

GERO 498: Nutrition, genes, longevity and diseases

Maymester Spring/Summer 2020

4 Units

Time: 2:00pm - 4:50pm California time OR 9-12 AM California time (See specific classes)

Room: All Lectures will be held online using the Zoom application

Course Instructors:

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Office Hours: By appointment

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Office hour: by appointment on Zoom (please schedule a meeting by email)

Please note that E-mail is the best way to be sure to contact the instructors

Course Description

This course is intended to teach students about the important role of nutrition and genes and the impact each has on longevity and diseases, particularly diseases related to aging. This course is unique in that it approaches these subjects through a traditional didactic approach as well as a “on location” approach to learning. This is accomplished by allowing students to have the opportunity to learn in an environment that has proven to be conducive to healthy aging. Students will be encouraged to observe and compare the lifestyle choices people make through their activities of daily living and dietary choices. Students will also be strongly encouraged to live as much as possible the Mediterranean life style with emphasis on the Mediterranean diet and an active lifestyle. In particular the class will try to emphasize the Mediterranean diet and life style of 50-100 years ago, which is still adopted by the older population but often not by younger individuals. For many students, this month-long immersion in the Mediterranean life style, could have a life-long impact.

In the classroom students will examine the effect of nutrition and genes modulated by nutrients on aging and life span in simple organisms and humans. The course will provide an introduction to the biology of aging and to the mechanisms for the extension of the healthy life span and the prevention of age-related diseases. The course will also describe the effect of common but also extreme diets and of diets adopted by very long-lived populations from around the world on aging and diseases. Specific populations with unusually long life spans will be examined as part of the course. Finally the course will discuss the role of diets, dietary restriction and fasting in the treatment of diseases with emphasis on cancer, diabetes, cardiovascular and neurodegenerative diseases. Students will be given actual case reports from doctors and/or clinical trials describing the translation of these approaches to disease prevention and treatment. For example, they will learn about the effects of fasting on the side effects caused by chemotherapy and they will see the effects of dietary restriction on hypertension and diabetes. Students will be responsible for more in-depth study of selected topics through assigned readings.

Prerequisite

It is recommended that students have had 1 prior undergraduate-level courses in biology. However, students without this background, can still perform well in the class with the appropriate effort.

Course Objectives

By the conclusion of the course, students are expected to be able to:

- 1) Understand the fundamental biology underlying aging and age-related diseases.
- 2) Understand the role of different dietary components on gene expression, cell function and protection, aging and diseases.
- 3) Describe the type of diets that can extend the healthy life span and why.
- 4) Understand how biogerontology can be applied to disease treatment and its role in medicine.
- 5) Have a general understanding of the role of different types of exercise on physiology, aging and diseases.
- 6) Understand how to apply evolutionary and comparative biology approaches to the optimization of health, disease prevention and treatment.
- 7) Understand the differences in the diet and lifestyle of people from Mediterranean area and Americans. Students should be able to identify the differences that are known to affect aging and diseases.

Online class organization

All lectures are held on line using the USC Zoom application. During lectures, students attendance in class is mandatory (see “participation points”). Students that are following the course from different countries or time zones could be eventually exempted on a case by case basis, **prior communication of their current location**. Lecture recordings will be accessible to all students.

Online Course Materials:

Course materials and announcements will be posted on the Blackboard website. Your USC e-mail username and password will allow you to access the secure site: <https://blackboard.usc.edu> (if you have trouble with Blackboard, please contact blackboard@usc.edu)

Students are responsible for checking additional postings and announcements on Blackboard website on a daily basis.

Students with Disabilities (the information below was provided by the office of the Provost)

“Any student requesting academic accommodations based on a disability is required to register with Disability Services and Programs (DSP) each semester. A letter of verification for approved accommodations can be obtained from DSP. Please be sure that the letter is delivered to any of the Instructors as early in the semester as possible. DSP is located in on campus in STU 301, and is open from 8:30 a.m. - 5:00 p.m., Monday through Friday. The phone number for DSP is (213) 740-0776.”

Statement on Academic Integrity

USC seeks to maintain an optimal learning environment. General principles of academic honesty include the concept of respect for the intellectual property of others, the expectation that individual work will be submitted unless otherwise allowed by an instructor, and the obligations both to protect one’s own academic work from misuse by others as well as to avoid using another’s work as one’s own. All students are expected to understand and abide by these principles. *Scampus*, the Student Guidebook, contains the Student Conduct Code in Section 11.00, while the recommended sanctions are located in Appendix A: <http://www.usc.edu/dept/publications/SCAMPUS/gov/>. Students will be referred to the Office of Student Judicial Affairs and Community Standards for further review, should

there be any suspicion of academic dishonesty. The Review process can be found at:
<http://www.usc.edu/student-affairs/SJACS/>.

Textbook

None. Articles will be used instead of the textbook and distributed at the beginning of the class. Students will have to become familiar with pubmed searches and with identifying and downloading articles

Full text journals

Many full text journals are available to free to USC students at:
http://www.usc.edu/e_resources/hsl/lists/journal_A.php

If signing in from outside USC, the USC username and password used for emails will be required.

Student Evaluation

Students will be evaluated on the basis of:

- 1) Midterm (45%)
- 2) Final (45%)
- 3) Attendance and participation (10%)

Gero 498 CLASS SCHEDULE

WEEK 1 class meets remotely

Tuesday, May 19: Remotely. 2-4:50 pm. Valter Longo, Introduction to Aging.

Reading: In Northern Italy, the Agony of Aging not so Gracefully. New York Times Sept. 22 2006.

<http://www.nytimes.com/2006/09/22/world/europe/22genoa.html>

Readings:

<http://www.sciencemag.org/content/328/5976/321/suppl/DC2>

(a slide show introduction to aging by *Science* magazine)

Extending the Healthy Life span: from yeast to humans. Fontana, L, Partridge, L., Longo VD. *Science*, April 16, 328, 321-6.

Wednesday, May 20 Aging and pollution. Remotely, 2-4:50 pm. Caleb Finch
Guest lecturer

Readings:

Finch CE, Crimmins EM. **Constant molecular aging rates vs. the exponential acceleration of mortality.**

Proc Natl Acad Sci U S A. 2016 Feb 2;113(5):1121-3. doi: 10.1073/pnas.1524017113. Epub 2016 Jan 20.

Trumble BC, Finch CE. **THE EXPOSOME IN HUMAN EVOLUTION: FROM DUST TO DIESEL.**

Q Rev Biol. 2019 Dec;94(4):333-394. doi: 10.1086/706768.

Wann LS, Narula J, Blankstein R, Thompson RC, Frohlich B, Finch CE, Thomas GS. **Atherosclerosis in 16th-Century Greenlandic Inuit Mummies.**

JAMA Netw Open. 2019 Dec 2;2(12):e1918270. doi: 10.1001/jamanetworkopen.2019.18270.

Longo VD, Finch CE. **Evolutionary medicine: from dwarf model systems to healthy centenarians?**

Science. 2003 Feb 28;299(5611):1342-6.

Finch CE, Morgan TE. **Developmental Exposure to Air Pollution, Cigarettes, and Lead: Implications for Brain Aging.**

Annual Review of Developmental Psychology Volume 2 (2020)

Saenz J, Finch CE. **Air Pollution, Aging and Lifespan: Air Pollution Inside and Out Accelerates Aging.**

Encyclopedia of Biomedical Gerontology, Volume 1, 2020, 203–213

Finch CE. **Organisms with negligible senescence.** MolBiolAging 2015

Beltrán-Sánchez H, Austad SN, Finch CE. **Comment on "The plateau of human mortality: Demography of longevity pioneers".**

Science. 2018 Sep 28;361(6409). pii: eaav1200. doi: 10.1126/science.aav1200.

Burstein SM, Finch CE. **Longevity examined: an ancient Greek's very modern views on ageing.**

Nature. 2018 Aug;560(7719):430. doi: 10.1038/d41586-018-05986-1.

Thursday, May 21:

1) **Introduction to the biology of aging (continued), theories and aging mechanisms at the molecular, and cellular level.** Valter Longo. Remotely, 2-4:50 pm.

2) **Aging in microorganisms.** Valter Longo

Readings:

<http://www.sciencemag.org/content/328/5976/321/suppl/DC2>

(a slide show introduction to aging by *Science* magazine)

Extending the Healthy Life span: from yeast to humans. Fontana, L, Partridge, L., Longo VD. *Science*, April 16, 2010, 328, 321-6.

Longo, VD, Mitteldorf J., and Skulachev, V. Programmed and Altruistic Aging. *Nature Reviews Genetics* 2005, 6:866-872.

Sci Am. 2010 Sep;303(3):42-9. Why can't we live forever? Kirkwood T

Readings: Replicative aging in yeast: the means to the end. Steinkraus KA, Kaeberlein M, Kennedy BK *Annu Rev Cell Dev Biol.* 2008;24:29-54. Review,

Fabrizio P, Longo VD. The chronological life span of *Saccharomyces cerevisiae*. *Methods Mol Biol.* 2007;371:89-95.

Extending the Healthy Life span: from yeast to humans. Fontana, L, Partridge, L., Longo VD. *Science*, April 16, 2010, 328, 321-6.

Friday, May 22 : Christian Pike. Aging and Alzheimer's Disease. Remotely, 2-4:50 pm.

Readings

The Amyloid Hypothesis of Alzheimer's Disease: Progress and Problems on the Road to Therapeutics

John Hardy and Dennis J. Selkoe

Science **297**, 353 (2002);

DOI: 10.1126/science.1072994

When neurogenesis encounters aging and disease

Orly Lazarov¹, Mark P. Mattson², Daniel A. Peterson³, Sanjay W. Pimplikar⁴ and Henriette van Praag². *Trends in Neurosciences*, December 2010, Vol. 33, No. 12.

Microglia: scapegoat, saboteur, or something else? Aguzzi A, Barres BA, Bennett ML. *Science*. 2013 Jan 11;339(6116):156-61.

WEEK 2 class meets remotely

Monday, May 25: NO CLASS MEMORIAL DAY

Tuesday, May 26.

Sugar, obesity and diseases. Remotely, 2-4:50 pm. Michael Goran

“Role of Dietary Sugars in Obesity and Related Metabolic Diseases”

Michael Goran is a Professor of Preventive Medicine, Physiology and Biophysics He is the founding Director of the USC Childhood Obesity Research Center and holds the Dr Robert C and Veronica Atkins Endowed Chair in Childhood Obesity and Diabetes.

Dietary consumption patterns have shifted during the course of prior generations towards greater consumption of sugars, sugary beverages and fructose and an earlier introduction of these sugars to infants. These changes have important implications in the development of obesity and risk of metabolic diseases including type 2 diabetes, cardiovascular disease and non alcoholic fatty liver disease (NAFLD). These dietary shifts are also likely to have a greater impact during infancy and childhood because infants and children are also undergoing growth and development. Furthermore, increased dietary sugars have a greater impact on obesity and metabolic risk in certain segments of the population including Hispanics, those who are already obese, and in the case of NAFLD, those carrying

the PNPLA3 genotype. In this lecture, I will review emerging studies indicating that consumptions of sugars and sugar sweetened beverages is beginning to occur early in life and this early life exposure is associated with increased risk of obesity by early childhood. In addition, I will review the evidence linking dietary intakes of sugars, especially fructose with altered metabolism and early obesity in animal models and limited human studies. I will review the evidence suggesting that high fructose exposure during critical periods of development of the fetus, neonate and infant can act as an obesogen by affecting lifelong neuroendocrine function, appetite control, feeding behaviour, adipogenesis, fat distribution and metabolic systems. These changes ultimately favour the long-term development of obesity and associated metabolic risk. This lecture will be presented by Dr Michael I Goran from the Keck School of Medicine. Dr Goran is Professor of Preventive Medicine, Co-Director of the USC Diabetes and Obesity Research Institute and the holder of the Atkins Endowed Chair in Childhood Obesity and Diabetes.

Suggested Reading

1. Ebbeling CB, Feldman HA, Chomitz VR, Antonelli TA, Gortmaker SL, Osganian SK, et al. A Randomized Trial of Sugar-Sweetened Beverages and Adolescent Body Weight. *N Engl J Med*. 2012. Epub 2012/09/25.
2. Davis JN, Whaley SE, Goran MI. Effects of Breastfeeding and Low Sugar-Sweetened Beverage Intake on Obesity Prevalence in Hispanic Toddlers. *Am J Clin Nutr*. 2012;95(1):3-8. Epub 2011/12/16.
3. Yang Q, Zhang Z, Gregg EW, Flanders WD, Merritt R, Hu FB. Added Sugar Intake and Cardiovascular Diseases Mortality among Us Adults. *JAMA Intern Med*. 2014. Epub 2014/02/05.
4. Park S, Pan L, Sherry B, Li R. The Association of Sugar-Sweetened Beverage Intake During Infancy with Sugar-Sweetened Beverage Intake at 6 Years of Age. *Pediatrics*. 2014;134 Suppl 1:S56-62.
5. Goran MI, Dumke K, Bouret SG, Kayser B, Walker RW, Blumberg B. The Obesogenic Effect of High Fructose Exposure During Early Development. *Nat Rev Endocrinol*. 2013. Epub 2013/06/05.
6. Goran MI, Ventura EE. Genetic Predisposition and Increasing Dietary Fructose Exposure: The Perfect Storm for Fatty Liver Disease in Hispanics in the U.S. *Dig Liver Dis*. 2012;44(9):711-3.

Wednesday, May 27: Intermittent Fasting, Therapeutic Fasting, and Ketogenic Diets.

Raffaella Ghittoni, PhD. Remotely, 2-4:50 pm.

An introduction to: 1) The different and most popular intermittent fasting practices including alternate day fasting, 16:8, 5:2 and alternate day fasting, 2) Therapeutic fasting, as practiced by in patient clinics, 3) Ketogenic diets

Longo VD, Mattson MP. Fasting: Molecular Mechanisms and Clinical Applications. *Cell Metab.* 2014 Feb. 4;19(2):181-192. doi 10.1016 PMID:24440038

Mattson MP, Allison DB, Fontana L, Harvie M, Longo VD, Malaisse WJ, Mosley M, Notterpek L, Ravussin E, Scheer FA, Syefried TN, Varady KA, Panda S. Meal frequency and timing in health and disease. *Proc Natl Acad Sci USA* 2014 Nov 25; 111(47); 16647-53. Doi PMID:25404320 PMCID:PMC4250148

Longo VD, Panda S. Fasting, Circadian Rhythms, and Time-Restricted Feeding in Healthy Lifespan. *Cell Metab.* 2016;23(6):1048-59. doi: 10.1016/j.cmet.2016.06.001. PubMed PMID: 27304506.

Optimizing glycemic control in type 2 diabetic patients through the use of a low-carbohydrate, high-fat, ketogenic diet: a review of two patients in primary care. Rallis S. *Diabetes Metab Syndr Obes* 2019 Mar 5;12:299-303. doi: 10.2147/DMSO.S195994. eCollection 2019.

Thursday May 28

Genetics of Aging in mice and humans. Valter Longo. Remotely, 2-4:50 pm.

Yan L et al 2007 Type 5 adenylyl cyclase disruption increases longevity and protects against stress. *Cell.* 130:247-58.

Extending the Healthy Life span: from yeast to humans. Fontana, L, Partridge, L., Longo VD. *Science*, April 16, 2010, 328, 321-6.

Growth hormone receptor deficiency is associated with a major reduction in pro-aging signaling, cancer and diabetes in humans. Guevara-Aguirre J, Balasubramanian P, Guevara-Aguirre M, et al. *Science Transl Med.* 2011 Feb 16;3(70):

Friday, May 29: Hanno Pijl, MD, PhD. University of Leiden, Holland **CLASS AT 9-12 AM California Time**

Dr Hanno Pijl, MD, PhD is an endocrinologist and a professor of Diabetology at the Department of Internal Medicine of the Leiden University Medical Centre in Leiden, The Netherlands. He is also a member of the Dutch Health Council (“Gezondheidsraad”), Standing Committee on ‘Nutrition’.

First part

Nutrition and chronic disease: an evolutionary perspective

The first part of my lecture will cover the changes our food intake went through over millions of years, the mismatch between what we eat and our physiology and its impact on the pathogenesis of chronic disease.

Second part

Calorie restriction and the management of (type 2) diabetes mellitus

In the second part of my lecture I will discuss the pathophysiology of the metabolic syndrome and type 2 diabetes.

Readings

- a) Effects and clinical potential of very-low-calorie diets (VLCDs) in type 2 diabetes. Scott Baker *, George Jerums, Joseph Proietto diabetes research and clinical practice 85 (2009) 235–242
- b) Intermittent fasting vs daily calorie restriction for type 2 diabetes prevention: a review of human findings ADRIENNE R. BARNOSKY et. al Translational Research Volume 164, Number 4
- c) Origins and evolution of the Western diet: health implications for the 21st century^{1,2} Loren Cordain, S Boyd Eaton, et al. Am J Clin Nutr 2005;81:341–54.

WEEK 3 class meets remotely

Monday, June 1

Cancer and aging: from the mechanisms of tumorigenesis, to standard treatment to anti-aging approaches for its prevention and treatment. Valter Longo. Remotely, 2-4:50 pm.

Readings:

- a. Case reports from Safdie et al. Fasting and Cancer Treatment in Humans. A case series report. *Aging*. 2009, 1(12): 988-1007
- b. Hanahan and Weinberg. The Hallmarks of Cancer. *Cell*, Vol. 100, 57–70, January 7, 2000.
- c. Raffaghello, L. , Lee, C. , Safdie, F.M., Wei, M., Madia, F. , Gonidakis, S. Bianchi, G. , and Longo V.D. Starvation-dependent Differential Stress Resistance Protects Normal but not Cancer Cells Against High Dose Oxidants/Chemotherapy. *PNAS*, 2008 Mar 3.
- d. Longo VD., Lieber, M., and Vijg, J. Turning Anti-aging genes against Cancer. *Nature Reviews Molecular Cell Biology*, Nov. 2008, 902.

Tuesday June 2nd

MIDTERM

MIDTERM COVERS UP TO MONDAY LECTURE ON GENETICS OF AGING IN MICE AND HUMANS

Wednesday, June 3

Dietary restriction, Exercise in aging and cardiovascular risk factor/diseases. Valter Longo. Remotely, 2-4:50 pm.

Readings:

Exercise, aging and diseases Exercise and longevity. Studies in rats. Holloszy JO. J Gerontol. 1988 Nov;43(6):B149-51. Review.

Biological Mechanisms of Physical Activity in Preventing Cognitive Decline.

Lista et al *Cell Mol Neurobiol* (2010) 30:493–503.

Aging, training, and the brain: A review and future directions *Neuropsychol Rev*. 2009 December ; 19(4): 504–522.

Habitual exercise and vascular ageing. Seals et al. *J Physiol* 587.23 (2009) pp 5541–5549

Thursday, June 4:

Nutrition, dietary restriction, aging and diseases: Parts 1 and 2. From the fundamental role of various nutrients on aging in model organisms and mammals, to the Mediterranean diet to the diets of long-lived and short-lived populations from around the world and their effect on life span and diseases. Valter Longo. Remotely, 2-4:50 pm.

Readings:

Colman RJ, Anderson RM, Johnson SC, Kastman EK, Kosmatka KJ, Beasley TM, Allison DB, Cruzen C, Simmons HA, Kemnitz JW, Weindruch R. Caloric restriction delays disease onset and mortality in rhesus monkeys. *Science*. 2009 Jul 10;325(5937):201-4

Caloric restriction reduces age-related and all-cause mortality in rhesus monkeys *Nat Commun*. 2014 Apr 1;5:3557. Colman RJ1, Beasley TM2, Kemnitz JW3, Johnson SC4, Weindruch R4, Anderson RM4.

Impact of caloric restriction on health and survival in rhesus monkeys from the NIA study . *Nature*. 2012 Sep 13;489(7415):318-21. Mattison JA1, Roth GS, Beasley TM, Tilmont EM, Handy AM, Herbert RL, Longo DL, Allison DB, Young JE, Bryant M, Barnard D, Ward WF, Qi W, Ingram DK, de Cabo R.

Extending the Healthy Life span: from yeast to humans. Fontana, L, Partridge, L., Longo VD. *Science*, April 16, 328, 321-6

Longo VD, Fontana L. Calorie restriction and cancer prevention: metabolic and molecular mechanisms. *Trends Pharmacol Sci*. 2010 Feb;31(2):89-98

Low-carbohydrate diets and all-cause and cause-specific mortality: two cohort studies. Fung TT, van Dam RM, Hankinson SE, Stampfer M, Willett WC, Hu FB. *Ann Intern Med*. 2010 Sep 7;153(5):289-98

Vegetarian Dietary Patterns Are Associated With a Lower Risk of Metabolic Syndrome. Rizzo et al. *Diabetes Care* 34:1225–1227, 2011

Association between the Mediterranean diet and cancer risk: a review of observational studies. Verberne L, Bach-Faig A, Buckland G, Serra-Majem L. [Nutr Cancer](#). 2010;62(7):860-70

Am J Clin Nutr. 2010 Nov;92(5):1189-96. Epub 2010 Sep 1.
Accruing evidence on benefits of adherence to the Mediterranean diet on health: an updated systematic review and meta-analysis. Sofi F, Abbate R, Gensini GF, Casini A.

Olive Oil and Cardiovascular Health María-Isabel Covas. *Cardiovasc Pharmacol* Volume 54, Number 6, December 2009

Exp Gerontol. 2004 Sep;39(9):1423-9. Identification of a geographic area characterized by extreme longevity in the Sardinia island: the AKEA study. Poulain M, Pes GM, Grasland C, Carru C, Ferrucci L, Baggio G, Franceschi C, Deiana L.

Caloric Restriction, the Traditional Okinawan Diet, and Healthy Aging
The Diet of the World's Longest-Lived People and Its Potential Impact on Morbidity and Life Span BRADLEY J. WILLCOX^{1,2} et al *Annals of the New York Academy of Sciences* Volume 1114, Healthy Aging and Longevity: Third International Conference pages 434–455, October 2007.

Longo VD, Mattson MP. Fasting Molecular Mechanisms and clinical applications. *Cell Metab*. 2014 Feb 4;19(2):181-92. 2014 Jan 16.

Primary prevention of cardiovascular disease with a Mediterranean diet.
Estruch R et al N Engl J Med. 2013 Apr 4;368(14):1279-90. doi: 10.1056/NEJMoa1200303.
Epub 2013 Feb 25.

Association of nut consumption with total and cause-specific mortality. N Engl J Med. 2013 Nov 21;369(21):2001-11. doi: 10.1056/NEJMoa1307352. Bao Y1, Han J, Hu FB, Giovannucci EL, Stampfer MJ, Willett WC, Fuchs CS.

Low protein intake is associated with a major reduction in IGF-I, cancer and overall mortality in the 65 and younger but not older population. Levine ME, Suarez JA, Brandhorst S, Balasubramanian P, Cheng CW, Madia F, Fontana L, Mirisola MG, Guevara-Aguirre J, Wan J, Passarino G, Kennedy BK, Wei M, Cohen P, Crimmins EM, Longo VD. *Cell Metab*. 2014 Mar 4;19(3):407-17. doi: 10.1016/j.cmet.2014.02.006.

Friday June 5:

1) Continue June 3 lecture: Nutrition, dietary restriction, aging and diseases (Valter Longo). Remotely, 2-4:50 pm.

WEEK 4 class meets remotely

Monday, June 8: CLASS AT 9-12 AM California Time

Aging, healthcare and diseases in Genoa. Prof. P. Odetti and Prof. Dijk University of Genoa. How this port city reached one of the highest over 65 population in the world (estimated at over 26%) and how the City handles it. Lecture by Professor and Chief of Geriatrics at Genoa's San Martino Hospital Patrizio Odetti. Prof. Odetti is one of the leading experts in Geriatric medicine in Italy. Prof. Monacelli will focus on the geriatric community and healthcare in Liguria. Prof. Nencioni will instead focus on the basic and clinical aspects of cancer, with focus on treatment and the elderly.

Prof. P.Odetti

Demographic data on Liguria

Liguria is an Italian County characterized by an high prevalence of elderly (beyond 25% of >65 years old subjects). The main causes of this dramatic modification of the population lie on the low birth rate, the increased women/(men) longevity and the return of Italian emigrates. The demographic change has modified the health care request of the population. The elderly, when sick, turn to the Emergency Department to fulfil their medical need instead of addressing to the general practitioner causing a overcrowded and busy first aid. The strategy of health care local Authorities tries to face the problems as well as the new queries of the very old people.

Prof. Dijk

The Ligurian geriatric community health care and welfare network

Aging is associated with increased comorbidity and disability; on average 30% of subjects over 65 years need a kind of health care intervention and at least 10% of them suffer from disability or impairment in ADL. The general practitioner in Italy takes care of 200-300 geriatric patients, covering 70/80% of the overall geriatric medical care and assistance. The ongoing geriatric community health care network includes day hospital, daily , domestic health care stratified on intensity care levels, nursing homes both for non disabled and disabled patients and hospice for terminally ill patients. However the network is still fragmented and non homogeneous according to different geographical Italian areas with non conclusive outcomes in terms of economic and disability restraining. Then, there is a urgent need for integrated health care networks sharing multidisciplinary professionals, alternative to hospitalization, in order to fulfill the outgrowing and differentiated medical need of aging people.

Prof. A Nencioni, MD,

Cancer treatment in the elderly

Dr. Nencioni is an oncologist but also a leading basic researcher in the field of metabolism and cancer. He will talk about his work in the lab but also the standard therapies to treat age-related cancers including breast and prostate cancer. Since we are now in the midst of a demographic revolution as a result of aging of populations worldwide and approximately 60% of cancer incidence and 70% of cancer mortality occurs in individuals older than 65 the issue of proper management of elderly patients and, primarily, the avoidance of treatment-related toxicities has become of central importance. "Elderly patients are especially likely to experience complications from chemotherapy, such as febrile neutropenia, nausea, anemia, osteoporosis, depression, insomnia, and fatigue. For many patients, symptoms may be addressed both through lifestyle management and pharmaceutical approaches" (Naeim A, JCO, 2014). In addition, short courses of starvation (or of starvation-mimicking diets) may be useful for preventing or reducing at least some of the side effects of chemotherapy. Scores for predicting the toxicity of chemotherapy in the elderly are also available and they could be applied to identify those patients who should receive less toxic treatments or just palliative care vs. those that should be treated with standard chemotherapy (with or without biological agents) as if they were "young". Overall, "the key to improving quality of life in the elderly patient with cancer is an awareness of their specific needs and a familiarity with emergent treatment options" (Naeim A, JCO, 2014).

Clinical aspects of Alzheimer's diseases Fiammetta Monacelli, MD

Alzheimer disease: pathogenesis and natural history: focus on cognitive deficit, psycho affective and behavioural disturbances, neuropsychological assessment and therapeutic options. The presentation will focus on the cornerstones of Alzheimer disease (AD) pathogenesis, deal with the diagnostic assessment, the natural course of the disease and the most relevant clinical features of the neurodegenerative process. The presentation will also focus on the comprehensive geriatric assessment of AD patients, in order to assess the patient's cognitive domain, the comorbidity status, the functional status, the psychoaffective and behavioural disturbances, the gait and balance, summarizing the standard reference tools, with particular regard to the neuropsychological assessment. Then an overall view of the therapeutic options will be provided, discussing also the non pharmacological approaches to AD patients. Dr. Monacelli is a clinical geriatrician and an expert in Alzheimer's disease and glycooxidation.

Readings

- a. Alzheimer's disease: clinical trials and drug development. Mangialasche. Lancet Vol 9 July 2010
- b. Systematic Review: Factors Associated With Risk for and Possible Prevention of Cognitive Decline in Later Life. Plassman, et al. Ann Intern Med. 2010;153:182-193
- c. Probing the Biology of Alzheimer's Disease in Mice. Ashe et al. Neuron 66, June 10, 2010

- d. Surmeier DJ 2007 Calcium, ageing, and neuronal vulnerability in Parkinson's disease. Lancet Neurol. 6:933-8. Review.
- e. Thomas B, Beal MF. 2007 Parkinson's disease. Hum Mol Genet. Spec No. 2:R183-94.

Readings

Systematic review of preoperative, intraoperative and postoperative risk factors for colorectal anastomotic leaks F. D. McDermott¹, A. Heeney¹, M. E. Kelly¹, R. J. Steele², G. L. Carlson³ and D. C. Winter¹ *BJS* 2015; 102: 462–479

Naeim A, Apro Matti, Subbarao R, Balducci L, Supportive Care Considerations for Older Adults With Cancer *J Clin Oncol* 32: 2627-2634.

Web site: <http://www.census.gov/ipc/www/idb/informationGateway.php>

Reading: Effectiveness of the Mediterranean diet in the elderly. Roman B, Carta L, Martínez-González MA, Serra-Majem L. *Clin Interv Aging.* 2008;3(1):97-109

Lancet. 2009 October 3; 374(9696): 1196–1208. doi:10.1016/S0140-6736(09)61460-4. Ageing populations: the challenges ahead Kaare Christensen, MD1, Gabriele Doblhammer, PhD2, Roland Rau, PhD2, and James W Vaupel, PhD

The Assessment of Frailty in Older Adults Gabor Abellan van Kan, MDa,b,* , Yves Rolland, MD, PhDa,b, Mathieu Houles, MDa, Sophie Gillette-Guyonnet, PhDa,b, Maria Soto, MDa,b, Bruno Vellas, MD, PhDa,b *Clin Geriatr Med* 26 (2010) 275–286

Health of Immigrants in European countries. Solé-Auró A, Crimmins EM. Int Migr Rev. 2008;42(4):861-876.

A Tale of Two Countries—the United States and Japan: Are Differences in Health Due to Differences in Overweight? Sandra L. Reynolds,¹ Aaron Hagedorn,² Jihye Yeom,² Yasuhiko Saito,³ Eise Yokoyama,³ and Eileen M. Crimmins² *Journal of Epidemiology.* Vol. 18 (2008) , No. 6 pp.280-290

Tuesday, June 9

Nutrition, Fasting Mimicking Diets Stem cells and Regeneration in the treatment and prevention of diseases. A) An introduction to regenerative medicine, its potential and the difficulties and potential pitfalls. B) The use of fasting mimicking diets to promote regeneration and rejuvenation in disease prevention and treatment Valter Longo. Remotely, 2-4:50 pm.

Readings:

- a. Gass P, Riva MA 2007 CREB, neurogenesis and depression. Bioessays. 29:957-61.

- b. Morgan D. 2007 Amyloid, memory and neurogenesis. Exp Neurol. 205:330-5. Mar 14.
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Wednesday June 10

Final. Remotely, 2-4:50 pm

Weeks	Date	Time	Topics Covered
Week 1	M 05/18		NO CLASS
	Tu 05/19	2-4:50pm PDT	Valter Longo - Course Overview -Introduction to Aging
	W 05/20	2-4:50pm PDT	Caleb Finch - Aging and pollution
	Th 05/21	2-4:50pm PDT	Valter Longo - Introduction to the biology of aging (continued), theories and aging mechanisms at the molecular, and cellular level. Aging in microorganisms
	F 05/22	2-4:50pm PDT	Christian Pike - Aging and Alzheimer's Disease
Week 2	M 05/25		NO CLASS- MEMORIAL DAY
	Tu 05/26	2-4:50pm PDT	Michael Goran - Sugar, obesity and diseases.
	W 05/27	2-4:50pm PDT	Raffaella Ghittoni - Intermittent Fasting, Therapeutic Fasting, and Ketogenic Diets.
	Th 05/28	2-4:50pm PDT	Valter Longo - Genetics of Aging in mice and humans.
	F 05/29	9-12 AM PDT	Hanno Pijl - Nutrition and chronic disease: an evolutionary perspective. Calorie restriction and the management of (type 2) diabetes mellitus
Week 3	M 06/01	2-4:50pm PDT	Valter Longo - Cancer and aging
	Tu 06/02	2-4:50pm PDT	MIDTERM -Exam material covers up to Thursday May 28 lecture on genetic of aging in mice and humans included
	W 06/03	2-4:50pm PDT	Dietary restriction, Exercise in aging and cardiovascular risk factor/diseases.
	Th 06/04	2-4:50pm PDT	Nutrition, dietary restriction, aging and diseases: Parts 1
	F 06/05	2-4:50pm PDT	Nutrition, dietary restriction, aging and diseases: Parts 2
Week 4	M 06/08	9-12 AM PDT	Patrizio Odetti - Aging, healthcare and diseases in Genoa - Demographic data on Liguria Babette Dijk - The Ligurian geriatric community health care and welfare network Alessio Nencioni- - Cancer treatment in the elderly
	Tu 06/09	2-4:50pm PDT	Nutrition, Fasting Mimicking Diets Stem cells and Regeneration in the treatment and prevention of diseases
	W 06/10	2-4:50pm PDT	FINAL EXAM -