1. OVERVIEW

Subject Area	Immuno-nutrition and Nutrigenomics
Degree	Human Nutrition and Dietetics
School/Faculty	Biomedical and Health Sciences
Year	Fourth
ECTS	6
Type	Compulsory
Language(s)	Spanish
Delivery Mode	On campus and blended
Semester	Seventh
Coordinating professor	Dr Esmeralda Parra-Peralbo

2. INTRODUCTION

The subject area Immuno-nutrition and Nutrigenomics is part of the overall subject of Advanced Biology in Module 4: 'Nutrition, Dietetics and Health', and is optional. This subject area, worth 6 ECTS credits, is delivered in the first semester of the fourth year of the Bachelor's Degree in Human Nutrition and Dietetics.

The overall objective of this subject area is to learn how nutrition affects the immune response. The specific objectives of this subject area are:

- Know about mechanisms of immune response.
- Understand how gene expression is regulated by the different biomolecules that are part of nutrition (carbohydrates, lipids, amino acids, etc.).
- Understand how nutrition affects the epigenome, gene expression and phenotype.

3. SKILLS AND LEARNING OUTCOMES

Key Skills (CB, by the acronym in Spanish)

- CB2: Students can apply their knowledge to their work professionally and possess the necessary skills, usually demonstrated by forming and defending opinions, as well as resolving problems within their study area.
- CB3: Students have the ability to gather and interpret relevant data (usually within their study area) to form opinions which include reflecting on relevant social, scientific or ethical matters.
- CB4: Students can communicate information, ideas, problems and solutions to both specialist and non-specialist audiences.

General skills (CG, by the acronym in Spanish)

- CG12: Know about nutrients, their function in the body, bioavailability, requirements and recommendations, as well as the bases of energy and nutritional balance.
- CG13: Understand and assess the relationship between food and nutrition in situations of health and situations of illness.
- CG14: Apply scientific knowledge of physiology, pathophysiology, nutrition and food to dietary planning and advice for individuals and groups of all ages, including both healthy and unwell people.

Cross-curricular skills (CT, by the acronym in Spanish)

- CT1: Communication: ability to engage in active listening, ask questions and respond in a clear and concise way, as well as to effectively express ideas and concepts. This includes concise and clear written communication.
- CT6: Problem solving: ability to solve an unclear or complex issue or situation which has no established solution and requires skill to reach a conclusion.
- CT9: Ability to put knowledge into practice, using the skills acquired through the study of mock situations based faithfully on real life issues in the relevant profession.

Specific skills (CE, by the acronym in Spanish)

- CE117: Know concepts of nutrigenomics, nutrigenetics and nutritional epigenetics. Tools of nutrigenomics.
- CE118: Understand how gene expression is regulated by carbohydrates, lipids, amino acids and other nitrogenous compounds, vitamins and minerals, and other food components.
- CE119: Understand how nutrition affects the epigenetic pattern, gene expression and phenotype.

Learning outcomes (RA, by the acronym in Spanish):

- RA1: Know about mechanisms of immune response.
- Understand how gene expression is regulated by the different biomolecules that are part of nutrition (carbohydrates, lipids, amino acids, etc.).
- RA3: Understand how nutrition affects the epigenetic pattern, gene expression and phenotype.

The following table shows how the skills developed in the subject area match up with the intended learning outcomes:

Skills	Learning outcomes
CB2, CB3, CB4, CG12, CG13, CG14, CT1, CT6, CT9, CE117	Know about mechanisms of immune response.
CB2, CB3, CB4, CG12, CG13, CG14, CT1, CT6, CT9, CE117, CE118,	Understand how gene expression is regulated by the different biomolecules that are part of nutrition (carbohydrates, lipids, amino acids, etc.).

CB2, CB3, CB4, CG12, CG13, CG14, CT1, CT6, CT9, CE117, CE119	Understand how nutrition affects the epigenetic pattern, gene expression and phenotype.

4. CONTENTS

Unit 1: Immunology
- ✓ Topic 1. Fundamentals of Immunology
- ✓ Topic 2. Immune responses and disorders
- ✓ Topic 3. Inflammation

Unit 2: Immuno-nutrition
- ✓ Topic 4. History of Immuno-nutrition
- ✓ Topic 5. Microbiota and immunity
- ✓ Topic 6. Psycho-Neuro-Immune-Endocrine Axis

Unit 3. Nutrigenomics 1
- ✓ Topic 7. Nutrigenomics
- ✓ Topic 8(a). Vitamins and minerals as regulators of gene expression.
- ✓ Topic 8(b). Micronutrients, Nutrigenomics and non-infectious diseases.
- ✓ Topic 9. Carbohydrates as regulators of gene expression.

Unit 4. Nutrigenomics 2
- ✓ Topic 10(a). Lipids as regulators of gene expression. Obesity and Type 2 Diabetes
- ✓ Topic 10(b). Lipids as regulators of gene expression. Cardiovascular disease
- ✓ Topic 11. Regulation of gene expression by amino acids and derivatives
- ✓ Topic 12. Regulation of gene expression by other food components

Unit 5. Nutrigenetics.
- ✓ Topic 13(a). Nutrigenetics and macronutrients 1
- ✓ Topic 13(b). Nutrigenetics and macronutrients 2
- ✓ Topic 14. Nutrigenetics and micronutrients

Unit 6. Nutritional epigenetics
- ✓ Topic 15. Nutrition as a modifier of the epigenome
- ✓ Topic 16. Disorders related to nutrigenetics/nutritional epigenetics

5. TEACHING/LEARNING METHODS

The types of teaching/learning methods are as follows:

- Lecture
- Collaborative learning
- Case studies
- Problem-based and project-based learning
- Learning based on workshops/labs

6. LEARNING ACTIVITIES

The types of learning activities, plus the amount of time spent on each activity, are as follows:

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On campus

Learning activity	Number of hours
Lecture	50
Independent working	43
Case studies	11
Group activities	7
Written reports and strategies	9
Workshops and/or lab work	10
Tutorials	14
Knowledge test	6
TOTAL	**150 h**

Blended learning

Learning activity	Number of hours
Reading of content	29
Online seminars	21
Independent working	42
Case studies	12
Group activities	7
Written reports and strategies	9
Workshops and/or lab work	10
Online tutorials	14
Knowledge test	6
TOTAL	**150 h**

7. ASSESSMENT

The assessment methods, together with their respective weighting towards the final grade for the subject, are as follows:

On-campus and blended learning:

Assessment method	Weighting
Knowledge test	50%

Laboratory work	20%
Submission of reports and essays	10%
Performance observation	10%
Participation in debates	10%

On the Virtual Campus, when you open the subject area, you can see all the details of your assessment activities, including the deadlines and assessment procedures for each activity.

8. BIBLIOGRAPHY

The reference works for following this subject area are:

- Caterina, R. de, Martínez, J. A. y Kohlmeier, M. (2020). *Principles of nutrigenetics and nutrigenomics: Fundamentals for individualized nutrition.* London. Elsevier.
- Gordillo, D. y Gordillo, E. (2015). *Nutrición molecular.* México McGraw-Hill.
- Mahmoudi, M. y Rezaei, N. (2019). *Nutrition and immunity.* Cham, Switzerland. Springer.
- Marcos, A. (2020). *Inmunonutrición.* Madrid. Médica Panamericana.

The recommended bibliography is indicated below:

- Abbas, A., Lichtman, AH. y Pober, JS. (1995) Inmunología Celular y Molecular. 2ª Edic. Interamericana*McGraw-Hill
- Abrams, S.A., Griffin, I.J., Hawthorne, K.M., Liang, L., Gunn, S.K., Darlington, G., Ellis, K.J., 2005. A combination of prebiotic shortand long-chain inulin-type fructans enhances calcium absorption and bone mineralization in young adolescents. Am J Clin Nutr 82, 471- 476.
- Arabi, A., Zahed, L., Mahfoud, Z., El-Onsi, L., Nabulsi, M., Maalouf, J., El-Hajj Fuleihan, G., 2009. *Vitamin D receptor gene polymorphisms modulate the skeletal response to vitamin D supplementation in healthy girls*. Bone 45, 1091-1097.
- Belén Zapatera, Andreu Prados, Sonia Gómez-Martínez, Ascensión Marcos. 2015. Rev Esp Nutr Comunitaria; 21(Supl. 1): 144-153. DOI: 10.14642/RENC.2015.21.sup1.5061
- Berin, M.C., Sampson, H.A., 2013. *Food allergy: an enigmatic epidemic.* Trends Immunol, 34 (8), 390-397.
- Berna´, G., *et al*., 2014. *Nutrigenetics and nutrigenomics insights into diabetes etiopathogenesis*. Nutrients 6 (11), 5338-5369.
- Bifari, F., Nisoli, E. (2017). *Branched-chain amino acids differently modulate catabolic and anabolic states in mammals: a pharmacological point of view*. Br J Pharmacol 174, 1366-1377.
- Bleau, C., et al., 2015. *Crosstalk between intestinal microbiota, adipose tissue and skeletal muscle as an early event in systemic low-grade inflammation and the development of obesity and diabetes*. Diabetes Metabol Res Rev 31 (6), 545-561.
- Brosnan JT (2001). *Amino acids, then and now—a reflection on Sir Hans Kreb's contribution to nitrogen metabolism*. IUBMB Life 52: 265–270
- Campbell, D.E., Boyle, R.J., Thornton, C.A., Prescott, S.L., 2015. *Mechanisms of allergic disease e environmental and genetic determinants for the development of allergy*. Clin Exp Allergy 45 (5), 844- 858.
- Clarke, G. et al., 2019. *Gut Reactions: Breaking Down Xenobiotic-Microbiome*. Pharmacological Reviews 71: 198-224. doi: 10.1124/pr.118.015768
- Collen, A. (2019). *10 % humanos.* RBA - obra de divulgación científica, lectura recomendada.
- Cui, X.L., Soteropoulos, P., Tolias, P., Ferraris, R.P., 2004. *Fructose responsive genes in the small intestine of neonatal rats*. Physiol Genom 18, 206-217.
- Curis E, Crenn P, Cynober L. (2007). *Citrulline and the gut*. Curr Opin Clin Nutr Metab Care 10:620– 626.
- Dana C Dolinoy (2008). *The agouti mouse model: an epigenetic biosensor for nutritional and*

environmental alterations on the fetal epigenome. Nutr Rev.; 66(Suppl 1): S7–11

- Delves, Marin, Burton y Roitt (2008). Inmunología Fundamentos. 11ª Edic. Panamericana
- Emilsson, V., Thorleifsson, G., Zhang, B., Leonardson, A.S., Zink, F., Zhu, J., Carlson, S., Helgason, A., Walters, G.B., Gunnarsdottir, S., Mouy, M., Steinthorsdottir, V., Eiriksdottir, G.H., Bjornsdottir, G., Reynisdottir, I., Gudbjartsson, D., Helgadottir, A., Jonasdottir, A., Jonasdottir, A., Styrkarsdottir, U., Gretarsdottir, S., Magnusson, K.P., Stefansson, H., Fossdal, R., Kristjansson, K., Gislason, H.G., Stefansson, T., Leifsson, B.G., Thorsteinsdottir, U., Lamb, J.R., Gulcher, J.R., Reitman, M.L., Kong, A., Schadt, E.E., Stefansson, K., 2008. *Genetics of gene expression and its effect on disease*. Nature 452, 423-428.
- Fenech M. *et al*., 2011. Nutrigenetics and Nutrigenomics: Viewpoints on the Current Status and Applications in Nutrition Research and Practice. J Nutrigenet Nutrigenomics. 4:69–89
- Fernandez-Morera, J.L., Calvanese, V., Rodriguez-Rodero, S., Menendez-Torre, E., Fraga, M.F., 2010. *Epigenetic regulation of the immune system in health and disease.* Tissue Antigens 76 (6), 431 - 439.
- Ferrari, S., Manen, D., Bonlour, J.P., Slosman, D., Rizzoli, R., 1999. Bone mineral mass and calcium and phosphate metabolism in young men: relationships with vitamin D receptor allelic polymorphisms. J Clin Endocrinol Metab 84, 2043-2048.
- Ferrari, S., Rizzoli, R., Manen, D., Slosman, D., Bonjour, J.P., 1998. Vitamin D receptor gene start codon polymorphisms (FokI) and bone mineral density: interaction with age, dietary calcium and 3' end region polymorphisms. J Bone Miner Res 13, 925-930.
- Flynn NE, Bird JG, Guthrie AS (2008). Glucocorticoid regulation of amino acid and polyamine metabolism in the small intestine. Amino Acids. doi:10.1007/s00726-008- 0206-7
- Francini, F., Castro, M.C., Schinella, G., García, M.E., Maiztegui, B., Raschia, M.A., Gagliardino, J.J., Massa, M.L., 2010. *Changes induced by a fructose-rich diet on hepatic metabolism and the antioxidant system.* Life Sci 86, 965-971.
- Fu WJ, Haynes TE, Kohli R et al (2005). *Dietary L-arginine supplementation reduces fat mass in Zucker diabetic fatty rats.* J Nutr 135:714–721
- Fu WJ, Haynes TE, Kohli R et al (2005). *Dietary L-argininesupplementation reduces fat mass in Zucker diabetic fatty rats.* J Nutr 135:714–721
- Fuchsberger, C., Flannick, J., Teslovich, T.M., Mahajan, A., Agarwala, V., Gaulton, K.J., Ma, C., Fontanillas, P., Moutsianas, L., McCarthy, D.J., Rivas, M.A., Perry, J.R., Sim, X., Blackwell, T.W., Robertson, N.R., Rayner, N.W., Cingolani, P., Locke, A.E., Fernandez Tajes, J., Highland, H.M., Dupuis, J., *et al* 2016. *The genetic architecture of type 2 diabetes*. Nature 536, 41-47.
- Fuentes, F. *et al*., 2015. *Dietary Glucosinolates Sulforaphane, Phenethyl Isothiocyanate, Indole-3- Carbinol/3,3'-Diindolylmethane: Anti-Oxidative Stress/Inflammation, Nrf2, Epigenetics/Epigenomics and In Vivo Cancer Chemopreventive Efficacy*. Curr Pharmacol Rep. May; 1(3): 179–196.
- Fushan, A.A., Simons, C.T., Slack, J.P., Drayna, D., 2010. Association between common variation in genes encoding sweet taste signaling components and human sucrose perception. Chem Senses 35 (7), 579-592.
- Fushan, A.A., Simons, C.T., Slack, J.P., Manichaikul, A., Drayna, D., 2009. Allelic polymorphism within the TAS1R3 promoter is associated with human taste sensitivity tosucrose. Curr Biol 19, 1288-1293.
- Glass, C.K, Olefsky, J.M., 2012. *Inflammation and lipid signaling in the etiology of insulin resistance*. Cell Metab 15, 635-645.
- Glastonbury, C.A., Vinuela, A., Buil, A., Halldorsson, G.H., Thorleifsson, G., Helgason, H., Thorsteinsdottir, U., Stefansson, K., Dermitzakis, E.T., Spector, T.D., Small, K.S., 2016. *Adiposity-dependent regulatory effects on multi-tissue transcriptomes*. Am J Hum Genet 99, 567-579.
- Grillo MA, Colombatto S (2007). ***S***-*Adenosylmethionine and radicalbased catalysis*. Amino Acids 32:197–202
- Grimaldi, K. A. et al. (2017). Proposed guidelines to evaluate scientific validity and evidence for genotype-based dietary advice. *Genes & Nutrition, 12,* 35. doi: 10.1186/s12263-017-0584-0
- Grimble RF (2006). The effects of sulfur amino acids intake on immune function in humans. J Nutr 136:1660S–1665S
- Gross, B., Pawlak, M., Lefebvre, P., Staels, B., 2017. *PPARs in obesity-induced*
- Ha EM, Choi CT, Bae YS, Lee WJ (2005). *A direct role for dual oxidase in Drosophila gut immunity*.

Science 310:847–850

- Haenen, D., Zhang, J., Souza da Silva, C., Bosch, G., van der Meer, I.M., van Arkel, J., van den Borne, J.J., Perez Gutierrez, O., Smidt, H., Kemp, B., Muller, M., Hooiveld, G.J., 2013. *A diet high in resistant starch modulates microbiota composition, SCFA concentrations, and gene expression in pig intestine.* J Nutr 143, 274-283.
- Han, K.H., Sekikawa, M., Shimada, K., Sasaki, K., Ohba, K., Fukushima, M., 2004. *Resistant starch fraction prepared from kintoki bean affects gene expression of genes associated with cholesterol metabolism in rats*. Exp Biol Med 229, 787-792.
- Harb, H., Renz, H., 2015. *Update on epigenetics in allergic disease.* J Allergy Clin Immunol 135 (1), 15-24.
- Hong, F., Pan, S., Guo, Y., Pengfei Xu, P. and Zhai, Y. 2019. *PPARs as Nuclear Receptors for Nutrient and Energy Metabolism.* Molecules 2019, 24, 2545; doi: 10.3390**/**molecules24142545
- Honma, K., Mochizuki, K., Goda, T., 2007. *Carbohydrate/fat ratio in the diet alters histone acetylation on the sucrase**e**isomaltase gene and its expression in mouse small intestine*. Biochem Biophys Res Commun 357, 1124-1129.
- Hu CA, Khalil S, Zhaorigetu S. (2008). *Human **D**1-pyrroline-5- carboxylate synthase: function and regulation*. Amino Acids 35:665–672.
- Huang YF, Wang YX, Watford M (2007). Glutamine directly downregulates glutamine synthetase protein levels in mouse C2C12 skeletal muscle myotubes. J Nutr 137:1357–1362
- Jobgen W, Fu WJ, Gao H et al (2009). *High fat feeding and dietary Larginine supplementation differentially regulate gene expression in rat white adipose tissue.* Amino Acids. doi: 10.1007/s00726- 009-0246-7
- Jobgen WS, Fried SK, Fu WJ et al (2006). *Regulatory role for the arginine-nitric oxide pathway in metabolism of energy substrates*. J Nutr Biochem 17:571–588
- Kilberg MS, Pan YX, Chen H, Leung-Pineda V (2005). Nutritional control of gene expression: how mammalian cells respond to amino acid limitation. Annu Rev Nutr 25:59–85
- Kim SW, Wu G (2008). *Regulatory role for amino acids in mammary gland growth and milk synthesis.* Amino Acids. doi: 10.1007/s00726-008-0151-5.
- Kim, J.H. *et al*, 2010. Sulforaphane Increases Cyclin-Dependent Kinase Inhibitor, p21 Protein in Human Oral Carcinoma Cells and Nude Mouse Animal Model to Induce G2/M Cell Cycle Arrest. J Clin Biochem Nutr. Vol. 46(1): 60–67.
- Kohler, J., et al., 2017. Plant sterol enriched functional food and atherosclerosis. Br. J Pharmacil 174, 1281e1289.
- Koo, H., Wallig, M.A., Chung, B.H., Nara, T.Y., Cho, B.S., Nakamura, M.T., 2008. *Dietary fructose induces a wide range of genes with distinct shift in carbohydrate and lipid metabolism in fed and fasted rat liver*. Biochim Biophys Acta 1782, 341-348.
- Lal, G., Bromberg, J.S., 2009. *Epigenetic mechanisms of regulation of Foxp3 expression.* Blood 114 (18), 3727- 3735.
- Le, M.T., 2010. Factors Impacting Fructose Bioavailability and its Adverse Metabolic Effects. PhD thesis. University of Florida
- Legoux F, Bellet D, Daviaud C et al., 2019. *Microbial metabolites control the thymic development of mucosal-associated invariant T cells*. Science 25;366(6464):494-499.
- Leong HX, Simkevich C, Lesieur-Brooks A et al (2006). Short-term arginine deprivation results in large-scale modulation of hepatic gene expression in both normal and tumor cells: microarray bioinformatics analysis. Nutr Metab 3:37
- Li P, Yin YL, Li DF, Kim SW, Wu G (2007). *Amino acids and immune function*. Br J Nutr 98:237–252
- Li X, Bazer FW, Gao H et al (2009). *Amino acids and gaseous signaling*. Amino Acids. doi:10.1007/s00726-009-0264-5
- Liao XH, Majithia A, Huang XL, Kimmel AR (2008). *Growth control via TOR kinase signaling, an intracellular sensor of amino acids and energy availability, with crosstalk potential to proline metabolism.* Amino Acids 35:761–770
- Lyons, C.L., Kennedy, E.B., Roche, H.M., 2016. Metabolic inflammation-differential modulation by dietary constituents. Nutrients 8 (5), 1-21.
- M. Mesa-Villanueva, P.J. Patiño, 2006. Inmunología, Vol. 25, Núm 2, pp.:115-130.
- Macchiarulo A, Camaioni E, Nuti R, Pellicciari RC (2008). *Highlights at the gate of tryptophan catabolism: a review on the mechanisms of activation and regulation of indoleamine 2,3-*

dioxygenase (IDO), a novel target in cancer disease. Amino Acids. doi:10.1007/s00726-008-0137-3

- Manna P, Sinha M, Sil PC (2009). *Taurine plays a beneficial role against cadmium- induced oxidative renal dysfunction*. Amino Acids 36:417–428.
- Martino, D.J., Bosco, A., McKenna, K.L., Hollams, E., Mok, D., Holt, P.G., et al., 2012. *T-cell activation genes differentially expressed at birth in CD4⁺ T-cells from children who develop IgE food allergy*. Allergy 67 (2), 191-200.
- Melchior D, Le Floc'h N, Seve B (2003). *Effect of chronic lung inflammation on tryptophan metabolism in piglets.* Adv Exp Med Biol 527:359–362
- Miyamoto, J., Hasegawa, S., Kasubuchi, M., Ichimura, A., Nakajima, A., Kimura, I., 2016. *Nutritional signaling via free fatty acid receptors*. Int J Mol Sci 17, 450.
- Müller, M. y Kersten, S. (2003). Nutrigenomics: Goals and strategies. *Nature Reviews Genetics, 4,* 315-322. doi: 10.1038/nrg1047
- Netea MG, Joosten LAB, Latz E, Mills KHG, Natoli G, Stunnenberg HG, et al. 2016. *Trained immunity: a program of innate immune memory in health and disease*. Science (New York, NY) 352(6284): aaf1098.
- Netea MG. 2013. *Training innate immunity: the changing concept of immunological memory in innate host defence*. Eur J Clin Investig; 43(8):881–4.
- Opazo, M.ª C. et al. (2018). Intestinal microbiota influences non-intestinal related autoimmune disease. *Frontiers in Microbiology, 9,* 432. doi: 10.3389/fmicb.2018.00432
- Palii SS, Kays CE, Deval C et al (2008). Specificity of amino acid regulated gene expression: analysis of gene subjected to either complete or single amino acid deprivation. Amino Acids. doi: 10.1007/s00726-008-0199-2
- Parnell, L.D., Blokker, B.A., Dashti, H.S., et al., 2014. *CardioGxE, a catalog of gene- environment interactions for cardiometabolic traits*. BioData Min 7, 21. https://doi.org/10.1186/1756-0381-7-21.
- Parra-Peralbo E and Culi J, 2011. "*Drosophila* lipophorin receptors mediate the uptake of neutral lipids in oocytes and imaginal disc cells by an endocytosis- independent mechanism". PLoS Genetics, vol. 7(2): e1001297.
- Perez-Alonso, M., Briongos, S., Ruiz-Mambrilla, M., et al., 2019 Feb. Association between Bat Vitamin D receptor 30 haplotypes with vitamin D levels at baseline and worse response after increase of vitamin D by supplements and exposure to sunlight. Int J Vitam Nutr Res 21, 1-5.
- Perta-Kajan J, Twardowski T, Jakubowski H (2007). *Mechanisms of homocysteine toxicity in humans*. Amino Acids 32:561–572.
- Phillips, C.M., Tierney, A.C., Roche, H.M., 2008. *Gene-nutrient interactions in the metabolic syndrome.* J Nutrigenetics Nutrigenomics 1 (3), 136-151.
- Pintó Sala, X. 2000. *La homocisteína como factor de riesgo cardiovascular.* Medicina Integral, Vol. 36, Núm. 5, pp.: 179-185.
- Platten M, Ho PP, Youssef S et al (2005). Treatment of autoimmune neuroinflammation with a synthetic tryptophan metabolite. Science 310:850–855
- Ralston, J.C., et al., 2017. *Fatty acids and NLRP3 inflammasomee-mediated inflammation in metabolic tissues*. Annu Rev Nutr 37 (1), 77-102.
- Ramos-López, O., *et al.*, 2017. Guide for current nutrigenetic, nutrigenomic, and nutriepigenetic approaches for precision nutrition involving the prevention and management of chronic diseases associated with obesity. J Nutrigenetics Nutrigenomics 10, 43e62.
- Ramos-Lopez, O., Panduro, A., Martinez-Lopez, E., Roman, S., 2016. Sweet taste receptor TAS1R2 polymorphism (Val191Val) is associated with a higher carbohydrate intake and hypertriglyceridemia among the population of west Mexico. Nutrients 8, 101.
- Rev. chil. endocrinol. diabetes 2013; 6 (1): 15-22
- Ribera-Casado, J. M. (2017). Centenario de Elie Metchnikoff (1845-1916). *Educación Médica, 18*(2), 136-143. doi: 10.1016/j.edumed.2016.11.009
- Riedijk MA, Stoll B, Chacko S *et al.* (2007). *Methionine transmethylation and transsulfuration in the piglet gastrointestinal tract*. Proc Natl Acad Sci USA, 104:3408– 3413
- Rolland, F., Baena-Gonzalez, E., Sheen, J., 2006. *Sugar sensing and signaling in plants: conserved and novel mechanisms.* Annu Rev Plant Biol 57, 675-709.
- Rosato, V., et al., 2017. Mediterranean diet and cardiovascular disease: a systematic review and

meta-analysis of observational studies. Eur J Nutr 2e19.

- Rui, L., 2014. *Energy metabolism in the liver.* Compr Physiol 4 (1), 177-197.
- Safi-Stibler, S & Gabory, A, 2020. *Epigenetics and the Developmental Origins of Health and Disease: Parental environment signalling to the epigenome, critical time windows and sculpting the adult phenotype*. Semin Cell Dev Biol, Jan;97:172-180
- Sahai A, Pan XM, Paul R et al (2006). Roles of phosphatidylinositol 3-kinase and osteopontin in steatosis and aminotransferase release by hepatocytes treated with methionine-choline-deficient medium. Am J Physiol Gastrointest Liver Physiol 291:G55–G62
- Shi W, Meininger CJ, Haynes TE *et al* (2004). Regulation of tetrahydrobiopterin synthesis and bioavailability in endothelial cells. Cell Biochem Biophys 41:415–433
- Sicherer, S.H., Sampson, H.A., 2014. *Food allergy: epidemiology, pathogenesis, diagnosis, and treatment*. J Allergy Clin Immunol 133 (2), 291-307-308.
- Simmons, R., 2011. Epigenetics and maternal nutrition: nature *versus* nurture. Proc Nutr Soc 70 (1), 73-81.
- Simopoulos A.P., 2010. Nutrigenetics/Nutrigenomics. Annu. Rev. Public Health. 31:53–68
- Skinner, M.K., Guerrero-Bosagna, C., 2009. *Environmental signals and transgenerational epigenetics.* Epigenomics 1 (1), 111-117.
- Slaats, G.G., Reinius, L.E., Alm, J., Kere, J., Scheynius, A., Joerink, M., 2012. *DNA methylation levels within the CD14 promoter region are lower in placentas of mothers living on a farm*. Allergy 67 (7), 895-903.
- Spears, J. 2002. *Scientific Advances in Animal Nutrition. Promise for the New Century: Proceedings of a Symposium*, pp. 113-126.
- Stipanuk MH, Ueki I, Dominy JE et al (2008). Cysteine dioxygenase: a robust system for regulation of cellular cysteine levels. Amino Acids. doi:10.1007/s00726-008-0202- y
- Sun YP, Nonobe E, Kobayashi Y et al (2002). Characterization and expression of L- amino acid oxidase of mouse milk. J Biol Chem 277:19080–19086
- Suzuki, T., Douard, V., Mochizuki, K., Goda, T., Ferraris, R.P., 2011. *Diet-induced epigenetic regulation in vivo of the intestinal fructose transporter Glut5 during development of rat small intestine*. Biochem J 435, 43-53.
- *T2DM, dyslipidaemia and NAFLD*. Nat Rev Endocrinol 13, 36-49.
- Tain, Y., Chan, J.Y., Hsu, C., 2016. *Maternal fructose intake affects transcriptome changes and programmed hypertension in offspring in later life.* Nutrients 8, 757.
- Tan BE, Li XG, Kong XF et al (2008). *Dietary L-arginine supplementation enhances the immune status in early-weaned piglets.* Amino Acids. doi: 10.1007/s00726-008-0155- 1
- Tan BE, Yin YL, Liu ZQ et al (2008). *Dietary L-arginine supplementation increases muscle gain and reduces body fatmass in growing-finishing pigs.* Amino Acids. doi: 10.1007/s00726-008-0148-0
- The 1000 Genomes Consortium, 2015. A global reference for human genetic variation. Nature 526, 68-74.
- Tiffon, C., 2018. *The Impact of Nutrition and Environmental Epigenetics on Human Health and Disease.* Int. J. Mol. Sci., 19, 3425
- Todendi, P. F. et al., 2019. The role of the genetic variants *IRX3* rs3751723 and *FTO* rs9939609 in the obesity phenotypes of children and adolescents. Obesity Research & Clinical Practice, Vol. 13, Issue 2, Pages: 137 -142. https://doi.org/10.1016/j.orcp.2019.01.005
- Tujioka K, Okuyama S, Yokogoshi H et al (2007). *Dietary **c**aminobutyric acid affects the brain protein synthesis rate in young rats*. Amino Acids 32:255–260.
- Uyeda, K., Repa, J.J., 2006. *Carbohydrate response element binding protein, ChREBP, a transcription factor coupling hepatic glucose utilization and lipid synthesis*. Cell Metabolism 4, 107-110.
- Vaulont, S., Vasseur-Cognet, M., Kahn, A., 2000. *Glucose regulation of gene transcription.* J Biol Chem 275, 31555-31558
- Vickers, M.H., 2014. *Early Life Nutrition, Epigenetics and Programming of Later Life Disease*. *Nutrients*, *6*, 2165-2178.
- Vinood B. Patel, Victor R. Preedy (2019). *Handbook of Nutrition, Diet, and Epigenetics.* Edit.: Springer International Publishing
- Wang JJ, Chen LX, Li P et al (2008). *Gene expression is altered in piglet small intestine by weaning and dietary glutamine supplementation*. J Nutr 138:1025–1032

- Wang JJ, Wu G, Zhou HJ, Wang FL (2008). *Emerging technologies for amino acid nutrition research in the post-genome era*. Amino Acids. doi: 10.1007/s00726-008- 0193-8
- Wang WW, Qiao SY, Li DF (2008) *Amino acids and gut function*. Amino Acids. 37, pages: 105–110. doi: 10.1007/s00726-008-0152-4
- Wang, Y., Viscarra, J., Kim, S.J., Sul, H.S., 2015. *Transcriptional regulation of hepatic lipogenesis.* Nat Rev Mol Cell Biol 16, 678-689.
- Wolff, G.L. *et al*, 1998. *Maternal epigenetics and methyl supplements affect agouti gene expression in Avy/a mice*. FASEB J. 12 (11): 949-57.
- World Health Organization, 2016. Obesity and Overweight [Fact Sheet]; Updated June 2016. Trouvle 13.
- Wu G, Bazer FW, Datta S et al (2008). Proline metabolism in the conceptus: implications for fetal growth and development. Amino Acids 35:691–702
- Wu G, Bazer FW, Hu J et al (2005). Polyamine synthesis from proline n the developing porcine placenta. Biol Reprod 72:842–850
- Wu G, Fang YZ, Yang S et al (2004). *Glutathione metabolism and its implications for health*. J Nutr 134:489–492
- Wu G, Meininger CJ (2002). *Regulation of nitric oxide synthesis by dietary factors.* Annu Rev Nutr 22:61–86
- Wu, G. (2009). *Amino acids: metabolism, functions, and nutrition.* Amino Acids, 37:1–17. DOI 10.1007/s00726-009-0269-0
- Yao K, Yin YL, Chu WY et al (2008). *Dietary arginine supplementation increases mTOR signaling activity in skeletal muscle of neonatal* pigs. J Nutr 138:867–872

Recommended websites

- http://immunonutrition-isin.org/
- https://nutritionandgenetics.org/
- https://nutritionandgenetics.org/Links
- https://omim.org/
- https://www.cancer.gov
- https://www.library.ucdavis.edu/database/scrivers-online-metabolic-and-molecular- bases-of-inherited-disease-ommbid/
- https://www.lshtm.ac.uk/newsevents/expert-opinion/100-questions-peter-piot-lshtm-director
- https://www.who.int/cardiovascular_diseases/about_cvd/es/
- https://www.who.int/es/news-room/fact-sheets/detail/malnutrition
- http://www.metahit.eu
- https://www.microbiota-site.com
- http://hmpdacc.org