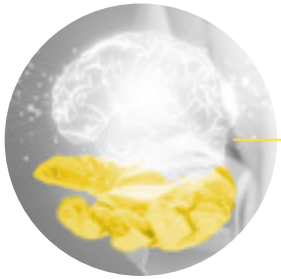


3.1.3 Neuroprotective Strategies in Neurodegenerative Diseases Group

Publications: 14
Q1: 14

COMPOSITION

Ana Isabel Rojo Sanchís. Profesora Contratado Doctor. Dpto. Bioquímica. Facultad Medicina. Universidad Autónoma de Madrid

Daniel Carnicero Senabre. Investigadora Predoctoral. Universidad Autónoma de Madrid

Eduardo Cazalla Ibáñez. Investigadora Predoctoral. Universidad Autónoma de Madrid

Antonio Cuadrado Pastor. Catedrático. Dpto. Bioquímica. Facultad Medicina. Universidad Autónoma de Madrid

María Isabel Escoll Guerrero. Investigadora Postdoctoral. CIBERNED

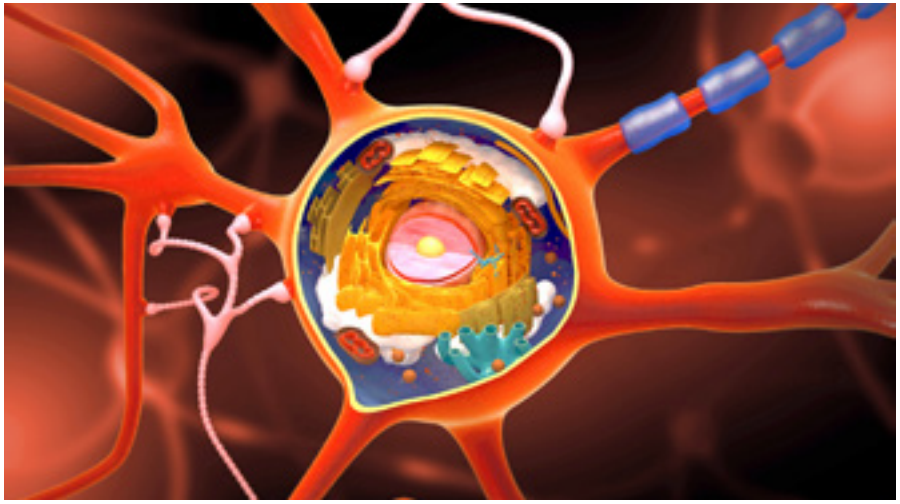
Raquel Fernández Ginés. Investigadora Predoctoral. Universidad Autónoma de Madrid

Ángel Juan García Yagüe. Investigador Postdoctoral. Universidad Autónoma de Madrid

José Jiménez Villegas. Investigador Predoctoral. Universidad Autónoma de Madrid

Ángela Martínez Valverde. Cientifico titular CSIC. IIb "Alberto Sols"/UAM-CISC

Patricia Rada Llano. Investigadora Postdoctoral. IIb "Alberto Sols"/UAM-CISC



STRATEGIC OBJECTIVE

Oxidative stress is a key element in the aetiopathogenesis of neurodegenerative diseases and their comorbidities. Our laboratory studies the antioxidant protection mechanisms activated by extracellular signals and how this response ould be regulated pharmacologically to provide a therapeutic benefit in these diseases.

To meet these two objectives, we are studying signalling pathways that regulate antioxidant metabolism and provide a general protective response. An important finding of this group was the observation that the PI3K/AKT/GSK-3 survival pathway regulates the transcription factor NRF2, guardian of cellular redox homeostasis, that provides protection against oxidative, inflammatory and proteotoxic stress.

For the past year we have been working on the validation this transcription factor as a new therapeutic target to modify progression of Parkinson's and Alzheimer's disease as well co-morbid retinopathy and type II diabetes.

RESEARCH LINES

- Role of oxidative stress in neuronal death and neuroinflammation in neurodegenerative diseases.
- Validation of NRF2 as a new therapeutic target in neurodegenerative diseases.
- Use of NRF2 transcriptional signature as a biomarker of prognosis, progression and therapeutic efficacy.
- Identification of NRF2 activating compounds by inhibiting their interaction with ß-TrCP.
- Relevance of NRF2 transcriptional signature in altered molecular processes in ALS models.
- Molecular basis of the role of Nrf2 in type 2 diabetes and its complications (diabetic retinopathy and nephropathy).

RESEARCH ACTIVITY

Doctoral theses

Barahona Sanz I. PTPN1 delection protects oval cells against lipoapotosis by targeting cellular processes that favour lipit droplet formation and dynamics[dissertation]. Madrid: UAM: 2022(27/01/2022).

Directors: Martínez Valverde AM, Valdecantos Jiménez de Andrade MP.

European Mention

Duarte Flórez P. Nuevos inductores de NRF2 e inhibidores selectivos de MAO-B para el tratamiento de la enfermedad de Parkinson[dissertation]. Madrid: UAM: 2022(19/09/2022).

Directors: León Martínez R, Cuadrado Pastor A.

Fernández Ginés R. Desarrollo de nuevos moduladores de actividad del factor de transcripción NRF2.[dissertation]. Madrid: UAM: 2022(24/11/2022).

Directors: Cuadrado Pastor A, Rojo Sanchís AI.

Master theses

Cazalla Ibáñez E. Role of transcription factor NRF2 in the regulation of the Blood-Brain Barrier component TIE2 receptor[dissertation]. Madrid: UAM: 2022(08/07/2022).

Directors: Cuadrado Pastor A, García-Yagüe AJ.

Publications

- Cuadrado A. Brain-Protective Mechanisms of Transcription Factor NRF2: Toward a Common Strategy for Neurodegenerative Diseases. Annu Rev Pharmacol. 2022; 62: 255-77. Review. IF: 12.5; D1
- Cucos CA, Milanesi E, Dobre M, Musat IA, Manda G, Cuadrado A. Altered blood and brain expression of inflammation and redox genes in Alzheimer's Disease, common to APP(V717I) x TAU(P301L) mice and patients. Int J Mol Sci. 2022; 23(10): 5799. Article. IF: 5.6; Q1
- del Hierro JN, Cantero-Bahillo E, Fernández-Felipe MT, García-Risco MR, Fornari T, Rada P, Doblado L, Ferreira V, Hitos AB, Valverde AM, Monsalve M, Martín D. Effects of a mealworm (Tenebrio molitor) extract on metabolic syndrome-related pathologies: In vitro insulin sensitivity, inflammatory response, hypolipidemic activity and oxidative stress. Insects. 2022; 13(10): 896. Article. IF: 3; Q1
- Duarte P, Michalska P, Crisman E, Cuadrado A, León R. Novel series of dual NRF2 inducers and selective MAO-B inhibitors for the treatment of Parkinson's disease. Antioxidants. 2022; 11(2): 247. Article. IF: 7; D1
- Fernández-Ginés R, Encinar JA, Hayes JD, Oliva B, Rodríguez-Franco MI, Rojo AI, Cuadrado A. An inhibitor of interaction between the transcription factor NRF2 and the E3 ubiquitin ligase adapter beta-TrCP delivers anti-inflammatory responses in mouse liver. Redox Biol. 2022; 55: 102396. Article. IF: 11.4; D1
- Ferreira V, Folgueira C, Guillén M, Zubiaur P, Navares M, Sarsenbayeva A, López-Larrubia P, Eriksson JW, Pereira MJ, Abad-Santos F, Sabio G, Rada P, Valverde AM. Modulation of hypothalamic AMPK phosphorylation by olanzapine controls energy balance and body weight. Metabolism. 2022; 137: 155335. Article. IF: 9.8; D1
- Jiménez MTB, Frenis K, Hahad O, Steven S, Cohen G, Cuadrado A, Muenzel T, Daiber A. Protective actions of nuclear factor erythroid 2-related factor 2 (NRF2) and downstream pathways against environmental stressors. Free Radical Bio Med. 2022; 187: 72-91. Review. IF: 7.4; Q1
- Jiménez-Villegas J, Kirby J, Mata A, Cadenas S, Turner MR, Malaspina A, Shaw PJ, Cuadrado A, Rojo AI. Dipeptide repeat pathology in C9orf72-ALS is associated with redox, mitochondrial and NRF2 pathway imbalance. Antioxidants. 2022; 11(10): 1897. Article. IF: 7; D1
- Kopacz A, Rojo AI, Patibandla C, Lastra-Martínez D, Piechota-Polanczyk A, Kloska D, Jozkowicz A, Sutherland C, Cuadrado A, Grochot-Przeczek A. Overlooked and valuable facts to know in the NRF2/KEAP1 field. Free Radical Bio Med. 2022; 192: 37-49. Review. IF: 7.4; Q1
- Lastra D, Escoll M, Cuadrado A. Transcription factor NRF2 participates in cell cycle progression at the level of G1/S and mitotic checkpoints. Antioxidants. 2022; 11(5): 946. Article. IF: 7; D1
- Manda G, Milanesi E, Genc S, Niculite CM, Neagoe IV, Tastan B, Dragnea EM, Cuadrado A. Pros and cons of NRF2 activation as adjunctive therapy in rheumatoid arthritis. Free Radical Bio Med. 2022; 190: 179-201. Article. IF: 7.4; Q1
- Srivastava R, Fernández-Ginés R, Encinar JA, Cuadrado A, Wells G. The current status and future prospects for therapeutic targeting of KEAP1-NRF2 and beta-TrCP-NRF2 interactions in cancer chemoresistance. Free Radical Bio Med. 2022; 192: 246-60. Review. IF: 7.4; Q1
- Uribe-Carretero E, Martínez-Chacón G, Yakhine-Diop SMS, Duque-González G, Rodríguez-Arribas M, Alegre-Cortes E, Paredes-Barquero M, Canales-Cortes S, Pizarro-Estrella E, Cuadrado A, González-Polo RA, Fuentes JM, Niso-Santano M. Loss of KEAP1 causes an accumulation of nondegradative Organelles. Antioxidants. 2022; 11(7): 1398. Article. IF: 7; D1
- Val-Blasco A, Prieto P, Jaen RI, Gil-Fernández M, Pajares M, Domenech N, Terron V, Tamayo M, Jorge I, Vázquez J, Bueno-Sen A, Vallejo-Cremades MT, Pombo-Otero J, Sánchez-García S, Ruiz-Hurtado G, Gómez AM, Zaragoza C, Crespo-Leiro MG, López-Collazo E, Cuadrado A, Delgado C, Boscá L, Fernández-Velasco M. Specialized proresolving mediators protect against experimental autoimmune myocarditis by modulating Ca2+ handling and NRF2 activation. JACC Basic Transl Sci. 2022; 7(6): 544-60. Article. IF: 9.7; D1

Research projects

Cuadrado Pastor A, Seabra M. NRF2 as a novel therapeutic target in age-related macular degeneratio (HR22-00569). Fundación La Caixa. 2022-2026.

Managment centre: UAM

Cuadrado Pastor A. Activation of NRF2 by 6-MISTC, role in AD (2021/0175). Kiinjirushi Ltd. Co. 2021-2023.

Managment centre: Fundación UAM

Cuadrado Pastor A. Desarrollo de fármacos activadores de NRF2 para terapias innovadoras de la enfermedad de Alzheimer - GT2 (2018/00050/001). CM. 2018-2022.

Managment centre: UAM

Cuadrado Pastor A. Investigación traslacional sobre la regulación farmacológica NRF2 en enfermedades no transmisibles (10.2J.01.03). MICIN. 2020-2022.

Managment centre: UAM

Cuadrado Pastros A, Rojo Sanchís AI. Desarrollo de nuevos fármacos antiinflamatorios basados en la activación del factor de transcripción NRF2 (PDC2021-121421-I00). Agencia Estatal de Investigación. 2021-2023.

Managment centre: UAM

Cuadrado Pastros A, Rojo Sanchís AI. El factor de transcripción NRF2 en la patofisiología de la enfermedad de Alzheimer (1004020167). MICIN. 2020-2023.

Managment centre: UAM

Martínez Valverde A. Extenting the knowledge of the cellular and molecular mediators in the progression and treatment of non-alcoholic fatty liver disease linked to obesity (FATLiV). (RTI2018-094052-B-I00). MICIN. 2019-2022.

Managment centre: CSIC

Martínez Valverde A. Extracelular vesicles: new insights into their role in liver-pancreas interactome in T2D. European Association for the Study of Diabetes. 2021-2023.

Managment centre: CIBER

Martínez Valverde A. Identification of metabolic biomarkers for chronic diseaseds and treatmentsIdentificacion de biomarcadores metabolicos para enfermedades cronicas y sus tratamientos. (EIN2020-112263). MICIN. 2021-2022.

Managment centre: CSIC

Martínez Valverde A. Mecanismos moleculares y comunicación intertisular en la resistencia a la insulina (B2017/BMD-3684 MOIR2-CM). CM. 2018-2022.

Managment centre: CISC

Martínez Valverde A. New messengers in the interactome of hepatic and extrahepatic cells in non-alcoholic fatty liver disease with diagnostic value. Fundación Ramón Areces. 2019-2022.

Managment centre: CSIC

Rojo Sanchís AI. NRF2: Biomarcador y evaluación como diana terapéutica para la esclerosis lateral amiotrófica (ref-P024.FTPGB 2018). Fundación Tatiana Pérez de Guzmán el Bueno. 2018-2022.

Managment centre: UAM

Cibers and Retics

Cuadrado Pastor A. Centro de Investigación Biomédica en Enfermedades Neurodegenerativas. (CB06/05/0010). ISCIII. (31/12/2022).

Managment centre: UAM

Martínez Valverde A. Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas. (CB07/08/0033). ISCIII. (31/12/2022).

Managment centre: CSIC

Cuadrado Pastor A, Rojo Sanchís AI. Bench to bedside transition for pharmacological regulation of NRF2 in noncommunicable diseases (BenBedPhar). (CA20121). EU Cost Actions. (18/10/2025).

Managment centre: Victor Babes Research Institute (Romania)

Patents and trademarks

Cuadrado Pastor A, Innamorato NG, inventors: CSIC, UAM. Use of sulforaphane as supplementary therapy for early-stage neurodegenerative disease. P201231693; 2012 November 06.

León Martínez R, Egea Maíquez J, Buendía Abaitua I, Parada Pérez E, Navarro González de Mesa E, inventors; Fundación para la Investigación Biomédica del Hospital Universitario de La Princesa, UAM, CSIC, DNS NEUROSCIENCE S.A., assignees. Use of 3-(2-isothiocyanatoethyl)-5-methoxy-1H-indole for the treatment of neurodegenerative diseases. P201300667; 2013 July 17.

León Martínez R, Buendía Abaitua I, Navarro González de Mesa E, Michalska P, Gameiro Ros I, López Vivo A, Egea Maíquez J, García López M, García García A, inventors; Fundación para la Investigación Biomédica del Hospital Universitario de La Princesa, UAM, DNS NEUROSCIENCE S.A., assignees. Compounds derived from 3-alkylamine-1H-indolyl acrylate and its use for the treatment of neurodegenerative diseases. P201400810, PCT/ES2015/000139, CA2964309; 2014 October15.

Cuadrado Pastor A, Fernández-Ginés R, León Martínez R, Encinar JA, Rodríguez Franco MI, García López MG, Rojo Sanchís AI, inventors. UAM, CSIC, UMH y Fundación de Investigación Biomédica del Hospital Universitario de la Princesa, assigness. Treatment of NRF2-Related diseases. PCT/2022/382025.1.