

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

|                      |   |
|----------------------|---|
| <b>Code</b>          | 43102   |
| <b>Name</b>          | Integrating metabolic, nutrition and therapy: The example of arginine |
| <b>Cycle</b>         | Master's degree   |
| <b>ECTS Credits</b>  | 4.5   |
| <b>Academic year</b> | 2021 - 2022   |

**Study (s)**

| <b>Degree</b>   | <b>Center</b>                  | <b>Acad. year</b> | <b>Period</b> |
|---|--------------------------------|-------------------|---------------|
| 2142 - M.U. en Aproximaciones Moleculares CC Salud 12-V.2 | Faculty of Biological Sciences | 1                 | Second term   |

**Subject-matter**

| <b>Degree</b>   | <b>Subject-matter</b>                    | <b>Character</b> |
|---|--|------------------|
| 2142 - M.U. en Aproximaciones Moleculares CC Salud 12-V.2 | 2 - Metabolic regulation and integration | Obligatory       |

**Coordination**

| <b>Name</b>                   | <b>Department</b>                       |
|-------------------------------|---|
| ALONSO IGLESIAS, EULALIA      | 30 - Biochemistry and Molecular Biology |
| O'CONNOR BLASCO, JOSE ENRIQUE | 30 - Biochemistry and Molecular Biology |

**SUMMARY**

In recent years, remarkable progress and development of analytical techniques has greatly supplemented our vision of metabolism. Becoming ever more evident principles that guide our organic functioning: integration, utilization and economics. From a limited number of biomolecules, and thanks to the clustering and partitioning enzyme, our body is able to synthesize a vast diversity of metabolites that enable their functioning and adaptation to different pathophysiological situations.

In this context we must frame the renewed interest in the analysis of metabolism. Together with genomics and proteomics, metabolomics information provided by it is essential to understand the basis of our performance (base rate), and analyze their possible answers, among others, against nutritional or pharmacological interventions (interest charged).

In the course "Integrating Metabolism, Nutrition and Therapy", the student will become familiar with these principles on the subject matter of arginine metabolism. Arginine is an amino acid extraordinarily



versatile protein for which have been discovered in recent years in key metabolic fates organic operation. In fact, many of its derived metabolites (nitric oxide, polyamines) are involved in such important processes such as growth, differentiation, proliferation and cell death, often with dual or conflicting roles.

Furthermore, it was recently demonstrated a close relationship between arginine metabolism and oxidative stress, and both processes alterations in numerous pathologies are highly prevalent diseases as cardiovascular risk. Since arginine is a common component of the diet, these results have opened the door to the analysis of its use in the prevention and / or therapy of these diseases as well as in the improvement and control of other pathophysiological processes.

## PREVIOUS KNOWLEDGE

### Relationship to other subjects of the same degree

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

### Other requirements

none

## OUTCOMES

### 2142 - M.U. en Aproximaciones Moleculares CC Salud 12-V.2

- 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.
- Conocer en profundidad y comprender la organización a nivel molecular de células, sistemas y procesos de relevancia en las Ciencias de la Salud.
- Conocer en profundidad y comprender las bases moleculares de la enfermedad.
- Conocer en profundidad y comprender las metodologías de investigación básica aplicables a las Ciencias de la Salud.
- Tener capacidad de analizar y sintetizar un problema.



- Tener capacidad de comunicación oral y escrita en una segunda lengua científica.
- Tener capacidad de trabajar en equipo
- Conocer, comprender y aplicar en la práctica las técnicas de estudio de la Integración Metabólica en Nutrición y Terapia en situaciones relacionadas con la investigación básica y clínica.
- Aprender a identificar, manejar y presentar adecuadamente en informes y exposiciones públicas, conocimientos existentes sobre la Integración Metabólica en Nutrición y Terapia, usando como vehículo la lengua inglesa.
- Aprender a identificar, manejar y presentar adecuadamente en informes y exposiciones públicas, conocimientos existentes sobre aspectos básicos y clínicos de señalización intercelular e intracelular, usando como vehículo la lengua inglesa.

## LEARNING OUTCOMES

1. To know and to understand the basic concepts and applications in basic and clinical research of arginine metabolism.
2. To know, to understand and to apply in practice the knowledge on the metabolism of arginine in particular, and metabolomics in general situations related to basic and clinical research, particularly in the area of nutrition.
3. Learn to identify, to manage and to present reports and statements properly public knowledge on the metabolism of arginine, using the English language as a vehicle.

## DESCRIPTION OF CONTENTS

### 1. General overview of metabolism of arginine: Arginine in its metabolic and physiological context

Overview of course content. Introduction to the arginine metabolic versatility, its origins and destinations, biochemical and metabolic importance of its metabolites, physiological and pathological importance. Current research interests and future potential related to arginine

### 2. Arginine biosynthesis in mammals: Nutritional Importance of arginine

Analysis of the origins of arginine in mammals: nutritional and endogenous biosynthesis. Metabolic pathways, enzymes and organs involved. Importance of arginine intake and metabolic conditioning: contrasting experimental results, critical analysis and methodological

### 3. Arginine and urea cycle



Analysis of the role of arginine in the detoxification of ammonia in mammals (Urea Cycle): metabolic pathway enzymes and organs involved. Arginine as an intermediary and cycle regulator. Metabolic Effects of arginine intake in performance: contrasting experimental results, critical analysis and methodological, pathophysiological and referrals

#### **4. Arginine and polyamine synthesis**

Overview and particular analysis and derivation of arginine metabolism towards polyamine biosynthesis: metabolic pathways, enzymes and organs involved. Functions and importance of polyamine homeostasis. Circulating levels of polyamines as pathophysiological indicators: contrasting experimental results, critical analysis and methodological.

#### **5. Arginine and nitric oxide.**

Arginine as a substrate precursor of nitric oxide (NO): enzymology of NO synthesis and metabolic and physiological importance of NO. Functions and relevance of NO homeostasis. The dietary content of arginine as metabolic conditioning of NO synthesis. Assessment of endogenous NO synthesis: indicators, contrasting experimental results, critical analysis and methodological and pathophysiological implications.

#### **6. Arginine and creatine synthesis. Arginine and releasing hormones**

Arginine as a substrate precursor in the synthesis of creatine metabolic pathway enzymes and organs involved. Metabolic and physiological importance of creatine, and dietary intake of arginine in their biosynthesis. Assessing creatine levels: indicators, contrast experimental results, critical analysis and methodological and pathophysiological implications.

Arginine as secretagogue. Arginine intake, release of hormones and body nutrient homeostasis: indicators, contrast experimental results, critical analysis and methodological and pathophysiological implications.

#### **7. Post-translational Arginylation**

Regulation of protein function by addition of arginine to post-translational level: mechanism, involved enzymes and biochemical and molecular effects. Analysis of specific cases: from particularity to generalization. Contrast experimental results, critical analysis and methodological and pathophysiological implications.

#### **8. Flow regulators elements between different metabolic pathways arginine**

Integrative view of the functionality of arginine metabolism "in vivo". Consideration of the role and importance of additional regulatory elements: arginine transporters and their metabolites (ornithine, polyamines, etc.), Isoenzymes and tissue and cellular localization of the enzymes involved in the different pathways. Relevance of cooperation between organs in the final destinations of arginine.



**9. Antioxidant role of arginine and its metabolites.**

Physiopathological importance of oxidative stress. Antioxidant systems of the organism and oxidative balance. Markers of oxidative damage. Molecular connections between arginine metabolism and oxidative stress: possible mechanisms of the antioxidant action of arginine and its metabolite. Therapeutic possibilities of arginine administration: indicators, contrast of experimental results, critical analysis, and methodological and therapeutic implications.

**10. Potential therapeutic uses of arginine: molecular basis**

Analysis of the molecular basis of potential therapeutic uses of arginine in various pathophysiological conditions: post-trauma recovery, improved immune status, drug transport, impaired oxidative balance and vascular risk diseases (obesity, diabetes, hypertension, hypercholesterolemia, ...). Indicators, contrast of experimental results, critical analysis and methodology, and referral practices

**WORKLOAD**

| ACTIVITY                  | Hours         | % To be attended |
|---------------------------|---------------|------------------|
| Group work                | 15,00         | 100              |
| Theory classes            | 15,00         | 100              |
| Seminars                  | 15,00         | 100              |
| Development of group work | 37,50         | 0                |
| Preparing lectures        | 30,00         | 0                |
| <b>TOTAL</b>              | <b>112,50</b> |                  |

**TEACHING METHODOLOGY**

The subject is devised to be developed in the form of presential and non-presential work. Actual teaching is done through lectures, interactive seminars and tutoring assistance. In the lectures will present an overview of the topic, with special emphasis on the key concepts. At the same meeting it will indicate the most appropriate resources for a deepening of the subject so that students complete their education in the same. In the interactive seminars the teacher and students critically analyze and contrast the methodological aspects and experimental results that support the key concepts of the various topics covered in the course in relation to arginine metabolism and its implications in nutrition and therapy.

**EVALUATION**

Assessment of student learning will be made by assessing the following sections:

- 1) Theoretical exam test type to be held in the classroom. This test will be worth up to 40% of the final grade and will be held at the end of the semester of the academic year in which the course is taught.
- 2) Practical work written and stated about on one of the themes of the course in relation to the metabolism



of arginine and its practical applications in nutrition and therapy. Be worth up to 50% of the final grade.

3) Involvement of the student in the subject, expressed as participation in organized discussions, the answers to the questions asked by professor during the sessions, assistance to personal tutoring and / or any other type of activity carried out by the student in relation to the subject. Of these concepts can be achieved up to 10% of the final grade for the course.

## REFERENCES

### Basic

- Wu G and Morris SM (1998). Arginine metabolism: nitric oxide and beyond. *Biochem J.*, 336:1-17.
- Morris SM (2002). Regulation of enzymes of urea cycle and arginine metabolism. *Annu Rev Nutr.*, 22:87-105.
- Morris SM (2004). Arginine metabolism: enzymology, nutrition, and clinical significance. *J Nutr.*, 134:2743S-2747S.
- McKnight J et al (2010). Beneficial effects of L-arginine on reducing obesity: potential mechanisms and important implications for human health. *Amino Acids*, 39:349-357.
- Morris SM (2006). Arginine beyond protein. *Am J Clin Nutr.*, 83:508S-512S.
- Wallance HM et al (2003). A perspective of polyamine metabolism. *Biochem J.*, 376:1-14.
- Moinard C (2005). Polyamines: metabolism and implications in human diseases. *Clin Nutr.*, 24:184-197.
- Wyss M and Kaddurah-Daouk R (2000) Creatine and creatinine metabolism. *Physiol Rev.*, 80:1107-1213.
- Saha S et al (2011). Posttranslational arginylation as a global biological regulator. *Develop Biol.*, 358 (Volumen 1).
- Proceedings of the 6th amino acid assessment workshop (2007). *J Nutr.*, 137:6S-II
- Stancic A et al (2012). L-Arginine in nutrition: multiple beneficial effects in the etiopathology of diabetes. *J Nutr Therap*, 1:114-131.
- Rath M (2014). Metabolism via arginase or nitric oxide synthase: two competing arginine pathways in macrophages. *Front Immunol*, 5: Article 532.
- Hou Y, Yin Y and Wu G (2015). Dietary essentiality of nutritionally non-essential amino acids for animals and humans. *Exp Biol Med*, 240:997-1007.
- Patel JJ et al (2016) When is it appropriate to use arginine in critical illness?. *Nutr Clin Pract*, 31(4): 438-444.
- LPatel VB, Preedy VR and Rajendram Eds.(2017) Arginine in Clinical Nutrition. ISBN 978-3-319-26007-5.



## ADDENDUM COVID-19

This addendum will only be activated if the health situation requires so and with the prior agreement of the Governing Council

In the event that the health situation so requires:

A) Face-to-face teaching will be replaced by online teaching, through synchronous or asynchronous presentations by teachers of the teaching materials, using the tools made available to teachers and students in the Virtual Classroom.

B) The tutorials will be carried out exclusively telematically.

C) The evaluation of student learning will be carried out in its entirety through continuous evaluation of the knowledge acquired through the performance of group work. The following sections will be valued in the final grade:

1) **Written work and commented presentation in PDF** on one of the topics of the course in relation to arginine metabolism and its practical applications in nutrition and therapy. It will have a value of up to 50% of the final grade.

2) **Project-Work: design of a product based on arginine** (or some of its metabolites) with potential application in the field of nutrition and / or therapy. It will have a value of up to 40% of the final grade.

3) **Ability to approach**, through specific questions and their resolution, the essential aspects of arginine metabolism. It will have a value of up to 10% of the final grade.