Biology 78 w22 Molecular Mysteries of Human Biology

Lectures: Monday, Wednesday & Friday, 9L (8:50-9:55 AM) **X-hour**: Thursday, (9:05-9:55 AM)

Text/Reading:

1. **Recommended text:** Any biochemistry text (e.g.Voet, Voet & Pratt, Berg, Tymoczko & Stryer, or Garrett & Grisham) may provide important background information.
2. **Course Readings**: 17 research manuscripts that are required course reading are posted on web site. Additional background information (also required) and helpful reviews (optional) for each topic also posted.

Course Web Site: http://canvas.dartmouth.edu

Date	Topic	Prob Set Posted	Prob Set Due
Watch on Tuesday, Jan 4	**Video**: The Hidden Epidemic: Heart Disease in America		
Wed, Jan 5	Atherosclerosis: The Loch Ness Monster and John Hunter's Ossified Arteries		
Fri, Jan 7	Plasma Lipoproteins: The Legacies of Michel-Eugène Chevruel and Mona Lisa		
Mon, Jan 10	Readings: Schoenheimer Effect Explained: Cholesterol Regulates Itself		
Wed, Jan 12	Readings: Hepatic Steatosis, PCSK9 Induction and LDL Receptor Expression	**#1**	
Thurs, Jan 13, **X-hour**	**Dr. John Butterly:** A Patient with Atherosclerosis		
Fri, Jan 14	Otto Warburg and the Mysterians: Metabolism in Cancer Cells		
Mon, Jan 17	**MLK Day**: NO CLASS		**#1**
Wed, Jan 19	Readings: Fructose Metabolism Drives Colon Cancer Metastasis in Liver		
Thurs, Jan 20, **X-hour**	Readings: CyclinD3-CDK6 Complex Regulates Metabolism in Cancer	**#2**	
Fri, Jan 21	Cachexia: Agostino Levanzin, the Irish Republican Army and Steve Jobs		
Mon, Jan 24	Readings: Tumor Blockade of Factors Affecting Muscle Mass		**#2**
Wed, Jan 26	Readings: Reversing Cancer Cachexia via Inhibition of GFRAL/RET Signaling	**#3**	
Fri, Jan 28	Bathsheba's Breast: Hendrickje Stoffels, Anne of Austria, Susan Sontag and Jill Ireland		
Mon, Jan 31	Readings: Fasting & Hormone Therapy Induce Breast Cancer Regression		**#3**
Wed, Feb 2	Readings: Fasting-mimicking Diets and Triple-Negative Breast Cancer	**#4**	
Friday, Feb 4	Exercise: Sled Dogs, Toadfish, Frogs, Geese & Lance Armstrong		
Mon, Feb 7	Readings: Prolyl Hydroxylase, AMPK and ACC-β in Muscle Performance		**#4**
Wed, Feb 9	Readings: Interleukin-13 and Metabolic Conditioning in Endurance Exercise	**#5**	
Fri, Feb 11	Diabetes Mellitus: Paul Cezanne's Vision and Shirley Horn's Feet		
Mon, Feb 14	Readings: CaMKII, O-linked Glycosylation and Cardiac Disease		**#5**
Wed, Feb 16	Readings: Fatty Acid Uptake and Progression of Diabetic Nephropathy	**#6**	
Thurs, Feb 17, **X-hour**	**Dr. Richard Comi**: Patient with Type 1 Diabetes Mellitus		
Watch on Thurs, Feb 17	**Video:** The Forgetting: A Portrait of Alzheimer's Disease		
Fri, Feb 18	Alois Alzheimer and Auguste D: Sailing Into Darkness		
Mon, Feb 21	Readings: LRP1: Master Regulator of Tau Uptake & Spread		**#6**
Wed, Feb 23	Readings: Astrocytes, Microglia & Interleukin-3 (IL3): Protective Pairings in AD	**#7**	
Thurs, Feb 24, Evening	**Dinner (?)/Movie: Iris: A Tale of Iris Murdoch & Discussion**		
Fri, Feb 25	Aging: In Vino Veritas: Luigi Cornaro & *Discorsi della Vita Sobria*		
Mon, Feb 28	Readings: Alternate Day Fasting & Molecular Markers of Aging		**#7**
Wed, March 2	Readings: Exercise and the Aging Brain: A Liver, Muscle & Adipose Tissue Connection		
Fri, March 4	Readings: "NAD Boosters": NMN Supplementation & Skeletal Muscle Biology	**#8**	
Mon, March 7	**TBD**		
Thurs, March 10			**#8**

Biology 78 Course Format & Expectations

Biology 78 COVID-related Obligations

Due to the pandemic and in the interests of the health & safety of me and you, **I need your ABSOLUTE ASSURANCE that you are adhering daily to all COVID protocols (especially during your "out-of-class" time, but also during class and my "in-person" office hours) and are getting regularly tested. The winter weather will bring people in closer proximity and infection numbers are likely to climb. PLEASE DO NOT** for the safety/health of your classmates, their contacts and me and my families including my children and grandchildren (whom I will be visiting hopefully frequently during the term in nearby Vermont) waiver from this commitment. **Masking is required for all of the time you spend in the LSC. DO NOT COME** to class or office hours if you have any COVID or respiratory symptoms and/or are awaiting the results of a COVID test taken when you have these symptoms. You also **CANNOT EAT** in the classroom, though you can remove your mask briefly to drink. **If you feel you cannot give these assurances, then please register for a different class.**

Course Goals and Format

Knowledge of molecular mechanisms allows new approaches to understanding human biology and disease. This course will explore the normal and abnormal biology of several human conditions relying on biochemistry, molecular genetics, and physiology as tools of inquiry. Examples will be drawn from the histories of Mona Lisa, Michel-Eugène Chevruel, Otto Warburg, Steve Jobs, Hendrickje Stöffels. Bobby Sands, Paul Cézanne, Lance Armstrong, Auguste D and Luigi Cornaro. among others.

The eight class topics are organized in blocks of approximately one week, the introduction of which will begin with a lecture (or two) by Professor Witters who will discuss an area of normal or abnormal human biology to be investigated. He will include information on the relevant physiology/pathophysiology and basic biochemical & molecular background to set the context for further discussions. In the following two classes, the assigned reading will be discussed. Students (in groups of 2) have been assigned to TWO papers for the term (see below) and will analyse, critique and present the papers to which they are assigned. **For each of these classes, ALL students will be expected to have read the background & research papers AND to participate in the discussion**. Some review papers on the course web site are also valuable in setting the context and will provide supplementary information to assist students in their preparation of their paper presentations. Following the final presentation within each topic, a to-be-graded problem set based on issues raised by one/both of the papers/topic. *These assignments will be due as indicated on the course schedule and can be completed in an open-book format with full consultation with any source of information, including others in the class (see below).*

Throughout the course, it will be important to put a human face/context to the biochemical/molecular events we are studying, illustrating the "life" experience where biology is normal or abnormal. We will hope to achieve this aim in several ways. The **background reading** is a very important complement to the molecular details. In some class meetings, we will have a **guest physician** discussing a patient dealing with one of the topics under discussion. We will preview two of the course blocks with **out-of-class viewing of videos** that will help introduce or amplify some of these topics.

Expectations and Grading

Expectations for and grading of students consists of several elements. **Students are expected to attend class, to have done the reading and to complete all assignments on time unless the reasons for the lateness have been discussed with Professor Witters in advance. In general, the only possible excuses for lateness will be illness or unavoidable conflicts (e.g. job or grad school interview). In each of these, however, PRIOR approval from him will be required.**

- **A 1% deduction per hour in grade will be assigned for any assignment that is late.**
- **Again, students are expected to communicate with Professor Witters in advance about any possible deviation from submission of assignments on time.**

It is possible to accumulate **100 points** in the course in 3 ways **anticipating the median grade to be A/A-.**

- **(40% of grade; 10 points for each submitted; 40 points total) Eight (8) problem assignments, each worth 10 points,** will be distributed during the term. **Each student must complete four (4) of these**, automatically excluding the problems on the topic of their 2 assigned papers AND two others of their choosing (the latter declared in advance). Each problem will relate to an aspect of the assigned reading/topic; answers are limited to two typewritten pages. **In the last offering of this course, grades ranged 7.5-9.7 points on each problem set).** *The distribution and due dates are indicated on the course schedule, on the student presentation assignments spreadsheet & on the Canvas course calendar.*

- **(40% of grade; 40 points/20 points per paper) Preparation and presentation of the assigned papers**. Each student (in groups of 2) will be expected to prepare a scholarly presentation of **TWO** papers, providing background on the topic, an exposition and review of the data and the methodology of the papers under review and a critique of the paper's findings and conclusions. Each presentation should be accompanied by a PP set, including a bibliography. **In the last offering of this course, grades ranged from 16-19 points per paper.** *More details below.*

- **(20% of grade; 20 points) Engagement of and participation in class discussions and analysis of reading through thoughtful questions and comment** will be an important part of the grading. Participation is the key word, not whether the student is "right or wrong". Evidence that student has read/prepared for each discussion will also be sought for. Other "evidence" of participation will include the use of office hours and use of Slack on the course web site for thoughtful questions, comments or postings. **In the last offering of this course, grades ranged from 16-20 points.**

- **There are no midterms, final exam or paper** in this course.

Course Materials

The **course readings** are included as .pdfs on the web site (along with links to each), as well as pertinent review articles & commentaries on the readings that may be of value in preparing paper presentations. **External links** to all the research manuscripts are included, which can be value in viewing in color and in examination of supplemental data.

A **biochemistry text**, either Berg, Tymoczko & Stryer, Biochemistry or Voet, Voet & Pratt, Biochemistry or Garrett & Grisham might be very valuable in the review of material and preparation of presentations.

The **course web site** is on Canvas (http://canvas.dartmouth.edu) where readings, Powerpoint slides, lecture/presentation Panopto videos (see below), web links, Q&A module (Slack) and other materials will be maintained.

Technologic snafus aside, we will be doing Panopto videos of all class sessions. While I do NOT regard this as a substitute for class attendance, it might be helpful for several of you if you have an unavoidable absence from class or would simply like to review aspects of a lecture or discussion (you can start and stop me!). Historically, many students have found these useful as a course study adjunct.

Other Course Issues

Office Hours: Students are very much encouraged to utilize weekday office hours for discussion and questions and to work on their assigned presentations. I enjoy getting to know you all well and to work with you on course material, "life after Dartmouth", things you are up to, etc. You can schedule **individual office hours using Calendly (see Canvas site for link)**. I will also be offering a **group Zoom office hour** in advance to posting of the weekly problem set (beginning Week #2) for last minute questions (times TBA). Students are also encouraged to utilize the **Slack** section of the Canvas site. By posting questions (and having public answers), everyone in the class benefits. Students can also use Slack to post interesting articles or web links to information they encounter during the course. Lastly, I will be arranging **specific office hours to help each group prepare their paper presentation**.

X-hours/Class Schedule: We will use some of the X-hours for visits from physicians to present patient cases or lead discussions. I will NOT be recording these sessions consistent with patient confidentiality. We will also use one X-hour for a paper presentation, as well (during MLK week).

Course Accommodations: Students with **disabilities,** including chronic illnesses, learning disabilities, and psychiatric disabilities are encouraged to discuss with me appropriate accommodations that might be helpful. **Please do this EARLY in the course**. This conversation will help to establish how your accommodations will be implemented in this course and what role Student Accessibility Services (SAS) or its Testing Center may play in assisting. In order for accommodations to be authorized, students are required to register with SAS (Getting Started with SAS webpage; student.accessibility.services@dartmouth.edu; 603-646-9900) and to request an accommodation email be sent to me in advance of the need for an accommodation. If students have questions about whether they are eligible for accommodations, they should contact the SAS office. All inquiries and discussions will remain confidential. It is **very important that we then continue to communicate** over the term to assure that your needs are being met. Receiving accommodations **does NOT** relieve you of the responsibility of communicating with me about any deviations from course requirements **BEFORE the fact.** *We will then work together with SAS if accommodations need to be modified based on the learning environment*. **Again, any requested deviation from course deadlines MUST be sought in advance of deadline dates irrespective of the authorized accommodations.**

Religious Observances: Some students may wish to take part in religious observances during the term. If you have such a conflict, please discuss with me, so we can make appropriate arrangements. *If you have a religious observance that conflicts with your participation in the course, please meet with me before the end of the second week of the term to discuss appropriate accommodations.*

Mental Health & Wellbeing Support: I recognize that the pandemic and the academic environment at Dartmouth are both challenging, that our terms are intensive, and that classes are not the only demanding part of your life. There are a number of resources available to you on campus to support your wellness, including: your undergraduate dean (http://www.dartmouth.edu/~upperde/), Counseling and Human Development (http://www.dartmouth.edu/~chd/), and the Student Wellness Center (http://www.dartmouth.edu/~healthed/). The student-led Dartmouth Mental Health Union and their Peer Support Program in Collis (and other programs) may additionally be helpful to you. **I especially encourage you to use these resources AND speak with me to help you take care of yourself throughout the term.**

Our Community: At Dartmouth, I/we value integrity, responsibility, and respect for the rights and interests of others, all central to our Principles of Community. I/we are dedicated to establishing and maintaining a safe and inclusive campus where all have equal access to the educational and employment opportunities Dartmouth offers. I/we strive to promote an environment of sexual respect, safety, and well-being. In its policies and standards, Dartmouth demonstrates unequivocally that sexual assault, gender-based harassment, domestic violence, dating violence, and stalking are not tolerated in our community.

The Sexual Respect Website (sexual-respect.dartmouth.edu) provides a wealth of information on your rights and obligations with regard to sexual respect and resources that are available to all in our community. **As a faculty member, I am obligated to share disclosures made to me regarding conduct under Title IX with Dartmouth's Title IX Coordinator.** Confidential resources are also available, and include licensed medical or counseling professionals (e.g., a licensed psychologist), staff members of organizations recognized as rape crisis centers under state law (such as WISE), and ordained clergy. Should you have any questions, please feel free to contact Dartmouth's Title IX Coordinator (Kristi.Clemens@Dartmouth.edu) (and deputies if appropriate).

Preparation of Assignments and the Dartmouth Academic Honor Principle: The Dartmouth College Student Handbook states: "Fundamental to the principle of independent learning are the requirements of honesty and integrity in the performance of academic assignments, both in the classroom and outside. Dartmouth operates on the principle of academic honor, without proctoring of examinations. Students who submit work which is not their own or who commit other acts of academic dishonesty forfeit the opportunity to continue at Dartmouth." Students are responsible for the information concerning plagiarism and proper citation found at:
https://students.dartmouth.edu/community-standards/policy/academic-honor-principle
https://writing-speech.dartmouth.edu/learning/materials/sources-and-citations-dartmouth
Some specific issues about adherence to the Honor Principle for your assigned papers and the problem sets follows:

- **Assigned paper presentations (more details below)** For completion of this Biology 78 assignment, students are free to consult other sources of information, but ALL THESE SOURCES must be documented in a bibliography. Possible sources include classmates, other non-class students (except students who have previously enrolled in Bio78), textbooks and the biomedical literature. INTERNET RESOURCES (as URLs) ARE **NOT** ACCEPTABLE AS THE SOLE SOURCES OF INFORMATION; STUDENTS ARE EXPECTED TO USE STANDARD TEXTBOOKS AND THE BIOMEDICAL LITERATURE (You are free to use the Internet, of course, to identify these primary sources, but must consult them directly). *All presentation materials (PP, other documents) must be passed onto Professor Witters for posting on the course web site after the presentation.*

- **Problem sets (more details below)** Eight (8) problem sets will be distributed, each on the final class day of each of the topic to be covered. Students must complete and submit four (4) of these. Two are automatically excluded for each student, namely the ones on the topics they presented. Students should then choose two others for exclusion, declared **in advance** of the distribution of the problem.

  Class students are encouraged to work together in discussing and researching the assignments, but everyone is expected to INDEPENDENTLY PREPARE their written answer. You will be required to list the names of the students you worked with on the problem sets. However, students MAY NOT consult with the students who prepared presentations about that particular topic. The completed assignments by individuals who discuss the assignment may reflect ideas developed by them together, but each student must phrase their assignment answer in their own words and acknowledge the "helpful discussions" with their collaborators in the bibliography. **Therefore DO**

NOT share the computer files for your written answers (in draft or final form)! For completion of this Biology 78 assignment, students are free to consult other sources of information, but ALL THESE SOURCES must be documented in a bibliography. **In general, the problem sets can be answered entirely based on information that has been communicated in class and outside references are not necessary (and, in some instances, could confuse).**

Some Specifics Regarding the Paper Assignments/Presentations and Problem Sets

Paper Assignments

Students have been "pre-assigned" (in groups of two) to two papers, using a random group generator and are assigned to a paper in both the first and second halves of the course (with a different partner for the second paper). At the beginning of the course, students can "swap" with others regarding their assignments (TBA).

Each student group is to prepare a scholarly 40-45 min (~20+ min per student) presentation using Powerpoint that includes a bibliography of any additional readings beyond that provided in class. This time leaves ~20 minutes for additional discussion/questions. For completion of all Biology 78 assignments (problem sets, class presentations), students are free to consult other sources of information, but ALL THESE SOURCES must be documented in a bibliography. Possible sources include classmates, other non-class students, Professor Witters/other faculty, textbooks and the biomedical literature. INTERNET RESOURCES (as URLs) ARE **NOT** ACCEPTABLE AS SOLE SOURCES OF INFORMATION; STUDENTS ARE EXPECTED TO USE STANDARD TEXTBOOKS AND THE BIOMEDICAL LITERATURE (You are free to use the Internet, of course, to identify these primary sources, but must consult them directly). *All presentation materials (PP, other documents) must be passed onto Professor Witters for posting on the course web site after the presentation.*

The presentation should include the **following FOUR elements**:

1. A **brief background** on the biology and clinical issues of the relevant topic addressed by the paper
2. **Presentation of the important data** displayed in the paper (it is not necessary to present ALL the data; attention should be paid to the data which supports the major experimental conclusions). *Indeed, your ability to identify which are the key data is part of your grade!* When presenting the data, the figure from the text should be shown where applicable and the experimental technique(s) used to generate the data briefly explained. The data presentation should include any critique about the techniques used or conclusions drawn about any of the data sets. **Each student group will be given all the main figures (as .jpg files) from the assigned paper to assist in their preparation. Supplemental data to many of the papers can be linked to from the Canvas site. In general, the supplemental data should not be a major part of your analysis (give the sheer density of many of these supplements).** However, you certainly can use these data if you think they are particularly important. Note also some supplements have valuable summary figures (as do the review articles and "visual abstracts" accompanying some of the paper postings).
3. A **summary and critique (to be solicited first from the class) of the major conclusions** of the paper and the ramifications of the study in terms of future research and comment about the "mystery" solved!
4. **Engagement of the rest of the class** through provocative or interesting questions. This is a crucial (and "graded") element of the presentation. The questions should be analytical and thought-provoking, not just regurgitative of what everyone has read or can see (i.e. not "softball"). Asking classmates to interpret data, to provide alternative explanations for conclusions, to critique the information presented and to synthesize different pieces of data are all examples of the kinds of engagement that should be elicited by the presenters.

Other important points about presentations:

1. The time limit of ~40-45 minutes allows sufficient time for Q&A and discussion, so rehearsal of the presentations is STRONGLY ENCOURAGED.
2. Students will be informed of their grade shortly after the class presentations. Twenty (20) course points are assigned to each presentation. For simple completion of the assignment, 15 points would be the expected grade; more (or fewer) points will be awarded depending on the quality of the presentation and the effort of the presenters to engage the rest of the class.

3. Powerpoint slides are a useful way to illustrate key points, and these sets will be distributed to all class members via the web site after the presentation. Professor Witters will give each student group the main figures from the paper as .jpg files. There are several guidelines regarding the use and preparation of PP slides in your presentation.
   a. **Plan about 35-40 total slides (i.e. ~1/minute of presentation).**
   b. **PP slides** are best used to display images and to "bullet" key points. Keep font size large and avoid putting too much text on one slide. Large figures with many panels should be "broken up" and presented in parts of clarity and readability. AVOID reading your slides to the class. REHEARSE!! Use your presentation to amplify your bullet points and to review an image, figure, graph or table. Highlighting (by animation, arrows, boxes, call-outs, etc) key points in the data helps draw focus. The best slides have a declarative title at the top that states succinctly what the slide is trying to illustrate (example: 'PCSK9 Diminishes Expression of the LDL receptor" is the title on a slide that has a graph containing these data). Adding questions to the slides (unanswered) for the class is a good way to initiate discussion. *A summary slide is always a good way to end (and to start)! "Roadmap" slides are also useful to inform the class what the flow of information will be.* BE CREATIVE!
   c. Many student groups will create their PP set as a Google document. **Rather than send a link to your PP set, please download after your presentation and send to Professor Witters for posting after your presentation.** This avoids the occasional problem with access to the Google document.
   d. All slide sets should contain one slide as your critique and one with your bibliography.
   e. Each student group should e-mail their PP set (**as a .pptx, not .pdf file**) to Professor Witters after completion of the presentation for posting on the web site.

I really want to work with all students to help you in the construction of a high-quality presentation. In the past, this has generally involved two (2) meetings, one to go over any questions you have about your paper after an initial reading and for me to review a few presentation points and a second meeting (often the day before a presentation) to preview your PP slides, so I can offer suggestions. Contact me at an early date to arrange these meetings.

Written Problem sets

Eight (8) problem sets requiring submission of a written answer will be distributed during the term. They will be posted on-line at the end of each course topic at 5 PM and **are due by 8AM on the dates indicated** (see the course schedule indicating the distribution and due dates). An **electronic version (as a .docx or .doc file)** MUST be submitted through the Canvas web site at the deadline. Optonal is a submission of a paper copy to the Bio78 dropbox adjacent to my office (122 LSC). Any deviation from the announced deadlines **MUST** be sought in advance. A **1% reduction in grade per hour late** will be strictly enforced unless **prior permission for late submission** has been granted by communication with me.

Students must complete and submit four (4) of these. Two are automatically excluded for each student, namely the ones on the topics they presented. The third & fourth to be excluded should be made known to Professor Witters in advance of the distribution of the problem.

Students are encouraged to work together in discussing and researching the assignments, but everyone is expected to INDEPENDENTLY PREPARE their written answer. **You will be required to list the names of the students you worked with on the problem**

sets. However, students MAY NOT consult with the students who prepared a presentation on that particular topic (or previously enrolled in this class). The completed assignments by two or more individuals who had discussed the assignment may reflect ideas developed by together, but each student must phrase their assignment in their own words and acknowledge the "helpful discussions" with their collaborators in the bibliography. **Therefore DO NOT share the computer files for your written answers (in draft or final form)!**

For completion of all Biology 78 problem sets, students are free to consult other sources of information, but ALL THESE SOURCES must be documented in a bibliography. Possible sources include classmates (**see exception in above paragraph**), other non-class students (if they have not previously enrolled in this class), textbooks and the biomedical literature. INTERNET RESOURCES (as URLs) ARE **NOT** ACCEPTABLE AS THE SOLE SOURCES OF INFORMATION; STUDENTS ARE EXPECTED TO USE STANDARD TEXTBOOKS AND THE BIOMEDICAL LITERATURE (You are free to use the Internet (e.g. PubMed), of course, to identify these primary sources, but must consult them directly). **In general, the problem sets can be answered entirely based on information that has been communicated in class and outside references are not necessary (and, in some instances, could confuse).**

The assignment (to be submitted through the Canvas site) is limited to **2 pages (as a .docx or .doc file in 12 font with the SAME MARGINS as the problem itself), exclusive of a bibliography, which will constitute a 3rd page (and should also list the names of the other students you consulted with about the problem).** Problem sets will be graded not only on the "correctness" of the answer, but the succinctness & clarity of the explanation and the perceived effort in creating a first-class scholarly document. Where appropriate, tables are a good way to display some answers. *I will also be grading these answers for the* ***quality of the expository writing****, including spelling, syntax, sentence structure, punctuation and organization.*