NFS 1226S: Nutrition and Cancer

Course Leader/Instructor:
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Office Hours: By appointment.
Class Hours: Winter 2018, Tuesdays 1:00-3:00 pm
Location: Health Sciences (HS) 108 (Dalla Lana School of Public Health, 155 College St)

Course Materials:
All readings will be available from the course website. There are no required texts for this course.

Course Objectives:
The purpose of this course is to provide students with an overview of the role of nutrition in the etiology of cancer development. Introductory lectures will provide a background to the scientific principles of cancer development (i.e., mechanisms of carcinogenesis, pathology) as well as an overview of study designs for conducting research programs of diet and cancer (i.e., animal models, epidemiologic studies, use of biomarkers). This will be followed by a series of lectures and discussion sessions on the role that foods and specific components of foods play in the development and progression of cancer at specific sites, including the colon, breast, and prostate. There will also be a chance for the graduate students to present the background of their proposed grant topic and to receive feedback from the group. The course will conclude with lectures on epigenetics and conducting studies of diet and cancer in high-risk populations.

At the completion of the course, you will be able to:

1. Develop the skills to discuss, analyze and critically appraise scientific literature on nutrition and cancer.
2. Have a broad understanding of carcinogenesis, use of biological markers, nutritional epigenetics and the concept of disease heterogeneity by population subtype.
3. Design a study (*in vitro*, animal or epidemiologic) evaluating the role of a nutritional factor on cancer risk (specific site), as well as write a grant proposal on this topic.

Class Schedule:

Date	Topic	Lecturer
Jan 9	Intro/Tips on Writing a Grant	Dr. J. Kotsopoulos, PhD/Dr. D. Harney, PhD
Jan 16	Pathology of Cancer	Dr. Michelle Downes, MD
Jan 23	Biomarkers of Risk and Exposure	Dr. J. Kotsopoulos, PhD
Jan 30	*In vitro* and Animal Studies of Diet and Cancer	Dr. L. Salmena, PhD
Feb 6	Diet and Prostate Cancer	Dr. N. Fleshner, MD
Feb 13	Diet and Colon Cancer	Dr. Y. Kim, MD
Feb 20	Reading week – no class	n/a
Feb 27	Diet and Breast Cancer	Dr. Victoria Kirsh PhD.
March 6	Diet and Cancer in High-Risk Populations	Dr. J. Kotsopoulos, PhD
March 13	Nutrition and Epigenetics	Dr. M. Akbari, MD, PhD
March 20	Epidemiologic Studies of Diet and Cancer	Beatrice Boucher
March 27	Presentations	Students
April 3	Presentations	Students
April 10	Feedback on Presentations/Summing Up	Dr. J. Kotsopoulos, PhD

Lecturers:

Departmental:

Dr. Joanne Kotsopoulos	Department of Nutritional Sciences and Dalla Lana School of Public Health, Women's College Research Institute, Women's College Hospital
Dr. Young In Kim	Departments of Medicine & Nutritional Sciences, University of Toronto & St. Michael's Hospital
Beatrice Boucher	Cancer Care Ontario & Department of Nutritional Sciences

Guest:

Dr. Michelle Downes	Department of Pathology, University Health Network
Dr. Leonardo Salmena	Department of Pharmacology and Toxicology & Ontario Cancer Institute, Princess Margaret Hospital
Dr. Neil Fleshner	Department of Surgical Oncology, Princess Margaret Hospital
Dr. Mohammad Akbari	Women's College Research Institute, Women's College Hospital
Dr. Daniel Harney	Grants and Awards Editor, Office of the Vice Dean, Research & Innovation, Faculty of Medicine, University of Toronto

Reading List:

January 9: Tips for Writing a Grant

Useful URLs:

January 16: Pathology of Cancer

Required:

Any undergraduate Pathology textbook chapter on 'Neoplasia' in the General Pathology section. Robbins and Cotran "Pathologic Basis of Disease" is the most comprehensive textbook but is heavy reading. The *'Neoplasia'* chapter (Chapter 7; 9th edition) or any general pathology textbooks will cover aspects of *'Neoplasia'*.

Journal Club: - no journal club

Optional:

These articles are of interest but do not have to be read prior to the lecture. They cover some aspects of neoplasia (i.e., infectious aetiologies) that are interesting but not essential reading.

Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell. 2011 Mar 4;144(5):646-74. doi: 10.1016/j.cell.2011.02.013. Review. PubMed PMID: 21376230.

Ward PS, Thompson CB. Metabolic reprogramming: a cancer hallmark even warburg did not anticipate. Cancer Cell. 2012 Mar 20;21(3):297-308. doi: 10.1016/j.ccr.2012.02.014. Review. PubMed PMID: 22439925; PubMed Central PMCID: PMC3311998.

Gramolelli S, Schulz TF. The role of Kaposi sarcoma-associated herpesvirus in the pathogenesis of Kaposi sarcoma. J Pathol. 2015 Jan;235(2):368-80. doi: 10.1002/path.4441. PubMed PMID: 25212381.

Tsao SW, Tsang CM, To KF, Lo KW. The role of Epstein-Barr virus in epithelial malignancies. J Pathol. 2015 Jan;235(2):323-33. doi: 10.1002/path.4448. PubMed PMID: 25251730.

January 23: Biomarkers of Exposure and Risk

Required:

Vineis and Perera. Molecular Epidemiology and Biomarkers in Etiologic Cancer Research: The New in Light of the Old. *Cancer Epidemiol Biomarkers Prev* 2007;16:1954-1965.

Schatzkin and Gail. The promise and peril of surrogate end points in cacner research. *Nat Rev Cancer.* 2002;2:19-27. Review.

Tworoger and Hankinson. Collection, processing, and storage of biological samples in epidemiologic studies: sex hormones, carotenoids, inflammatory markers, and proteomics as examples. *Cancer Epidemiol Biomarkers Prev*. 2006 Sep;15(9):1578-81.

Journal club: Jan 23 – Biomarkers of Exposure and Risk: Shana Kim (guest journal club speaker)
Am J Clin Nutr. 2016 Sep;104(3):671-7. doi: 10.3945/ajcn.116.133470. Epub 2016 Jul 27. Plasma folate, vitamin B-6, and vitamin B-12 and breast cancer risk in BRCA1- and BRCA2-mutation carriers: a prospective study. Kim SJ, Zuchniak A, Sohn KJ, Lubinski J, Demsky R, Eisen A, Akbari MR, Kim YI, Narod SA, Kotsopoulos J.

Optional:
Tworoger and Hankinson. Use of biomarkers in epidemiologic studies: minimizing the influence of measurement error in the study design and analysis. *Cancer Causes Control*. 2006 Sep;17(7):889-99. Review.

January 30: *In vitro* and Animal Studies of Diet and Cancer
Required:

Journal club:

Optional:
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February 6: Diet and Prostate Cancer
Required:

Journal club:

Optional:

February 13: Diet and Colon Cancer
Required:

Journal club:

Optional:

February 20: Reading Week – no class

February 27: Diet and Breast Cancer
Required:

Journal club:

Optional:

March 6: Diet and Cancer in High-Risk Populations
Required:
Nkondjock A et al. Coffee consumption and breast cancer risk among BRCA1 and BRCA2 mutation carriers. *Int J Cancer.* 2006 Jan 1;118(1):103-7.

Kotsopoulos J, et al. Prospective study of high-risk, BRCA1/2-mutation negative women: the 'negative study'. BMC Cancer. 2014 Mar 25;14:221.

Journal club:

Optional:
Kotsopoulos J, Kim YI, Narod SA. Folate and breast cancer: what about high-risk women? *Cancer Causes Control.* 2012 Sep;23(9):1405-20.

Kotsopoulos J et al. Changes in body weight and the risk of breast cancer in BRCA1 and BRCA2 mutation carriers. *Breast Cancer Res.* 2005;7(5):R833-43.

Kotsopoulos J, Narod SA. Towards a dietary prevention of hereditary breast cancer. *Cancer Causes Control.* 2005 Mar;16(2):125-38.

March 13: Nutrition and Epigenetics
Required:

Journal club:

Optional:

March 20: Epidemiologic Studies of Diet and Cancer
Required:

Journal club:

Optional:

April 10: Summing up/last class

Outcome Measures and Grading Scheme (100%)

1. Class participation (15% of total grade)

The course will be conducted as weekly lectures with class discussion. Active learning through class participation and discussion are an important component of this class and students are expected to attend and participate in all the classes. **There are no wrong questions!!**

2. Journal Club (15% of total grade)

You (and a fellow student if numbers permit) will lead a journal club session (i.e., *critical appraisal* of a scientific article) at the end of the selected session. You will prepare a 10 minute presentation on a pre-determined scientific article, and lead the discussion for the remaining 15-20 minutes. It is expected that you will prepare questions for your audience about the study design choices, as well as challenges you encountered while reading the paper. Please, electronically send your Power Point presentation to the instructor (Joanne Kotsopoulos) before class or bring to class on a USB key. Each student is marked separately based on their level of preparedness and quality of their answers to questions.

Your assignment should follow the guidelines below:

1. Brief introduction of the topic – including some biological background.
2. Why is this study important? What gap in the literature does it fill (or what the authors claim it does?
3. Present the method section with a focus on the study design and analytic strategies.
4. What are the most important results?
5. Significance – Is the study important? Why/why not? What's next?
6. Be prepared with questions for your audience – even some for which you do not have answers!
7. Additional points: Pay attention to the quality of your slides. Here, I do not refer to "how pretty" these can be but rather how "readable" they are e.g., not too much information per slide, font that can be read by the audience. Make sure that each slide has a purpose. The text on the slide should be concise i.e., present the most relevant information but be ready to discuss the details during the discussion if necessary. The presentation should not last more than 10 minutes (excluding interruption time for questions); 10-15 slides should be sufficient.

A journal club presentation is a bit like a critical appraisal with the exception that you are not expected to be an expert on the topic that you are presenting. This means that you are not only allowed to ask questions to your audience about what you did not understand, but you are encouraged to do so! **Now, have fun preparing it!**

Journal Club - Marking scheme

1. Brief introduction of the topic – including some biological background. (/1)
2. Rationale (why is this study important)? What gap in the literature does it fill (or what the authors claim it does? (/2)
3. Present the method section with a focus on the study design and analytic strategies. (/2)
4. What are the most important results? (/2)
5. Significance – Is the study important? Why/why not? What's next? (/3)
6. Be prepared with questions for your audience – even some for which you do not have answers! (/2)
7. Leading class discussion (/2)
8. Overall presentation (pay attention to the quality of your slides). (/1)

Journal Club Topics and Presenters:

Jan 30 – *In vitro* and Animal Studies of Diet and Cancer

Feb 6 – Diet and Prostate Cancer

Feb 13 – Diet and Colon Cancer

Feb 27 – Diet and Breast Cancer

March 6 – Epidemiologic Studies of Diet and Cancer

March 27 – High Risk Populations

April 3 – Epigenetics

Mock Grant Assignment

There will be two components to this assignment:
1) the grant proposal presentation and
2) the final written grant proposal.

Details for each section are outlined below.

Modified call from the Canadian Cancer Society Research Institute – Innovation Grants and the National Cancer Institute – Program Project Grants

Purpose
The goal of this grant program is to support unconventional concepts, approaches or methodologies to address problems in nutrition cancer research. Innovation projects will include elements of creativity, curiosity, investigation, exploration and opportunity. Successful projects may involve higher risk ideas, but will have the potential for "high reward", i.e. to significantly impact our understanding of the relationship between diet and cancer and to generate new possibilities to combat the disease by introducing novel ideas into use or practice. This grant program will fund research into the effects of diet, nutrition, body fatness and physical activity on cancer.

This Funding Opportunity Announcement encourages research grant applications from institutions/organizations that propose to examine associations between nutrition and cancer development in humans, animals or *in vitro* models. The goal of this program announcement is to stimulate a broad range of research on the role of nutrition in the development, prevention, and treatment of cancer. Study designs may include biomedical research, epidemiologic approaches, and intervention studies.

Priority will be given to studies that explore areas of uncertainty in the links between food, nutrition, physical activity, body fatness and cancer where the results have a reasonable prospect of adding important information to the overall body of evidence.

Read more:
http://cancer.ca/research/Grants%20and%20Awards/Current%20funding%20opportunities.aspx?sc_lang=en#ixzz2fMMM1Hcl

http://deais.nci.nih.gov/foastatus/?nt=P

3. Grant Proposal Oral Presentation (20% of final grade)

Students will present the background, rationale, specific objectives, hypotheses and proposed methodology for their mock grant proposal evaluating the relationship between a specific nutritional factor and cancer risk. The overall goal is to provide an overview of your proposed grant topic and to receive feedback from the class and instructor. This is a work *'in-progress'* and the feedback is meant to help you during the writing phase of the final mock grant proposal. Ensure to approach a topic that is currently NOT your specific area of research and/or expertise.

The presentation should:

a. Describe the rationale for the proposed study including literature review of the evidence and context as to why the study is important.
b. Outline the specific objectives.
c. Provide an overview of the study design and methodology.
d. Questions you may have for the group to aid in the development of your grant.

The presenter will receive feedback on the study proposal from the instructor and the students in the class that will help finalize the objectives of their grant proposal during the assigned date.

Proposal Presentation - Marking scheme

1. Adequate literature review and background knowledge of the topic of interest as well as insight. (/4)
2. Sound rationale: Why is this study important? How will it contribute to the current knowledge? (/5)
3. Specific aims and objectives reasonable for scope of the grant call. (/3)
4. Well-planned study design, methodology. (/4)
5. Discussion and engagement of audience (/2).
6. Overall quality of presentation (/2)

4. Written Mock Grant Proposal (50% of final grade):

A written grant proposal based on what was proposed in the oral presentation above will be submitted according to a modified call from the Canadian Cancer Society Research Institute (CCSRI). This will entail a short 4 – 5 page grant proposal.

A. Document Format

The proposal must be clear and legible and conform to the following guidelines:

- Use a font size of 12 point, black type.
- Use Times New Roman font type.
- Maximum of six lines per inch. No condensed/narrow fonts, type, or spacing.
- Insert a margin of 2 cm (3/4 inch) - minimum - around the page.
- Observe page limitations, additional pages may NOT be added unless specified.
- Use only letter size (21.25 X 27.5 cm / 8.5" X 11") white paper/background for all attachments.
- Photo-reduce the supporting documents if the originals are larger than (21.25 X 27.5 cm / 8.5" X 11").

B. Grant Components

1. Public Summary of the Project ~ 2-3 sentences

Summarize the proposal in simple, easy-to-understand, non-technical language, e.g. "Dr X is working to…" or "Dr X will be studying…"

2. Scientific Abstract ~ 1 page maximum

Provide a detailed summary of your research project, stating the problem to be investigated, the objectives of the investigation, a brief indication of the methodology to be used, as well as the significance of the research to cancer.

3. Keywords/Technical Terms ~10 words maximum

Provide up to a maximum of ten specific keywords or descriptive technical terms/methodologies that best describe the scientific and technical aspects of your project.

4. Research Proposal ~ 5 pages single spaced maximum

Provide a scientific proposal that includes the following components:

A. Background Data

Review of relevant literature, relevant preliminary data and/or consultations that led to the development of this project

B. Rationale for the Project

Explain why this project is being proposed and what you hope to achieve and demonstrate how the project builds upon existing knowledge and/or expertise.

C. Hypothesis/Research Question

Identify the key concept(s) or correlation(s) to be tested or the research question(s) to be answered.

D. Objectives
Identify a limited number of specific objectives for the project that are concise and measurable.

E. Study Design and Research Methodology
Describe the experimental design, methods and data analysis to be used.

F. Research Team
Describe which member of the research team will be responsible for which aspect of the project, including a rationale for their inclusion in the project and a description of the research environment where the work will take place.

G. Impact
Describe the relevance of the grant to the mission and priorities of the agency. How will the findings impact prevention strategies, disease risk, influence healthcare systems and/or direct patient care?

5. References – no page limit
Please attach reference list directly after the proposal.

6. Appendix – no page limit
Include any relevant figures, tables, charts, questionnaires, etc. in an appendix.

7. Budget and Budget Justification – table (Appendix 1) and 3-page maximum justification (Appendix 2)

Requests for budgets up to 2 years will be considered in this competition for a total of **$200,000.**

a) Budget – please complete the attached table for Year 1 and Year 2 of the grant.

See attached template.

b) Budget Justification – Attach a detailed justification for all line items requested in this budget category in the first and second year. Requested items must be justified to allow the grants panel to evaluate. It is not necessary to repeat the narrative for each subsequent year unless there are substantial differences (see attached sample *Budget Justification* for guidance).

Example of salary support
Summer students – $1,500 per month
MSc/PhD students – $19,500 per year
Postdoctoral fellows – $42,915 per year

8. Common Scientific Outline (CSO)
Select a maximum of 3 codes which best describe the research. Full details of the Common Scientific Outline can be found at the International Cancer Research Portfolio website (https://www.icrpartnership.org/CSO.cfm).

Mock Grant Proposal - Marking scheme

1. Public Summary: appropriate for lay audience? what is key message? (/3)
2. Abstract: appropriate scientific abstract including key aspects of the study (i.e., rationale, objectives, methodology, impact) (/7)
3. Keywords: relevant, comprehensive (/1)
4. Proposal (/30): each section out of 5 marks
    i. Introduction
    ii. Rationale
    iii. Objectives
    iv. Methodology
    v. Team
    vi. Impact
5. References (/1)
6. Budget (including justification): adequate, appropriate, well-described (/5)
7. CSO codes: relevant, comprehensive (/1)
8. Overall style, grammar, editing (/2)
9. Bonus: appendices, figures, tables (must be relevant and not just fluff!) (+1)

Appendix 1

Budget Template – please feel free to modify as necessary.

Year	2014	2015	TOTAL
Budget Item			
1. Supplies and Expenses			
Total for Supplies and Expenses			
2. Salaries and Wages			
Total for Salaries and Wages			
3. Equipment			
Total for Equipment			
TOTAL REQUESTED FUNDING			

Appendix 2:

BUDGET JUSTIFICATION

A. PERSONNEL JUSTIFICATION

TBD, Research Assistant, (1.0 FTE), funds are requested for one full-time research assistant in years 1, 2 and 3. This individual has earned a Master's in Public Health degree. She will oversee all aspects of this study including administering the supplemental questionnaire, following up with subjects who have not returned completed study materials and coordinating biological sample shipment of specimens for plasma folate quantification. She will be responsible for all data entry, database management and will work closely with the PI and collaborating centers in Canada and Poland. **Years 1-2.**

Year 1: $50,000 + (0.27%benefits) x 0.5FTE = $31,750
Year 2: $50,000 + (0.27%benefits) + 3% increase x 0.5FTE = $32,703

TOTAL = $XX

TBD, Research Assistant, (1.0 FTE), funds are requested for one full-time research assistant in Poland for years 1 and 2. This individual has a Bachelor's of Science degree. Her primary role will be questionnaire administration and follow-up, as well as sample shipment for the Polish participants. She will be responsible for all data entry and will work closely with the PI, research assistant in Canada and the collaborating centers in Poland. **Years 1-2.**

Year 1: $50,000
Year 2: $50,000

TOTAL = $100,000

TBD, Summer Student, (1.0 FTE), funds are requested for an undergraduate summer student with an interest in nutrition and cancer epidemiology. S/he will work with the Principal investigator and will take a lead in subject recruitment, data entry, and the interim statistical analyses. **Years 1-2**.

Year 1: $10.25/hr + (0.11% in lieu of benefits) x 37.5hrs/week x 12 weeks = $5,120
Year 2: $10.25/hr + (0.11% in lieu of benefits) x 37.5hrs/week x 12 weeks = $5,120

TOTAL = $10,240

TBD, Research Technician, (0.15 FTE), funds are requested for 0.15FTE of a research technician in years 1 and 2. This individual has a Master's of Science degree and more than 10 years experience in analyses of folate quantification. Her primary role will be folate level determination in the laboratory of Dr. Young-In Kim. **Years 1 and 2.**

Year 1: **$50,000 + (0.27%benefits) x 0.15FTE = $9,525**
Year 2: **$50,000 + (0.27%benefits) x 0.15FTE + 3% increase = $9,810**

TOTAL = $19,335

TBD, PhD, Statistician, (0.25 FTE), will be responsible for quality control of the data and data editing. He has expertise in the area of cancer genetics and statistics and has been associated with our projects at Women's College Hospital for over ten years and is highly experienced. Further, Dr. Sun has been involved in prior analyses specifically using data from the *BRCA* registry. He will work closely with the PI and applicants to perform interim and final analyses of the data. He will be in regular contact with the research assistants and investigators. **Years 1 and 2.**

Year 1: **$72,000 + (0.27% benefits) x 0.25FTE = $22,860**
Year 2: **$72,000 + (0.27% benefits) x 0.25FTE + 3% increase = $23,545**

TOTAL = $46,405

TOTAL PERSONNEL COSTS = $

B. NON-PERSONNEL JUSTIFICATION

1. Office Supplies, Stationary and Printing
Miscellaneous office and computer supplies, copy paper, file folders, writing implements, toner cartridges. Stationary and printing will be required for letters to subjects, consent forms, and questionnaires.

$500/year * 3 years = $1,500

2. Postage
Supplemental questionnaires will be mailed to all eligible subjects (n = 500) in addition to return postage being included on the envelopes to be returned by the subjects (n = 500). Each envelope will require $1.50 in postage + tax (2.3%HST) for mailing plus return postage. It is anticipated that 15% of the study packages will be re-mailed to non-responders. Costs for postage in Poland is not requested from this grant.

1,075 x $1.50 + tax (2.3%HST) = $1,650

3. FedEx Shipment
Funds are requested to ship ~1,000 plasma samples from Poland to Toronto for plasma folate analysis.

$1,800

4. Subject Compensation
Each participant will be compensated $20 for participating in the research study.

$20/subject * 500 = $10,000

5. Dissemination of Research Results
Funds are requested for the dissemination of research findings through publications (i.e., publication expenses). This includes all aspects of manuscript preparation and correspondence with journals such as printing fees, postage, and courier. We will also consider submitting manuscripts to the open access journals which charge fees of approximately $1,000-3,000 per publication.

$2,000

6. Travel
Results of this project will be presented at scientific meetings such as the American Association for Cancer Research. Costs are requested for one investigator to travel to a conference and will cover airfare, conference registration fees, food allowance, and accommodation. **Years 1-3.**

$2,500 * 3 = $7,500

7. Laboratory Assays:
Plasma folate levels:
Plasma folate will be measured in the laboratory Dr. Young In Kim (Co-Applicant) at the Keenan Research Centre, St. Michael's Hospital (Toronto, Canada) using a standard microbiological microtiter plate assay [1]. **Years 1-3.**

$30 per sample * 1,500 samples + 200 (10% QC samples) = $51,000

TOTAL NON-PERSONNEL COSTS = $

TOTAL GRANT COSTS = $

REFRENCES

1. Tamura T. Microbiological assay of folate. In: Piccairo M, Stokstad R, Gregory J, eds. Folic acid metabolism in health and disease. New York: Wiley-Liss; 1990:121-37.