# EYES Research Observership Program

## Maimonides Biomedical Research Institute of Cordoba (IMIBIC)

**Research overview**:
OncObesity and Metabolism Group is a basic-clinical multidisciplinary group composed of Postdocs researchers, PhD students, clinicians and laboratory technicians experts in different areas of the Biomedicine field.

We focus on the study of cellular, molecular and pathophysiological bases that underlie the development and progression of metabolic diseases (such as obesity and diabetes), tumor pathologies and cancer and, on the pathophysiological association and interaction between both pathologies. More specifically, we have a special interest in the study of the function of some endocrine-metabolic factors (hormonal, inflammatory and lipidic systems, chemokines, miRNAs, etc), as well as the molecular and cellular mechanisms underlying in the pathophysiological relationship between obesity and cancer, such as the machineries that control the expression and secretion of inflammatory components (inflammasome), regulators of the senescence-associated secretory phenotype (SASP), factors associated with the regulation of the expression and secretion of miRNAs (DROSHA, DICER, etc.) and extracellular vesicles, as well as machineries and factors that control the splicing process [spliceosome and non-sense mediated mRNA decay (NSMD) and related factors/variants], etc.

The different research lines of our group have as a common aim: the identification of new diagnostic, prognostic and therapeutic opportunities in the interaction between metabolic dysregulations (mainly obesity) and tumoral pathologies, in order to promote their transfer to the Society and improve the Public Health Systems.

**Research topics:**
Our research is based on reaching four different goals:

1) Identification of key endocrine-metabolic factors in the pathophysiological interaction between tumoral pathologies (prostate, liver, brain cancer, etc.) and metabolic dysregulations (obesity, diabetes, etc.)
2) Study of novel cellular and molecular mechanisms involved in the development, progression and aggressiveness of endocrine-metabolic tumoral pathologies
3) Identification of new biomarkers associated to the diagnosis, prognosis, aggressiveness and resistance to drugs in endocrine-metabolic tumoral pathologies

4) Generation and characterization of preclinical animal models to develop new diagnostic, prognostic and therapeutic tools in the study of the pathophysiological association between obesity and cancer

**Techniques:**
To make science happen, we employ many different experimental techniques which include:

- In vitro primary cell culture and cell lines (including functional assays such as determination of cell viability, apoptosis, clonogenic assay, etc.)
- Experimental manipulation of mouse models
- Protein analyses by ELISA
- Flow cytometry
- DNA, RNA, and protein extraction from human/mouse tissues and cells
- Immunohistochemistry and immunofluorescence
- Analysis of gene expression by microfluidic-base qPCR array
- Analysis and integration of clinical and molecular data

**Contacts:**
Prof Raúl M. Luque, raul.luque@uco.es
Antonio J. Montero, b4mohia@uco.es

For more information, please check:

- Website: https://www.imibic.org/grupo/52
- Twitter: @OncMet27

**Selected publications**:

1. Fuentes-Fayos, AC; Perez-Gomez, JM; G-Garcia, ME; et al; Luque, RM. 2022. SF3B1 inhibition disrupts malignancy and prolongs survival in glioblastoma patients through BCL2L1 splicing and mTOR/beta-catenin pathways imbalances J. Exp. Clin. Cancer Res.41. https://doi.org/10.1186/s13046-022-02241-4
2. Fuentes-Fayos, AC; G-Garcia, ME; Perez-Gomez, JM; et al; Luque, RM. 2022. Somatostatin Receptor Splicing Variant sst5TMD4 Overexpression in Glioblastoma Is Associated with Poor Survival, Increased Aggressiveness Features, and Somatostatin Analogs Resistance Int. J. Mol. Sci.23. https://doi.org/10.3390/ijms23031143
3. Jiménez-Vacas JM; Montero-Hidalgo AJ; Gómez-Gómez E; et al; Luque RM. 2022. Tumor suppressor role of RBM22 in prostate cancer acting as a dual-factor regulating alternative splicing and transcription of key oncogenic genes.Translational research : the journal of laboratory and clinical medicine. ISSN 1931-5244. https://doi.org/10.1016/j.trsl.2022.08.016
4. Fuentes-Fayos, AC; Luque, RM. 2021. A novel human tumoroid 3D model of sustained ACTH-secreting cell cultures to study critically needed therapies for Cushing's disease EBioMedicine. 67. ISSN 2352-3964. https://doi.org/10.1016/j.ebiom.2021.103368
5. Jimenez-Vacas, JM; Montero-Hidalgo, AJ; Gomez-Gomez, E; et al; Luque, RM. 2021. In1-Ghrelin Splicing Variant as a Key Element in the Pathophysiological Association Between Obesity and Prostate Cancer JCEM. 106. ISSN 0021-972X. https://doi.org/10.1210/clinem/dgab516
6. Jiménez-Vacas JM; Herrero-Aguayo V; Montero-Hidalgo AJ; et al; Luque RM. 2020. Clinical, cellular and molecular evidence of the additive antitumor effects of biguanides

and statins in prostate cancer.J Clin Endocrinol Metab. https://doi.org/10.1210/clinem/dgaa877
7. Jiménez-Vacas JM; Herrero-Aguayo V; Montero-Hidalgo AJ; et al; Luque RM. 2020. Dysregulation of the splicing machinery is directly associated to aggressiveness of prostate cancer.EBioMedicine. https://doi.org/10.1016/j.ebiom.2019.11.008
8. Herrero-Aguayo V; Jiménez-Vacas JM; Sáez-Martínez P; et al; Luque RM. 2020. Influence of obesity in the miRNome: miR-4454, a key regulator of insulin response via splicing modulation in prostate.J Clin Endocrinol Metab. https://doi.org/10.1210/clinem/dgaa580
9. Fuentes-Fayos AC; Vázquez-Borrego M; Jiménez-Vacas JM; et al; Luque RM. 2020. Splicing machinery dysregulation drives glioblastoma aggressiveness: oncogenic role of SRSF3.Brain. https://doi.org/10.1093/brain/awaa273
10. Vázquez-Borrego MC; Gupta V; Ibáñez-Costa A; et al; Luque RM. 2019. A Somatostatin Receptor Subtype-3 (SST<sub>3</sub>) Peptide Agonist Shows Antitumor Effects in Experimental Models of Nonfunctioning Pituitary Tumors.Clinical cancer research : an official journal of the American Association for Cancer Research. 26, pp.957-969. ISSN 1078-0432. https://doi.org/10.1158/1078-0432.CCR-19-2154
11. del Rio-Moreno, M; Alors-Perez, E; Gonzalez-Rubio, S; et al; Luque, RM. 2019. Dysregulation of the Splicing Machinery Is Associated to the Development of Nonalcoholic Fatty Liver Disease JCEM. 104. ISSN 0021-972X. WOS (1) https://doi.org/10.1210/jc.2019-00021
12. Jimenez-Vacas, JM; Herrero-Aguayo, V; Gomez-Gomez, E; et al; Luque, RM. 2019. Spliceosome component SF3B1 as novel prognostic biomarker and therapeutic target for prostate cancer.Translational Research. WOS (3) https://doi.org/10.1016/j.trsl.2019.07.001
13. Gahete MD; Del Rio-Moreno M; Camargo A; et al; Luque RM. 2018. Changes in Splicing Machinery Components Influence, Precede, and Early Predict the Development of Type 2 Diabetes: From the CORDIOPREV Study. EBioMedicine. https://doi.org/10.1016/j.ebiom.2018.10.056.
14. Montero-Hidalgo, AJ; Perez-Gomez, JM; Gahete, MD; Jimenez-Vacas, JM; Luque, RM. 2022. Alternative splicing in bladder cancer: potential strategies for cancer diagnosis, prognosis, and treatment WILEY INTERDISCIPLINARY REVIEWS-RNA. ISSN 1757-7004. https://doi.org/10.1002/wrna.1760