Instruction and Work Expectations

This course includes lectures, directed readings, in-class exercises and discussions, and a group project and presentation. The lectures will be given to introduce basic concepts and will be followed by seminars to practice application of the gained knowledge and to discuss assigned readings. The group project will include writing a biomarker-based research proposal (not longer than 3 pages) and a discussion of proposals written by individual groups. Students are expected to attend all of the classes.

**Lecture topics will include:**

- Introduction to biomarker classification, characteristics, development and validation approaches, and overview of the current status of biomarker application in environmental health

  - Biomarkers of chemical exposures
    - Air pollutants
    - Occupational exposures
    - Organic chemicals
    - Metals
    - Food contaminants
    - Tobacco smoke/Environmental Tobacco Smoke

  - Genetic toxicity markers
    - Specific DNA adducts as biomarkers of DNA damage
    - Mutations caused by environmental carcinogens

  - Biomarkers of genetic susceptibility
    - Genetic variations in xenobiotic metabolizing genes
    - Genetic variations in DNA repair genes

  - Organ and systems biomarkers
    - Markers of organ toxicity
    - Oxidative damage and inflammation
    - Immunotoxicity markers
    - Epigenetics

  - Tools and technologies for biomarker measurement and discovery
    - Analytical techniques and instrumentation
    - Metabolomics
    - Proteomics
    - Adductomics
    - Exposome

  - Analysis of human biomonitoring data

  - Ethics, data protection, communication

  - Application in public health policies and interventions
Grading percentages will be based on total performance on the assignments. Course grades will be determined by the following:

- **Assigned readings and classroom activities (40%)**

  The purpose of these activities is to involve students in active learning process and to apply the gained knowledge to the analysis of case studies.

  Students will read assigned research papers and prepare for class presentation by writing a brief summary of the study hypothesis, design, methods and conclusions, focusing on the critique of issues relevant to the specific course topic (as indicated by the instructor). The summaries are due on the day of paper presentation in class, and will be used to guide the presentation and discussion. There will be five reading assignments over the course of the semester (each worth 4%). Points will be awarded for clearly and concisely addressing the major strengths and weaknesses of the reviewed research study.

  Classroom exercises (worth 2% on week 1 and 3% on weeks 4, 7, and 9-12) will include group discussions, small group projects, quizzes, and minute papers. For selected activities, students will be required to enter their notes in the questionnaires provided on the Moodle site (https://moodle.umn.edu/). Points will be awarded for active participation and turning in completed written assignments.

- **Course Project (50%)**

  Students will design a biomarker-based study in the form of a research proposal. The proposal must follow the format outlined by the instructor, which will be close to the NIH proposal format. The proposals will be 3 pages maximum, and will coherently incorporate a statement of specific aims, significance of the problem, study design and methodology, and a discussion of potential limitations and solutions. Students will have 6 weeks to complete this project. Each proposal will be graded according to the rubric which will provided by the instructor at the time of project assignment.

  Several choices of proposal topics will be offered, however students can propose their own topic in the area of environmental health.

- **Evaluation of the course project (10%)**

  Each student will prepare a written critique of a proposal prepared by another student (as assigned by the instructor). This will be the final assignment. Students will have one week to complete this assignment and will follow rubrics provided by the instructor. Points will be awarded for clearly and concisely addressing the major strengths and weaknesses of the reviewed proposal.

After completion of this assignment, each project will be discussed in class in a study section format.

V. **Course Text and Readings**

This course is based on the practical aspects of current biomarker applications. Most readings will include recent research papers and reviews of works that are focused on current issues in human health and use state-of-the art technologies. Copies of, or web links to, research papers, reviews, and book chapters will be provided on the Moodle site (https://moodle.umn.edu/).

Recommended general reading:

*Casarett and Doull’s Toxicology. The Basic Science of Poisons* by Curtis D. Klaasen. This reference book is useful for reviewing toxicology concepts. This reference is available online through the University of Minnesota Biomedical Library: http://www.knovel.com/knovel2/Toc.jsp?BookID=95


environmental toxicants and provides examples of biomarker-based studies. Available at UM TC Bio-
Medical Library (WA670 B615 2012 )

*Biomarkers and occupational health. Progress and perspectives.* Mendelsohn, M.L., Peeters, J.P.,
(WA400 B6155 1994)

### VI. Course Outline/Weekly Schedule

<table>
<thead>
<tr>
<th>Week:</th>
<th>1st hour</th>
<th>2nd hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>September 14</td>
<td><strong>Week 1</strong> Lecture: Introduction to the course. Definitions, classifications, and characteristics of biomarkers. Development and validation. Overview of biomarker applications in environmental health.</td>
<td>Classroom activities: background knowledge probes, application cards, minute paper</td>
</tr>
<tr>
<td>September 21</td>
<td><strong>Week 2</strong> Lecture: Biomarkers of chemical exposures (Part 1)</td>
<td>Classroom activity: Presentation and analysis of assigned readings</td>
</tr>
<tr>
<td>September 28</td>
<td><strong>Week 3</strong> Lecture: Biomarkers of chemical exposures (Part 2)</td>
<td>Classroom activity: Presentation and analysis of assigned readings</td>
</tr>
<tr>
<td>October 5</td>
<td><strong>Week 4</strong> Lecture: Biomarkers of genetic susceptibility.</td>
<td>Classroom activity: Group discussions of brief articles on studies involving genetic susceptibility markers.</td>
</tr>
<tr>
<td>October 12</td>
<td><strong>Week 5</strong> Laboratory class – PAH biomarkers in urine</td>
<td>Note: Projects are assigned</td>
</tr>
<tr>
<td>October 19</td>
<td><strong>Week 6</strong> Lecture: Genetic toxicity markers</td>
<td>Classroom activity: Presentation and analysis of assigned readings</td>
</tr>
<tr>
<td>October 26</td>
<td><strong>Week 7</strong> Laboratory class – DNA adducts</td>
<td></td>
</tr>
<tr>
<td>November 2</td>
<td><strong>Week 8</strong> Lecture: Organ and systems biomarkers</td>
<td>Classroom activity: Presentation and analysis of assigned readings</td>
</tr>
<tr>
<td>November 9</td>
<td><strong>Week 9</strong> Lecture: Ethical and data protection issues in biomarker research.</td>
<td>Classroom activity: Group discussions of brief articles on ethical and data protection issues in biomarker research, followed up by the read around exercise.</td>
</tr>
</tbody>
</table>
November 16
Week 10
**Guest lecture:** Biomarker-based research at the U of M – Metabolomics

November 23
Week 11
**Lecture:** Application of biomarkers in public health policies and interventions
**Classroom activity:** Group projects: alternative biomarkers for real-life policies; ideas for biomarker-based interventions.

**Note:** Written proposals due

November 30
Week 12
**Guest lecture:** Biomarker-based research at the U of M – Aromatic amines

December 7
Week 13
**Guest lecture:** Biomarker-based research at the U of M - Adductomics

**Note:** Written critique of assigned proposals due

December 14
Week 14
Discussion and critique of proposals

VII. Evaluation and Grading

Grading percentages are based on total performance on the assignments. Extra credit projects will not be accepted to improve a grade or as a substitute for assignments. There is no final exam. Course grades will be determined by the following:

- **Assigned readings and classroom activities (40%)**
  When required, students must present assigned readings and turn in reports and written classroom assignments. When requested to enter class notes in the questionnaire provided on the Moodle site (https://moodle.umn.edu/), students must do so within 24 hours after class meeting. Late reports will not be accepted.

- **Group Project: Proposal (50%)**
  Each group will turn in a single proposal; all members of the team will receive the same grade. Criteria for the proposal evaluation will be handed out in class at the time of group and topic assignment. If a proposal is turned in after the due date, two points will automatically be deducted for each day after the deadline. Late proposals will not be accepted after the class meeting on Week 12.

- **Evaluation of group project (10%)**
  Each student must prepare a written critique of the proposal assigned for review, following the format which will be handed out in class at the time of critique assignment. Discussion of proposals will take place at the last class meeting on Week 14, and cannot be postponed or re-scheduled.

A/F letter grade will be determined by total effort as follows:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Percentage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>92-100%</td>
<td>(4.0) Represents achievement that is outstanding relative to the level necessary to meet course requirements.</td>
</tr>
<tr>
<td>A-</td>
<td>88-91.5%</td>
<td></td>
</tr>
</tbody>
</table>
B+ = 84-87.5%
B = 80-83.5%
  (3.0) Represents achievement that is significantly above the level necessary to meet course requirements.
B- = 76-79.5%
C+ = 72-75.5%
C = 68-71.5%
  (2.0) Represents achievement that meets the minimum course requirements.
C- = 64-67.5%
D+ = 60-63.5%
D = 56-59.6%
  (1.0) Achievement below minimum course expectations but sufficient to be awarded credit.
D- = 52-55.5
F = <51.5
  Represents failure (or no credit) and signifies that the work was either (1) completed but at a level of achievement that is not worthy of credit or (2) was not completed and there was no agreement between the instructor and the student that the student would be awarded an I.

Course Evaluation
Beginning in fall 2008, the SPH will collect student course evaluations electronically using a software system called CoursEval: www.sph.umn.edu/courseval. The system will send email notifications to students when they can access and complete their course evaluations. Students who complete their course evaluations promptly will be able to access their final grades just as soon as the faculty member renders the grade in SPHGrades: www.sph.umn.edu/grades. All students will have access to their final grades through OneStop two weeks after the last day of the semester regardless of whether they completed their course evaluation or not. Student feedback on course content and faculty teaching skills are an important means for improving our work. Please take the time to complete a course evaluation for each of the courses for which you are registered.

Incomplete Contracts
A grade of incomplete "I" shall be assigned at the discretion of the instructor when, due to extraordinary circumstances (e.g., documented illness or hospitalization, death in family, etc.), the student was prevented from completing the work of the course on time. The assignment of an "I" requires that a contract be initiated and completed by the student before the last official day of class, and signed by both the student and instructor. If an incomplete is deemed appropriate by the instructor, the student in consultation with the instructor, will specify the time and manner in which the student will complete course requirements. Extension for completion of the work will not exceed one year (or earlier if designated by the student’s college). For more information and to initiate an incomplete contract, students should go to SPHGrades at: www.sph.umn.edu/grades.

University of Minnesota Uniform Grading and Transcript Policy - A link to the policy can be found at onestop.umn.edu.

VIII. Other Course Information and Policies

Grade Option Change (if applicable)
For full-semester courses, students may change their grade option, if applicable, through the second week of the semester. Grade option change deadlines for other terms (i.e. summer and half-semester courses) can be found at onestop.umn.edu.

Course Withdrawal
Students should refer to the Refund and Drop/Add Deadlines for the particular term at onestop.umn.edu for information and deadlines for withdrawing from a course. As a courtesy, students should notify their instructor and, if applicable, advisor of their intent to withdraw.
Students wishing to withdraw from a course after the noted final deadline for a particular term must contact the School of Public Health Office of Admissions and Student Resources at sph-ssc@umn.edu for further information.

**Student Conduct Code**
The University seeks an environment that promotes academic achievement and integrity, that is protective of free inquiry, and that serves the educational mission of the University. Similarly, the University seeks a community that is free from violence, threats, and intimidation; that is respectful of the rights, opportunities, and welfare of students, faculty, staff, and guests of the University; and that does not threaten the physical or mental health or safety of members of the University community.

As a student at the University you are expected to adhere to Board of Regents Policy: **Student Conduct Code**. To review the Student Conduct Code, please see: 

Note that the conduct code specifically addresses disruptive classroom conduct, which means “engaging in behavior that substantially or repeatedly interrupts either the instructor’s ability to teach or student learning. The classroom extends to any setting where a student is engaged in work toward academic credit or satisfaction of program-based requirements or related activities.”

**Use of Personal Electronic Devices in the Classroom**
Using personal electronic devices in the classroom setting can hinder instruction and learning, not only for the student using the device but also for other students in the class. To this end, the University establishes the right of each faculty member to determine if and how personal electronic devices are allowed to be used in the classroom. For complete information, please reference: 
http://policy.umn.edu/Policies/Education/Education/STUDENTRESP.html

**Scholastic Dishonesty**
You are expected to do your own academic work and cite sources as necessary. Failing to do so is scholastic dishonesty. Scholastic dishonesty means plagiarizing; cheating on assignments or examinations; engaging in unauthorized collaboration on academic work; taking, acquiring, or using test materials without faculty permission; submitting false or incomplete records of academic achievement; acting alone or in cooperation with another to falsify records or to obtain dishonestly grades, honors, awards, or professional endorsement; altering, forging, or misusing a University academic record; or fabricating or falsifying data, research procedures, or data analysis. (Student Conduct Code: 
http://regents.umn.edu/sites/default/files/policies/Student_Conduct_Code.pdf) If it is determined that a student has cheated, he or she may be given an "F" or an "N" for the course, and may face additional sanctions from the University. For additional information, please see: 
http://policy.umn.edu/Policies/Education/Education/INSTRUCTORRESP.html

The Office for Student Conduct and Academic Integrity has compiled a useful list of Frequently Asked Questions pertaining to scholastic dishonesty: http://www1.umn.edu/oscai/integrity/student/index.html. If you have additional questions, please clarify with your instructor for the course. Your instructor can respond to your specific questions regarding what would constitute scholastic dishonesty in the context of a particular class—e.g., whether collaboration on assignments is permitted, requirements and methods for citing sources, if electronic aids are permitted or prohibited during an exam.

**Makeup Work for Legitimate Absences**
Students will not be penalized for absence during the semester due to unavoidable or legitimate circumstances. Such circumstances include verified illness, participation in intercollegiate athletic events, subpoena, jury duty, military service, bereavement, and religious observances. Such circumstances do not include voting in local, state, or national elections. For complete information, please see: 
http://policy.umn.edu/Policies/Education/Education/MAKEUPWORK.html

**Appropriate Student Use of Class Notes and Course Materials**
Taking notes is a means of recording information but more importantly of personally absorbing and integrating the educational experience. However, broadly disseminating class notes beyond the classroom community or accepting compensation for taking and distributing classroom notes undermines instructor
interests in their intellectual work product while not substantially furthering instructor and student interests in effective learning. Such actions violate shared norms and standards of the academic community. For additional information, please see: http://policy.umn.edu/Policies/Education/Education/STUDENTRESP.html.

**Sexual Harassment**
"Sexual harassment" means unwelcome sexual advances, requests for sexual favors, and/or other verbal or physical conduct of a sexual nature. Such conduct has the purpose or effect of unreasonably interfering with an individual’s work or academic performance or creating an intimidating, hostile, or offensive working or academic environment in any University activity or program. Such behavior is not acceptable in the University setting. For additional information, please consult Board of Regents Policy: http://regents.umn.edu/sites/default/files/policies/SexHarassment.pdf.

**Equity, Diversity, Equal Opportunity, and Affirmative Action**
The University will provide equal access to and opportunity in its programs and facilities, without regard to race, color, creed, religion, national origin, gender, age, marital status, disability, public assistance status, veteran status, sexual orientation, gender identity, or gender expression. For more information, please consult Board of Regents Policy: http://regents.umn.edu/sites/default/files/policies/Equity_Diversity_EO_AA.pdf.

**Disability Accommodations**
The University of Minnesota is committed to providing equitable access to learning opportunities for all students. Disability Services (DS) is the campus office that collaborates with students who have disabilities to provide and/or arrange reasonable accommodations.

If you have, or think you may have, a disability (e.g., mental health, attentional, learning, chronic health, sensory, or physical), please contact DS at 612-626-1333 to arrange a confidential discussion regarding equitable access and reasonable accommodations.

If you are registered with DS and have a current letter requesting reasonable accommodations, please contact your instructor as early in the semester as possible to discuss how the accommodations will be applied in the course.

For more information, please see the DS website, https://diversity.umn.edu/disability/.

**Mental Health and Stress Management**
As a student you may experience a range of issues that can cause barriers to learning, such as strained relationships, increased anxiety, alcohol/drug problems, feeling down, difficulty concentrating and/or lack of motivation. These mental health concerns or stressful events may lead to diminished academic performance and may reduce your ability to participate in daily activities. University of Minnesota services are available to assist you. You can learn more about the broad range of confidential mental health services available on campus via the Student Mental Health Website: http://www.mentalhealth.umn.edu.

**Academic Freedom and Responsibility: for courses that do not involve students in research**
Academic freedom is a cornerstone of the University. Within the scope and content of the course as defined by the instructor, it includes the freedom to discuss relevant matters in the classroom. Along with this freedom comes responsibility. Students are encouraged to develop the capacity for critical judgment and to engage in a sustained and independent search for truth. Students are free to take reasoned exception to the views offered in any course of study and to reserve judgment about matters of opinion, but they are responsible for learning the content of any course of study for which they are enrolled.*

Reports of concerns about academic freedom are taken seriously, and there are individuals and offices available for help. Contact the instructor, the Department Chair, your adviser, the associate dean of the college, or the Vice Provost for Faculty and Academic Affairs in the Office of the Provost. [Customize with names and contact information as appropriate for the course/college/campus.]

* Language adapted from the American Association of University Professors "Joint Statement on Rights and Freedoms of Students".