

**COURSE DATA****Data Subject**

Code	43084
Name	Physiology and physiopathology of free radicals and antioxidants
Cycle	Master's degree
ECTS Credits	4.0
Academic year	2023 - 2024

Study (s)

Degree	Center	Acad. year	Period
2141 - Master's Degree in Physiology	Faculty of Medicine and Odontology	1	Second term

Subject-matter

Degree	Subject-matter	Character
2141 - Master's Degree in Physiology	3 - Oxidative stress and its applications in biomedicine	Obligatory

Coordination

Name	Department
SASTRE BELLOCH, JUAN JOSE	190 - Physiology

SUMMARY

In this subject we will study the role of reactive oxygen and nitrogen species, specially oxygen free radicals, as well as oxidative stress and redox signalling in Biomedicine. To this end, firstly we will provide basic knowledge about reactive oxygen and nitrogen species, describing the major pro-oxidant species, their reactions and the cell organelles involved in their generation and their main targets. The most widely used biomarkers to detect the presence of oxidative and nitrosative stress in biological samples will be shown, explaining the most appropriate and updated techniques. In addition, the key role played by redox signalling in the mechanisms of cell adaptation, as well as the role of oxidative and nitrosative stress in cell death by necrosis, or other mechanisms. Special emphasis will be given to the great contribution of redox signaig and oxidative stress to a variety of physiological processes such as aging and physical exercise. Furthermore, the relevant role played by reactive oxygen species through redox signalling and oxidative stress in the pathogenesis and pathophysiology of a variety of diseases, such as neurodegenerative diseases, liver diseases, diabetes, and those related to acute and chronic inflammation and rare diseases will be dealt with in detail. Finally, the potential benefit of antioxidant administration in the treatment and prevention of diseases and its limitations will be shown.



PREVIOUS KNOWLEDGE

Relationship to other subjects of the same degree

There are no specified enrollment restrictions with other subjects of the curriculum.

Other requirements

It is recommended to have taken the subjects of Physiology and Biochemistry and Molecular Biology and subjects related to Pathology, such as Pathophysiology and General Pathology.

COMPETENCES (RD 1393/2007) // LEARNING OUTCOMES (RD 822/2021)

2141 - Master's Degree in Physiology

- Students should apply acquired knowledge to solve problems in unfamiliar contexts within their field of study, including multidisciplinary scenarios.
- Students should be able to integrate knowledge and address the complexity of making informed judgments based on incomplete or limited information, including reflections on the social and ethical responsibilities associated with the application of their knowledge and judgments.
- Students should communicate conclusions and underlying knowledge clearly and unambiguously to both specialized and non-specialized audiences.
- Students should demonstrate self-directed learning skills for continued academic growth.
- Students should possess and understand foundational knowledge that enables original thinking and research in the field.
- Know how to write and prepare presentations to present and defend them later.
- Search, order, analyze and synthesize scientific information (databases, scientific articles, bibliographic repertoires), selecting the pertinent to focus current knowledge on a topic of scientific interest in Physiology.
- Assess the need to complete the scientific training, in languages, computer science, ethics, etc., attending conferences or courses and/or carrying out complementary activities, self-evaluating the contribution that the performance of these activities implies for their comprehensive training.
- Manage the basic concepts of oxidative stress and antioxidants, identifying the bases of related cellular processes, in order to solve problems of redox physiology in the healthy organism and in the pathophysiology associated with the presence of free radicals.

LEARNING OUTCOMES (RD 1393/2007) // NO CONTENT (RD 822/2021)

To know the definition of free radical and the major free radicals in Biomedicine



To know the concept of oxidative stress and its biological markers

To know the role of free radicals, oxidative stress and redox signalling in cell death by necrosis and apoptosis

To know the role of free radicals, oxidative stress and redox signaling in Physiology, especially in physical exercise, and in Pathophysiology, particularly in the molecular basis of neurodegenerative diseases, diabetes, and cancer as well as in acute and chronic inflammatory processes.

To know the possible benefits of the administration of antioxidants in the treatment and prevention of diseases and their limitations.

DESCRIPTION OF CONTENTS

1. Biomarkers of oxidative stress

The most sensitive and easy to use biomarkers to detect the presence of oxidative stress in biological samples will be shown. It will be explained which are the most appropriate and updated techniques to measure those biomarkers, their limitations and how to interpret their changes.

2. Role of reactive oxygen and nitrogen species in cell death

The mechanisms involved in cell death by apoptosis and necrosis in which free radicals participate through redox signaling or oxidative and nitrosative stress will be described.

3. Role of free radicals, oxidative stress and redox signaling in Physiology

The important role of free radicals and redox signaling in a variety of physiological processes, such as fetal-to-neonatal transition, physical exercise, and aging will be shown. Emphasis will be given to the benefit of redox signaling as adaptive mechanism during sport training.

4. Role of free radicals, oxidative stress and redox signaling in Pathophysiology

The key role of oxidative stress in the molecular basis of neurodegenerative diseases, such as Alzheimer, as well as in acute and chronic inflammatory disorders, such as acute pancreatitis and liver cirrhosis will be shown.

5. Possible benefit of antioxidant administration in the treatment and also in the prevention of diseases and their limitations.

The most widely used exogen antioxidants and their mechanism of action, with special emphasis in their direct and indirect effects as well as in their action on endogen antioxidants will be explained. It will be shown when it may be beneficial the administration of antioxidants, and when blockade of the redox signaling by antioxidants may abrogate the protective adaptive mechanisms. In addition, possible detrimental effects of antioxidants that would limit their therapeutic potential will be dealt with.

**WORKLOAD**

ACTIVITY	Hours	% To be attended
Theory classes	24,00	100
Tutorials	3,00	100
Other activities	2,00	100
Development of individual work	20,00	0
Study and independent work	15,00	0
Readings supplementary material	5,00	0
Preparation of evaluation activities	15,00	0
Preparing lectures	6,00	0
Resolution of case studies	10,00	0
TOTAL	100,00	

TEACHING METHODOLOGY

- Theoretical lessons of master lectures with active participation
- Conferences of scientists with great expertise in the field
- Round table and discussion on the findings presented in the course.
- In person and online tutorials with professors

EVALUATION**Evaluation system:**

-Written exam consisting of short and/or development questions and/or preparation of an individual report related to the subject: evaluation up to 10 points.

Minimum passing grade: 5 points.

REFERENCES

**Basic**

- Rius-Pérez S, Pérez S, Toledano MB, Sastre J. p53 drives necroptosis via downregulation of sulfiredoxin and peroxiredoxin 3. *Redox Biol.* 2022;56:102423.
- Gomez-Cabrera MC; Carretero A; Millan-Domingo F; Garcia-Dominguez E; Correas AG; Olasso-Gonzalez G; Viña J. Redox-related biomarkers in physical exercise. *Redox Biology.* 2021.; 42: 101956.
- Rius-Pérez S, Pérez S, Martí-Andrés P, Monsalve M, Sastre J. Nuclear Factor Kappa B Signaling Complexes in Acute Inflammation. *Antioxid Redox Signal.* 2020; 33(3):145-165.
- Gomez Cabrera, M.C.; Arc-Chagnaud, Coralie; Salvador Pascual, A.; Brioché, T.; Chopard, A.; Olasso González, Gloria; Viña Ribes, José. Redox modulation of muscle mass and function. *Redox Biology.* 2020; 35: 101531.
- Viña J; Olasso-Gonzalez G; Arc-Chagnaud C; De la Rosa A; Gomez-Cabrera MC. Modulating Oxidant Levels to Promote Healthy Aging. *Antioxidants & Redox Signaling* 2020; 33(8): 570-579.
- Pamplona R; Borrás C; Jové M; Pradas I; Ferrer I; Viña J. Redox lipidomics to better understand brain aging and function. *Free Radical Biology and Medicine.* 2019; 144:310-321.
- Viña J; Borrás C; Gomez-Cabrera MC. A free radical theory of frailty. *Free Radical Biology and Medicine.* 2018; 124:358-363.
- Pérez S, Taléns-Visconti R, Rius-Pérez S, Finamor I, Sastre J. Redox signaling in the gastrointestinal tract. *Free Radic Biol Med.* 2017;104:75-103.
- Nóbrega-Pereira S; Fernandez-Marcos PJ; Brioché T; Gomez-Cabrera MC; Salvador-Pascual A; Flores JM; Viña J; Serrano M. G6PD protects from oxidative damage and improves healthspan in mice. *Nature Communications.* 2016; 1: 1-9.
- Markovic J, García-Gimenez JL, Gimeno A, Viña J, Pallardó FV. Role of glutathione in cell nucleus. *Free Radic Res.* 2010;44(7):721-33.
- Borrás, C.; Gambini, J.; Gómez-Cabrera, M.C.; Sastre, J.; Pallardó, F.V.; Mann, G.E.; Viña, J. Genistein, a soy isoflavone, up-regulates expression of antioxidant genes: involvement of estrogen receptors, ERK1/2, and NFkB. *Faseb Journal.* 2006; 20(12):2136-8.
- Sastre, J.; Martín, J.A.; Gomez-Cabrera, M.C.; Pereda, J.; Borrás, C.; Pallardo, F.V.; Vina, J. Age-associated oxidative damage leads to absence of gamma-cystathionase in over 50% of rat lenses: relevance in cataractogenesis. *Free Radical Biology and Medicine.* 2005; 38(5): 575-582.

Additional

- Borrás C, Gómez-Cabrera MC, Viña J. The dual role of p53: DNA protection and antioxidant. *Free Radic Res.* 2011;45(6):643-52.
- Gomez-Cabrera MC, Viña J, Ji LL. Interplay of oxidants and antioxidants during exercise: implications for muscle health. *Phys Sports Med.* 2009 Dec;37(4):116-23.



- Mas-Bargues C, Viña-Almunia J, Inglés M, Sanz-Ros J, Gambini J, Ibáñez-Cabellos JS, García-Giménez JL, Viña J, Borrás C. Role of p16(INK4a) and BMI-1 in oxidative stress-induced premature senescence in human dental pulp stem cells. *Redox Biol.* 2017;12:690-698.
- Matheu A, Maraver A, Klatt P, Flores I, Garcia-Cao I, Borrás C, Flores JM, Viña J, Blasco MA, Serrano M. Delayed ageing through damage protection by the Arf/p53 pathway. *Nature.* 2007;448(7151):375-9.
- Nascimento CM, Ingles M, Salvador-Pascual A, Cominetti MR, Gomez-Cabrera MC, Viña J. Sarcopenia, frailty and their prevention by exercise. *Free Radic Biol Med.* 2019 20;132:42-49.
- Pallardó FV, Markovic J, García JL, Viña J. Role of nuclear glutathione as a key regulator of cell proliferation. *Mol Aspects Med.* 2009;30(1-2):77-85.
- Pérez S, Pereda J, Sabater L, Sastre J. Pancreatic ascites hemoglobin contributes to the systemic response in acute pancreatitis. *Free Radic Biol Med.* 2015;81:145-55.
- Pérez S, Rius-Pérez S, Tormos AM, Finamor I, Nebreda ÁR, Taléns-Visconti R, Sastre J. Age-dependent regulation of antioxidant genes by p38 MAPK in the liver. *Redox Biol.* 2018;16:276-284.
- Quintana-Cabrera R, Fernández-Fernández S, Bobo-Jimenez V, Escobar J, Sastre J, Almeida A, Bolaños JP. gamma-Glutamylcysteine replaces glutathione on reactive oxygen species detoxification and neuroprotection. *Nature Comm.* 2012; 6(3):718.
- Rius-Pérez S, Pérez S, Torres-Cuevas I, Martí-Andrés P, Taléns-Visconti R, Paradela A, Guerrero L, Franco L, López-Rodas G, Torres L, Corrales F, Sastre J. Blockade of the trans-sulfuration pathway in acute pancreatitis due to nitration of cystathionine -synthase. *Redox Biol.* 2020 Jan;28:101324.
- Romagnoli M, Gomez-Cabrera MC, Perrelli MG, Biasi F, Pallardó FV, Sastre J, Poli G, Viña J. Xanthine oxidase-induced oxidative stress causes activation of NF-kappaB and inflammation in the liver of type I diabetic rats. *Free Radic Biol Med.* 2010;49(2):171-7.
- Yeo D, Kang C, Gomez-Cabrera MC, Vina J, Ji LL. Intensified mitophagy in skeletal muscle with aging is downregulated by PGC-1alpha overexpression in vivo. *Free Radic Biol Med.* 2019;130:361-368.