MINISTERIO DE CIENCIA E INNOVACIÓN

CURRICULUM VITAE (maximum 4 pages)

AGENCIA ESTATAL DE INVESTIGACIÓN

Part A. PERSONAL INFORMATION

CV date	12/04/2021

First and Family name	JOSE NEPTUNO RODRIGUEZ LOPEZ		
Social Security, Passport, ID number	05167786P	Age	56
Researcher codes	Open Researcher and Contributor ID (ORCID**)	0000-0001-6863-1173	
	SCOPUS Author ID (*)	35584818100	
	WoS Researcher ID (*)	F-5012-2016	

(*) Optional
(**) Mandatory

A.1. Current position

Name of University/Institution	Universidad de Murcia			
Department	Departamento de Bioquímica y Biología Molecular A / Facultad de Biología			
Address and Country	DUQUES DE LUGO 26, BAJO B, 30009, MURCIA			
Phone number	669954726	E-mail	neptuno@um.es	
Current position	Full Professor		From	2011
Key words	Epigenetics; melanoma; breast cancer; pancreatic cancer; protein methylation; resistance mechanisms			

A.2. Education

PhD, Licensed, Graduate	University	Year
Doctor en Ciencias Biológicas	Universidad de Murcia	1993
Licenciado en Ciencias Sección Biológicas. Especialidad Bioquímica y Biología Molecular	Universidad Autónoma de Madrid	1987

A.3. General indicators of quality of scientific production

Nº Sexenios Research = 5 (last in 2019); Nº Sexenios Transference = 1 (last in 2019)
No. Directed PhD Thesis = 5 (desde 2010)
Number of articles = 201
Corresponding author (last 10 years) = 43
Total Appointments = 5947
Average appointments/year (last 5 years) = 327
Total publications in Q1 = 140
Index h = 41
Group Leader (years) = 16
Principal Investigator Competitive Projects (Number of Projects) = 13

Part B. CV SUMMARY

Full Professor of Biochemistry and Molecular Biology (University of Murcia) and Doctor of Biological Sciences. Since 2004, I have led a Molecular Oncology Research Team that discovered the antifolate activity of tea catechins, the pathways that lead to melanoma resistance to methotrexate (MTX) and to the design of new dihydrofolate reductase enzyme inhibitors (DHFR). Currently we are working on three main lines of research: **(1) Epigenetics of cancer:** Know the epigenetic processes that control the pathophysiology of cancer. This line focuses on knowing the methylation of histones and transcription factors that are involved in the development of cancer, in order to design drugs and antimethylating combinations to control their proliferation and expansion (metastasis). **(2) Mechanisms of drug resistance:** The physiological processes that result in resistance to conventional treatments in different types of cancer of epithelial origin are studied in this line of research. Knowing the resistance phenomena can lead to more effective strategies for cancer treatment. **(3) Design and synthesis of new antitumor agents:** In collaboration with Prof. Alberto Tárraga of the Department of Organic Chemistry of the University of Murcia, our group works on the synthesis of new antifolates as antitumor drugs. Among the objectives of my research is to collaborate with various oncology professionals in order to design more effective and personalized treatments for cancer patients. The combination of epigenetic strategies with other

types of treatments such as radio or immunotherapy could generate new personalized lines of action for cancer treatment. In addition, we are working on protocols to transfer some of these epigenetic therapies to the clinic.

Part C. RELEVANT MERITS

C.1. Publications

1. Sánchez-Del-Campo L., Martí-Díaz R, Montenegro MF, González-Guerrero R, Hernández-Caselles, T, Martínez-Barba E, Piñero-Madrona A, Cabezas-Herrera J, Goding CR, Rodríguez-López JN. MITF induces escape from innate immunity in melanoma. J. Exp. Clin. Cancer Res. 2021. 40:117. (10/10)

2. Martí-Díaz R, Montenegro MF, Cabezas-Herrera J, Goding CR, Rodríguez-López JN, Sánchez-Del-Campo L. Acriflavine, a Potent Inhibitor of HIF-1α, Disturbs Glucose Metabolism and Suppresses ATF4-Protective Pathways in Melanoma under Non-Hypoxic Conditions. Cancers (Basel). 2021, 13(1):102.

3. Montenegro MF, González-Guerrero R, Sánchez-Del-Campo L, Piñero-Madrona A, Cabezas-Herrera J, Rodríguez-López JN. PRMT1-dependent methylation of BRCA1 contributes to the epigenetic defense of breast cancer cells against ionizing radiation. Sci Rep. 2020, 10, 13275. (6/6).

4. Piñero-Madrona A, Goméz-Ruiz AJ, Ruiz-Merino G, Martínez-Barba E, Cerezuela-Fuentes P, Rodríguez-López JN, Cabezas-Herrera J. Prognostic value of the Breslow:diameter ratio in cutaneous melanoma. J Am Acad Dermatol. 2019, 80, 806-808. (6/7).

5. Piñero-Madrona A, Ruiz-Merino G, Cerezuela Fuentes P, Martínez-Barba E, Rodríguez-López JN, Cabezas-Herrera J. Mitotic rate as an important prognostic factor in cutaneous malignant melanoma. Clin Transl Oncol. 2019, 21(10):1348-1356.

6. Hammouda MB, Riahi-Chebbi I, Souid S, Rodríguez-López JN, Essafi-Benkhadir K. Macrovipecetin, a C-type lectin from Macrovipera lebetina venom, inhibits proliferation migration and invasion of SK-MEL-28 human melanoma cells and enhances their sensitivity to cisplatin. Biochim Biophys Acta Gen Subj. 2018, 1862, 600-614. (12/13*). *Co-corresponding author.

7. Hammouda MB, Montenegro MF, Sánchez-Del-Campo L, Zakraoui O, Aloui Z, Riahi-Chebbi I, Karoui H, Rodríguez-López JN, Essafi-Benkhadir K. Lebein, a Snake Venom Disintegrin, Induces Apoptosis in Human Melanoma Cells. Toxins (Basel). 2016, 8(7):206.

8. Montenegro MF, Sánchez-Del-Campo L, González-Guerrero R, Martínez-Barba E, Piñero-Madrona A, Cabezas-Herrera J, Rodríguez-López JN. Tumor suppressor SET9 guides the epigenetic plasticity of breast cancer cells and serves as an early-stage biomarker for predicting metastasis. Oncogene. 2016, 35, 6143-6152. (7/7).

9. Montenegro MF, González-Guerrero R, Sánchez-del-Campo L, Piñero-Madrona A, Cabezas-Herrera J, Rodríguez-López JN. Targeting the epigenetics of the DNA damage response in breast cancer. Cell Death Dis. 2016, 7, e2180. (6/6).

10. Casado F, Teruel JA, Casado S, Ortiz A, Rodríguez-López JN, Aranda FJ. Location and Effects of an Antitumoral Catechin on the Structural Properties of Phosphatidylethanolamine Membranes. Molecules. 2016, 21(7):829.

11. Montenegro MF, Sánchez-del-Campo L, Fernández-Pérez MP, Sáez-Ayala M, Cabezas-Herrera J, Rodríguez-López JN. Targeting the epigenetic machinery of cancer cells. Oncogene. 2015, 34 135-143. (6/6).

12. Castillo-González AC, Pelegrín-Hernández JP, Nieto-Cerón S, Madrona AP, Noguera JA, López-Moreno MF, Rodríguez-López JN, Vidal CJ, Hellín-Meseguer D, Cabezas-Herrera J. Unbalanced acetylcholinesterase activity in larynx squamous cell carcinoma. Int Immunopharmacol. 2015, 29(1):81-6.

13. Castillo-González AC, Nieto-Cerón S, Pelegrín-Hernández JP, Montenegro MF, Noguera JA, López-Moreno MF, Rodríguez-López JN, Vidal CJ, Hellín-Meseguer D, Cabezas-Herrera J. Dysregulated cholinergic network as a novel biomarker of poor prognostic in patients with head and neck squamous cell carcinoma. BMC Cancer. 2015, 15:385.

14. López-Molina D, Chazarra S, How CW, Pruidze N, Navarro-Perán E, García-Cánovas F, García-Ruiz PA, Rojas-Melgarejo F, Rodríguez-López JN. Cinnamate of inulin as a vehicle for delivery of colonic drugs. Int J Pharm. 2015, 479(1):96-102.

15. Montenegro MF, Collado-González Mdel M, Fernández-Pérez MP, Hammouda MB, Tolordava L, Gamkrelidze M, Rodríguez-López JN. Promoting E2F1-mediated apoptosis in oestrogen receptor-α-negative breast cancer cells. BMC Cancer. 2014, 14:539.

16. How CW, Teruel JA, Ortiz A, Montenegro MF, Rodríguez-López JN, Aranda FJ. Effects of a synthetic antitumoral catechin and its tyrosinase-processed product on the structural properties of phosphatidylcholine membranes. Biochim Biophys Acta. 2014,1838(5):1215-24.

17. Sáez-Ayala M, Fernández-Pérez MP, Chazarra S, Mchedlishvili N, Tárraga-Tomás A, Rodríguez-López JN. Factors influencing the antifolate activity of synthetic tea-derived catechins. Molecules. **2013**,18(7):8319-41.

18. Sáez-Ayala M, Montenegro MF, Sánchez-Del-Campo L, Rodríguez-López JN. Directed phenotype switching as an effective antimelanoma strategy. Cancer Cell. 2013, 24, 105-119. (11/11).

19. Fernández-Pérez MP, Montenegro MF, Sáez-Ayala M, Sánchez-del-Campo L, Piñero-Madrona A, Cabezas-Herrera J, Rodríguez-López JN. Suppression of antifolate resistance by targeting the myosin Va trafficking pathway in melanoma. Neoplasia. 2013, 15, 826-839. (7/7).

20. Montenegro MF, Sáez-Ayala M, Piñero-Madrona A, Cabezas-Herrera J, Rodríguez-López JN. Reactivation of the tumour suppressor RASSF1A in breast cancer by simultaneous targeting of DNA and E2F1 methylation. PLoS One. 2012, 7(12):e52231.

21. Sáez-Ayala M, Fernández-Pérez MP, Montenegro MF, Sánchez-del-Campo L, Chazarra S, Piñero-Madrona A, Cabezas-Herrera J, Rodríguez-López JN. Melanoma coordinates general and cell-specific mechanisms to promote methotrexate resistance. Exp Cell Res. 2012, 318(10):1146-59.

22. Sáez-Ayala M, Sánchez-del-Campo L, Montenegro MF, Chazarra S, Tárraga A, Cabezas-Herrera J, Rodríguez-López JN. Comparison of a pair of synthetic tea-catechin-derived epimers: synthesis, antifolate activity, and tyrosinase-mediated activation in melanoma. ChemMedChem. 2011, 6(3):440-9.

23. Sánchez-del-Campo L, Chazarra S, Montenegro MF, Cabezas-Herrera J, Rodríguez-López JN. Mechanism of dihydrofolate reductase downregulation in melanoma by 3-O-(3,4,5-trimethoxybenzoyl)-(-)-epicatechin. J Cell Biochem. 2010, 110(6):1399-409.

24. Sánchez-del-Campo L, Sáez-Ayala M, Chazarra S, Cabezas-Herrera J, Rodríguez-López JN. Binding of natural and synthetic polyphenols to human dihydrofolate reductase. Int J Mol Sci. 2009, 10(12):5398-410.

25. Sánchez-del-Campo L, Montenegro MF, Cabezas-Herrera J, Rodríguez-López JN. The critical role of alpha-folate receptor in the resistance of melanoma to methotrexate. Pigment Cell Melanoma Res. 2009, 2(5):588-600.

26. Sánchez-del-Campo L, Tárraga A, Montenegro MF, Cabezas-Herrera J, Rodríguez-López JN. Melanoma activation of 3-o-(3,4,5-trimethoxybenzoyl)-(-)-epicatechin to a potent irreversible inhibitor of dihydrofolate reductase. Mol Pharm. 2009, 6(3):883-94.

27. Navarro-Perán E, Cabezas-Herrera J, Sánchez-Del-Campo L, García-Cánovas F, Rodríguez-López JN. The anti-inflammatory and anti-cancer properties of epigallocatechin-3-gallate are mediated by folate cycle disruption, adenosine release and NF-kappaB suppression. Inflamm Res. 2008 Oct;57(10):472-8.

28. Munoz-Munoz JL, García-Molina F, Molina-Alarcón M, Tudela J, García-Cánovas F, Rodríguez-López JN. Kinetic characterization of the enzymatic and chemical oxidation of the catechins in green tea. J Agric Food Chem. 2008, 56(19):9215-24.

29. Sánchez-del-Campo L, Rodríguez-López JN. Targeting the methionine cycle for melanoma therapy with 3-O-(3,4,5-trimethoxybenzoyl)-(-)-epicatechin. Int J Cancer. 2008, 123(10):2446-55.

30. Sánchez-del-Campo L, Otón F, Tárraga A, Cabezas-Herrera J, Chazarra S, Rodríguez-López JN. Synthesis and biological activity of a 3,4,5-trimethoxybenzoyl ester analogue of epicatechin-3-gallate. J Med Chem. 2008, 51(7):2018-26.

31. Martínez-López de Castro A, Nieto-Cerón S, Aurelio PC, Galbis-Martínez L, Latour-Pérez J, Torres-Lanzas J, Tovar-Zapata I, Martínez-Hernández P, Rodríguez-López JN, Cabezas-Herrera J. Cancer-associated differences in acetylcholinesterase activity in bronchial aspirates from patients with lung cancer. Clin Sci (Lond). 2008, 115(8):245-53.

32. Navarro-Perán E, Cabezas-Herrera J, Campo LS, Rodríguez-López JN. Effects of folate cycle disruption by the green tea polyphenol epigallocatechin-3-gallate. Int J Biochem Cell Biol. 2007;39(12):2215-25.

33. Martínez-Moreno P, Nieto-Cerón S, Torres-Lanzas J, Ruiz-Espejo F, Tovar-Zapata I, Martínez-Hernández P, Rodríguez-López JN, Vidal CJ, Cabezas-Herrera J. Cholinesterase activity of human lung tumours varies according to their histological classification. Carcinogenesis. 2006, 27(3):429-36.

34. Navarro-Perán E, Cabezas-Herrera J, Hiner AN, Sadunishvili T, García-Cánovas F, Rodríguez-López JN. Kinetics of the inhibition of bovine liver dihydrofolate reductase by tea catechins: origin of slow-binding inhibition and pH studies. Biochemistry. 2005, 44(20):7512-25.

35. Navarro-Perán E, Cabezas-Herrera J, García-Cánovas F, Durrant MC, Thorneley RN, Rodríguez-López JN. The antifolate activity of tea catechins. Cancer Res. 2005, 65(6):2059-64.

C.2. Research projects

I have participated in 28 competitive research projects (in 13 of them as Principal Investigator) including 6 EU actions (1 INTAS, 1 ERA, 2 COST, 1 HCM, 1 TMR).

C.3. Contracts, technological or transfer merits

I have participated as Principal Investigator (PI) in 8 projects with national and international companies. I have participated as a tutor in 3 actions/contracts of the Torres Quevedo Plan. I have been the tutor of 2 contracts financed by the Foundation of the Spanish Association against Cancer (AECC) and I have participated as principal investigator of the Spanish group in a project of the Oxford Cancer Research Center Foundation.

C.4. Patents

I participate as an inventor in 2 National Patents (1 of them licensed to the Bioprodin S.L Company) and 5 International Patents (all of them licensed to the British company Plant Bioscience Limited).

1. José Neptuno Rodríguez López. GB1214877.1. Compounds for treatment of tumours United Kingdom. 23/08/2012. Universidad de Murcia.

2. Jose Neptuno Rodríguez López; María Fernanda Montenegro Arce; María Piedad Fernández Pérez. GB1212586.0. Methods and compositions to overcome cytotoxic drug resistance in melanoma United Kingdom. 23/08/2012. Universidad de Murcia.

3. JOSE NEPTUNO RODRIGUEZ LOPEZ. WO2014029669. COMPOUNDS FOR TREATMENTS OF TUMORS 21/08/2012. Universidad de Murcia.

4. JOSE NEPTUNO RODRIGUEZ LOPEZ; MARIA FERNANDA MONTENEGRO ARCE; MARIA PIEDAD FERNANDEZ PEREZ. WO2014/012902A2. MELANOSOME TRANSPORT INHIBITION FOR THE TREATMENT OF MELANOMA United Kingdom. 16/07/2012. Universidad de Murcia.

C.5. Direction of students' research works.

I have been the director of 15 Doctoral Theses (5 of them as the unique director), 3 Bachelor's Theses, 6 Master's Final Project and 17 Final Degree Project. Tutor of 2 doctoral students within the EC Erasmus Mundus Program. A summary of the supervised Theses are numbered below:

C.6. Participation in evaluation tasks

I have been an evaluator of ANEP and ISCIII projects and member of the JDC/INCORP/2015/BMED, JDC/INCORP/2016/BMED and JDC/FORMACION/2018/BMED Evaluation Commissions. I have evaluated projects for various agencies and international research centers such as the National Institutes of Health (NIH) in the USA, the National Science Center in Poland, the German-Israeli agency (DKFZ-MOST) cooperation in cancer research and the University of Antwerp in Belgium.

C.7. International collaboration.

Prof Colin R. Goding, Melanoma Research, Ludwig Institute for Cancer Research, University of Oxford; **Dr. Mark Middleton**, Melanoma Research. Department of Oncology. Churchill Hospital. Oxford; **Dr. Essafi Khadija**, Cancer Research. Institute Pasteur of Tunis; **Dr. Magali Saez-Ayala**, Crystallography, AFMB, CNRS, Aix-Marseille Université, Marseille, France; **Prof. Alexander Rösch**, Centre for Medical Biotechnology, University of Duisburg-Essen, Germany; **Prof. Georgi Kvesitadze**, Tea chemistry & biochemistry, Durmishidze Institute of Biochemistry and Biotechnology of Agricultural University of Georgia (DIBBAUG), Tbilisi Georgia.