



Programul Operational Competitivitate 2014-2020

Axa Prioritară 1 – Cercetare, Dezvoltare Tehnologică și Inovare în Sprijinul Competitivității Economice și Dezvoltării Afacerilor  
Acțiunea 1.1.4 Atragerea de personal cu competențe avansate din străinătate pentru consolidarea capacității de CD

Titlul proiectului: Transfer de cunoștințe în domeniul biologiei redox pentru dezvoltarea de instrumente moleculare avansate în bolile neurodegenerative – semnătura factorului de transcripție Nrf2 pentru diagnostic și terapie” (REDBRAIN)

ID proiect: P37\_732, cod SMIS: 104294

## Publicatii (24)

### Articole cu rezultate originale in studii initiate in cadrul proiectului

- 1 Distinctive Under-Expression Profile of Inflammatory and Redox Genes in the Blood of Elderly Patients with Cardiovascular Disease; Milanese E, Manda G, Dobre M, Codrici E, Neagoe IV, Popescu BO, Bajenaru OA, Spiru L\*, Tudose C, Prada GI, Davidescu EI, Piñol-Ripoll G, Cuadrado A. *J Inflamm Res.* 2021 Feb 18;14:429-442. doi: 10.2147/JIR.S280328. (\***public-private partnership**). **Factor de impact 6.532.** [Link](#)
- 2 Whole blood expression pattern of inflammation and redox genes in mild cognitive; Milanese E, Dobre M, Cucos CA, Rojo AI, Jiménez-Villegas J, Capetillo-Zarate E\*, Matute C, Piñol-Ripoll G, Manda G, Cuadrado A, *Journal of Inflammation Research*, Volume 2021, 14: 6085—6102, doi: 10.2147/JIR.S334337 (\***public-private partnership**). **Factor de impact 6.532.** [Link](#)
- 3 Reduced blood RGS2 expression in mild cognitive impairment patients; Milanese E, Cucos CA, Matias-Guiu JA, Piñol-Ripoll G, Manda G, Dobre M, Cuadrado A, *Frontiers in Aging Neuroscience*, 29 September 2021, doi: 10.3389/fnagi.2021.738244. **Factor de impact 5.750.** [Link](#)
- 4 Sulfiredoxin-1 blood mRNA expression levels negatively correlate with hippocampal atrophy and cognitive decline; Cucos CA, Cracana I\*, Dobre M, Surcel M, Popescu BO, Tudose C, Spiru L, Manda G, Niculescu G, Milanese E, *F1000Res.* 2022 Jan 28;11:114. doi: 10.12688/f1000research.76191.2. (\***public-private partnership**). **Factor de impact 2.297.** [Link](#)
- 5 Viral oncogenesis in tumors of the central nervous system: reality or random association? A retrospective study on archived material; Arsene DE, Milanese E, Dobre M. *J Cell Mol Med.* 2022 Mar;26(5):1413-1420. doi: 10.1111/jcmm.17064. **Factor de impact 5.310.** [Link](#)
- 6 Increased MYD88 blood transcript in a mouse model of Alzheimer’s disease; Cucos CA, Dobre M, Dragnea EM, Manda G, Milanese E, *BMC Neurosci.* 2022 Mar 11;23(1):13. doi: 10.1186/s12868-022-00699-8. **Factor de impact 3.288.** [Link](#)
- 7 Altered Blood and Brain Expression of Inflammation and Redox Genes in Alzheimer's Disease, Common to APPV717I × TAUP301L Mice and Patients; Cucos CA, Milanese E, Dobre M, Musat IA, Manda G, Cuadrado A. *Int J Mol Sci.* 2022 May 21;23(10):5799. doi: 10.3390/ijms23105799. **Factor de impact 5.542.** [Link](#)

## Articole cu rezultate originale generate in studii initiate de alte grupuri de cercetare

- 8 miR-146a and miR-181a are involved in the progression of mild cognitive impairment to Alzheimer's disease; Ansari A, Maffioletti E, Milanese E, Marizzoni M, Frisoni GB, Blin O, Richardson JC, Bordet R, Forloni G, Gennarelli M, Bocchio-Chiavetto L; PharmaCog Consortium. *Neurobiol Aging*, 2019 Oct, 82:102-109. doi: 10.1016/j.neurobiolaging.2019.06.005. [Factor de impact 4.347. Link](#)
- 9 miR-146a Plasma Levels Are Not Altered in Alzheimer's Disease but Correlate With Age and Illness Severity; Maffioletti E, Milanese E, Ansari A, Zanetti O, Galluzzi S, Geroldi C, Gennarelli M, Bocchio-Chiavetto L., *Front Aging Neurosci*, 2020 Jan, 17;11:366. doi: 10.3389/fnagi.2019.00366. [Factor de impact 4.364. Link](#)
- 10 SIRT1, miR-132 and miR-212 link human longevity to Alzheimer's Disease; Hadar A, Milanese E, Walczak M, Puzianowska-Kuznicka M, Kuźnicki J, Squassina A, Niola P, Chillotti C, Attems J, Gozes I, Gurwitz D. *Scientific Reports* 2018, May, 8(1):8465, doi:10.1038/s41598-018-26547-6. [Factor de impact 4.12. Link](#)

## Articole de tip review

1. Oxidative stress and inflammation induced by environmental and psychological stressors: a biomarker perspective; Ghezzi P, Floridi L, Boraschi D, Cuadrado A, Manda G, Levic S, D'Acquisto F, Hamilton A, Athersuch TJ, Selley L. *Antioxidants and Redox Signaling*, May 2017, 28(9):852-872. doi: 10.1089/ars.2017.7147. [Factor de impact 6.73. Link](#)
2. NRF2 deficiency replicates transcriptomic changes in Alzheimer's patients and worsens APP and TAU pathology. Rojo AI, Pajares M, Rada P, Nuñez A, Nevado-Holgado AJ, Killik R, Van Leuven F, Ribe E, Lovestone S, Yamamoto M, Cuadrado A; *Redox Biology*, October 2017, 13:444-451. doi: 10.1016/j.redox.2017.07.006. [Factor de impact 6.760. Link](#)
3. Transcription factor NRF2 as a therapeutic target for degenerative diseases: a systems medicine approach. Cuadrado A, Manda G, Hassan A et al. *Pharmacol Rev*, 2018 Apr, 70(2):348-383. doi: 10.1124/pr.117.014753. [Factor de impact 18.886. Link](#)
4. Activators and inhibitors of NRF2: a review of its clinical development. Robledinos-Antón N, Fernández-Ginés R, Manda G, Cuadrado A; *Oxidative Medicine and Cellular Longevity*, 2019 July, 2019:9372182. doi: 10.1155/2019/9372182. [Factor de impact 4.580. Link](#)
5. Nordihydroguaiaretic acid: from herbal medicine to clinical development for cancer and chronic diseases. *Frontiers in Pharmacology, section Experimental Pharmacology and Drug Discovery*. Manda G, Rojo AI, Martínez-Klimova E, Pedraza-Chaverri J, Cuadrado A; *Front Pharmacol*. 2020 Feb 28;11:151. doi: 10.3389/fphar.2020.00151. [Factor de impact 4.225. Link](#)
6. NRF2 drug repurposing using a question-answer artificial intelligence system. Mickael ME, Pajares M, Enache I, Manda G, Cuadrado A. 2019 Jan, preprint. doi: <https://doi.org/10.1101/594622>. [Link](#)
7. Repurposing Zileuton as a Depression Drug Using an AI and In Vitro Approach. Kubick N, Pajares M, Enache I, Manda G, Mickael ME. *Molecules* 2020, 25(9), 2155; doi: 10.3390/molecules25092155. [Factor de impact 3.267. Link](#)
8. Can Activation of NRF2 Be a Strategy against COVID-19? Cuadrado A, Benito C, Jiménez-Villegas J, Escoll M, Fernández-Ginés R, Garcia Yagüe AJ, Lastra D, Manda G, Pajares M, Rojo AI, Dinkova-Kostova AT. *Trends in Pharmacological Sciences*, 2020 Sep; 41(9): 598–610. doi: 10.1016/j.tips.2020.07.003. [Factor de impact 11.523. Link](#)
9. Neuroinflammation in Parkinson's disease: mechanisms and therapeutic implications; Pajares M, Rojo AI, Manda G, Boscá L, Cuadrado A. *Cells* 2020, 9(7), 1687; doi:10.3390/cells9071687, [Factor de impact 4.366. Link](#)
10. Book chapter "Perspectives on the Clinical Development of NRF2-Targeting Drugs"; Diego L, Fernandez-Gines R, Manda G, Cuadrado A, within the book "Reactive Oxygen Species:

Sources, Targets and Therapeutic Implications”, Handbook of Experimental Pharmacology, Springer Nature, doi: 10.1007/164\_2020\_381. [Link](#)

11. The transcription factor NRF2 shapes the identity of radio-resistant tumor cells; Manda G, Cuadrado A, Journal of Cell Identity, October 20, 2020, vol. 1, p. 0049-0081, doi:10.47570/joci.2020.004. [Link](#)
12. What has single-cell RNA sequencing revealed about microglial neuroimmunology? Kubick N, Henckell Flournoy PC, Klimovich P, Manda G, Mickael ME, Immun Inflamm Dis. 2020 Dec;8(4):825-839. doi: 10.1002/iid3.362. **Factor de impact 2.5.** [Link](#)
13. Drugs Modulating CD4+ T Cells Blood–Brain Barrier Interaction in Alzheimer’s Disease. Kubick N, Henckell Flournoy PC, Enciu AM, Manda G, Mickael ME. *Pharmaceutics*, 12(9), 880, 2020. doi: 10.3390/pharmaceutics12090880. **Factor de impact 4.421.** [Link](#)
14. Pros and cons of NRF2 activation as adjunctive therapy in rheumatoid arthritis. Gina Manda, Elena Milanese, Sermin Genc, Cristina Mariana Niculite, Ionela Victoria Neagoe, Bora Tastan, Elena Mihaela Dragnea, Antonio Cuadrado. *Free Radical Biology & Medicine*. 2022 (In press) **Factor de impact 8.101.**

## Comunicari la manifestari stiintifice (36)

1. NRF2 deficiency in mice replicates transcriptomic alterations found in brain of elderly and Alzheimer’s disease patients and aggravates APP and TAU pathology. Antonio Cuadrado, *EMBO (European Molecular Biology Organization)*, 16-23.07.2017, Sankt Petersburg, Rusia.
2. NRF2 modulates neuroinflammation in Alzheimer’s disease, Antonio Cuadrado. A 47-a Conferință Anuală de Imunologie cu participare internațională, 4-6.10.2017, Bucuresti, Romania.
3. The NRF2-Neuroinflammation Network in Alzheimer’s Disease. Antonio Cuadrado. Conferinta Anuala a INCD „Victor Babes” si al 10-lea Simpozion de Patologie, 23-25.11.2017, Bucuresti, Romania.
4. The transcription factor NRF2: a new brain protective strategy in Alzheimer's disease. Antonio Cuadrado. Seminar organizat de Basque Center for Neurosciences, 25.05.2018, Achucarro Mintegiak, Bilbao, Spania.
5. The role of Nrf2 in neurodegenerative diseases. Antonio Cuadrado, Ana I. Rojo. Workshop - Transcription factor NRF2: New opportunities for pharmaceutical innovations in chronic diseases, 11-13.04.2018, Madrid, Spania.
6. Neuroprotective effects of NRF2 in neurodegeneration. Antonio Cuadrado. International course “Mitochondria and ROS signalling”, 12-14.06.2018, University of Eastern Finland, Kuopio, Finland.
7. Inflammation, oxidative stress and Alzheimer: a preliminary gene expression study. Dobre Maria, Milanese Elena, Manda Gina, Cuadrado Antonio. Aging 2018 – Bordeaux Neurocampus Conferences, 26-28.09.2018, Bordeaux, Franta.
8. Potential role of NRF2 in Alzheimer’s disease as a crucial modulator of the innate immune suppression. Rojo Ana, Milanese Elena, Pajares Marta, Mihai Simona, Surcel Mihaela, Lopez-Colazzo Eduardo, Varel A, Manda Gina, Cuadrado Antonio. Aging 2018 – Bordeaux Neurocampus Conferences, 26-28.09.2018, Bordeaux, Franta.
9. Molecular profiles in Alzheimer disease – The REDBRAIN project after two year. Antonio Cuadrado, Elena Milanese, Michel Edwar Mickael, Bogdan Ovidiu Popescu, Gabriel Prada, Ovidiu Bajenaru, Catalina Tudose, Luiza Spiru, Gina Manda. Sesiunea Stiintifica Anuala a INCD „Victor Babes” si al 11-lea Simpozion National de Patologie, 22-24.11.2018, Bucuresti, Romania.
10. 8 Arm Radial Maze test for assesement of memory performance in Nrf2-/- mice. Grigoras Stefania, Tiron Radu Ioan, Stefan Andreea Elena, Neagoe Ionela Victoria, Enciu Ana-Maria.

Sesiunea Stiintifica Anuala a INCD „Victor Babes” si al 11-lea Simpozion National de Patologie, 22-24.11.2018, Bucuresti, Romania.

11. Age-related gene expression changes: oxidative stress, inflammation, environment and cognition. Elena Milanesi, Maria Dobre, Ionela Victoria Neagoe, Mihaela Surcel, Gheorghita Isvoranu, Bogdan Ovidiu Popescu, Antonio Cuadrado. Sesiunea Stiintifica Anuala a INCD „Victor Babes” si al 11-lea Simpozion National de Patologie, 22-24.11.2018, Bucuresti, Romania.
12. La enfermedad de Alzheimer: de la neurodegeracion a la neuroproteccion. Antonio Cuadrado. Seminariile „Progrese in Biomedicina”, 1.02.2019, Facultatea de Medicina, Ciudad Real, Spania.
13. Transcription factor NRF2 modulates chaperone mediated autophagy. Seminar - Instituto de Investigación Sanitaria “La Paz” (IdiPAZ), 29.04.2019, Madrid, Spain.
14. New advances in the search for beta-TrCP or KEAP1 Protein-Protein Interaction (PPI) inhibitors. Seminar - Department of Pharmacology, Medical College, Autonomous University of Madrid, 15.05.2019, Madrid Spania.
15. Oxidative stress and inflammation gene expression changes in cognitive impairment. Elena Milanesi, Maria Dobre, Bogdan Ovidiu Popescu, Gabriel Prada, Ovidiu Bajenaru, Catalina Tudose, Luiza Spiru, Gina Manda, Antonio Cuadrado. The 44th FEBS Congress, 6-11.07.2019, Krakow, Polonia.
16. Targeting NRF2 for brain protection and monitoring biomarker in Alzheimer’s disease. Antonio Cuadrado, Elena Milanesi, Maria Dobre, Marta Pajares, Bogdan O. Popescu, Ana I. Rojo, Gerard Piñol, Gina Manda. The Environmental Response V /17th JBS Biofrontier Symposium, 12-14.09.2019, Sendai, Japonia.
17. Inflamación y estrés oxidativo en enfermedades neurodegenerativas. Antonio Cuadrado. INNO UAM\_Neuro, 24.10.2019, Madrid Spania.
18. Cognitive evaluation method in NRF2-KO mice using the eight-arm radial maze. Catalina Anca Cucos, Ana-Maria Enciu, Laurențiu Anghelache. Sesiunea Anuala a INCD „Victor Babes” si al 12-lea Simpozion National de Patologie, 21-23.11.2019, București, Romania.
19. Transcriptional signatures of NRF2 and NFkB as blood biomarkers in dementia. A Cuadrado, E. Milanes, M. Dobre, G. Piñol, G. Manda. XL Congreso del Grupo Español de Neurotransmisión y Neuroprotección (GENN), 18-21.12.2019, Segovia, Spania.
20. Targeting oxidative and inflammatory stress for brain protection and biomarker monitoring in Alzheimer’s disease, Antonio Cuadrado, CIBERNED Meeting, 20.10.2020, Madrid, Spania.
21. Blood transcript signatures in mild dementia: a targeted transcriptomics study, Antonio Cuadrado, Elena Milanesi, Maria Dobre, Anca Cucos, Gerard Piñol-Ripoll, Gabriela Niculescu, Gina Manda. Annual Scientific Meeting & 13th National Pathology Symposium, 5-7.11.2020, INCD “Victor Babes” (<https://www.ivb.ro/v3/project/symposium/>).
22. The NRF2-KEAP1 Signaling Pathway as a Pharmacological Target in Neurodegenerative diseases, Antonio Cuadrado, Redox Webinar Series - Oxidative Stress: Biochemical and Pharmacological Aspects, Sectiunea 2: Redox Therapies for Neurodegenerative Diseases: Lights and Shadows, 11.03.2021.
23. Distinctive under-expression profile of inflammatory and redox genes in the blood of elderly patients with cardiovascular disease”, Antonio Cuadrado, Elena Milanesi, Maria Dobre, Anca Cucos, Gerard Piñol-Ripoll, Catalina Tudose, Gabriela Niculescu, Gina Manda, SFRRI (Society for Free Radical Research International), 15-18.03.2021.
24. Altered inflammation and redox networks in the blood of patients with mild dementia, Antonio Cuadrado, Elena Milanesi, Maria Dobre, Anca Cucos, Gerard Piñol-Ripoll, Catalina Tudose, Gabriela Niculescu, Gina Manda, SFRRI (Society for Free Radical Research International), 15-18.03.2021.
25. The NRF2-KEAP1 signaling pathway as a pharmacological target in neurodegenerative disease, Antonio Cuadrado, April Seminars @ CEDOC, organizat de CHRONIC DISEASES RESEARCH CENTRE, 7.04.2021.

26. A novel NRF2-βTrCP Protein-Protein Interaction (PPI) inhibitor suppresses LPS-mediated inflammation, Antonio Cuadrado, Ligase Targeting Drug Development, 25-27.05.2021.
27. Targeting NRF2 for brain protection in Alzheimer's disease". Antonio Cuadrado. FEBS 2021, 3-8.07.2021 (<https://2021.febscongress.org/>).
28. Transcription factor NRF2 as a brain protective target in preclinical Alzheimer's disease. Antonio Cuadrado. International Pathology Conference of the Victor Babeş Institute, 4 – 6 noiembrie 2021.
29. Reduced blood RGS2 expression in mild cognitive impairment patients. Elena Milanesi, Cătălina Anca Cucos, Jordi A. Matias-Guiu, Gerard Piñol-Ripoll, Gina Manda, Maria Dobre, Antonio Cuadrado. International Pathology Conference of the Victor Babeş Institute, 4 – 6 noiembrie 2021.
30. MYD88 blood levels increase during Alzheimer's disease progression in a transgenic mouse model. Cătălina Anca Cucos, Maria Dobre, Elena Mihaela Dragnea, Elena Milanesi. International Pathology Conference of the Victor Babeş Institute, 4 – 6 noiembrie 2021.
31. Targeting Transcription Factor Nrf2 in Neurodegenerative Diseases. Antonio Cuadrado. Paris Redox Meeting, 13-15.10.2021.
32. The NRF2-KEAP1 Signaling Pathway as a Pharmacological Target in Neurodegenerative diseases, Antonio Cuadrado, BenBedPhar Online Scientific Marathon, 10-11.01.2022.
33. The expression pattern of inflammation and redox genes in the blood of mild AD patients – focus on the molecular signatures of NFκB and NRF2, Gina Manda, , BenBedPhar Online Scientific Marathon, 10-11.01.2022.
34. Doua comunicari la manifestarea stiintifica "International Medical Students' Summit of Bucharest, organizata la Bucuresti in perioada 8-12.12.2021.
35. Herpes viruses in brain of Alzheimer's Disease patients: a mini-review, Alexandra Boromiz, Alina Ioana Bucuroiu , Ioana Muşat, Elena Milanesi , Maria Dobre, International Medical Students' Summit of Bucharest, 8-12.12.2021.
36. Gut-brain axis: the link between inflammatory bowel disease and psychiatric disorders. Autori: Alina Ioana Bucuroiu, Alexandra Boromiz, Anastasia Andreev, Maria Dobre and Elena Milanesi, International Medical Students' Summit of Bucharest, 8-12.12.2021.

### **Comunicari pentru promovarea proiectului (3)**

37. Alzheimer's disease from the redox signaling perspective - the REDBRAIN project, Gina Manda, Ana-Maria Enciu, Antonio Cuadrado A. 46-a Conferință Anuală de Imunologie cu participare internațională, 5-7.10.2016, Bucuresti, Romania.
38. Alzheimer's disease from a redox perspective: The REDBRAIN project. Antonio Cuadrado. Bench to Bed Research on the Transcription Factor NRF2, 19.10.2016, Medical College of Autonomous University of Madrid (La Pagoda), Madrid Spania.
39. The REDBRAIN project, Antonio Cuadrado. New concepts and views in redox biology and oxidative stress research – achievements of COST Action BM1203 (EU-ROS)", organizată în perioada 7-10 noiembrie 2016, în Eilat, Israel.

### **Cerere de brevet la OSIM**

“METODĂ DE EVALUARE A DEZINHIBIȚIEI COMPORTAMENTALE ÎNTR-UN MODEL ANIMAL DE BOALĂ ALZHEIMER (ȘOARECI TRANSGENICI APP/TAU), UTILIZÂND LABIRINTUL RADIAL CU OPT BRAȚE” by Cucos CA, Milanesi E, Dobre M, Anghelache L, Cuadrado A, Manda G; OSIM registration number: A2021/00377. The abstract of the patent request is published in BOPI, volum 11/2021 of 29.11.2021, page A23J. [Link](#)