Part A. Personal Information

DATE	15/'3/2022

Surname(s)	Díaz Pereira	
Forename	José Fernando	
Sex	Male	
Age	56	
Researcher codes	WoS Researcher ID	U-3532-2017
	SCOPUS Author ID	56244961600
	Open Researcher and Contributor ID (ORCID)	0000-0003-2743-3319

A.1. Current position

Post/ Professional Category	Senior Staff Scientist/Investigador Científico de OPIS	
UNESCO Code	2302, 2390, 3209, 3302	
Key Words	Tubulin, Cancer, Antitumourals	
Name of the University/Institution	Consejo Superior de Investigaciones Científicas	
	Department/Centre	Centro de Investigaciones Biológicas Margarita Salas.
	Full Address	Ramiro de Maeztu 9, 28040 Madrid
	Email Address	fer@cib.csic.es
	Phone Number	+34911098069
Start date	2008	

A.2. Education

Year	*University*	*Degree*	*Title*
1988	*Complutense Madrid*	*Graduate*	*Chemistry*
1989	*Complutense Madrid*	*Masters (if appropriate)*	*Chemistry*
1993	*Complutense Madrid*	*PhD*	*Chemistry*

Indicators of Quality in Scientific Production

Sexenials: 6, last one 2014-2020.
Total number of citations: 8209
Average number of citations per year during the last five years: 512
Total number of publications 183
in the first quartile (Q1) 135 (75%)
and first decile (D1) 48 (25%)
h-index: 50
Thesis supervised: 8
Data from Google Academics
https://scholar.google.com/citations?user=GW3WUf0AAAAJ

Part B. Summary of CV

1.- Seek and discovery of new chemotherapeutic targets.

Tubulin and its assembly product, microtubules, are among the most successful targets in cancer chemotherapy. However, treatment of tumours with tubulin targeting agents is severely hampered by the development of resistance. An obvious way to address resistance is the seek for new binding sites in the same protein with different function and structural properties. When I started my scientific career in 1988 only three binding sites had been discovered in tubulin, those of colchicine, taxane and vinca. Since then four new binding sites have been discovered, (maytansine, pore site, laulimalide/peloruside and pironetin), all of them had been discovered and characterized by my group, either alone or in collaboration with other groups.

2.- Structural mechanisms of activation/deactivation of cancer related proteins.
Tubulin is labile and very difficult to crystallize which implied that the determination of its structure and the functional implications of its modulation by antitumoural drugs was a complex problem which was only fully solved in the last years. In coordination with a drug discovery group from Victoria University (New Zealand), a natural product synthesis group from the Swiss Institute of Technology and a crystallography group from the Paul Scherrer Institute (Switzerland), we provided the biochemical techniques needed to optimize the formation of drug/protein complexes allowing us to determine the structure of tubulin in complex with drugs and providing essential structural information about the interaction of these compounds with their binding site and the structural mechanism of activation of tubulin.

3.- Develop of methods for the in vitro evaluation of antitumoural drugs and of strategies able to predict their effectivity.
Another important problem that has occupied an important part of my scientific career is the search of methods that allow the in vitro evaluation of the potency of a drug in different tumoural cells. We have developed a method for the high throughput evaluation of the binding affinity of taxane binding site microtubule stabilizing agents which is now a standard for evaluating microtubule stabilizing agents. Later we have proof that the binding affinity of a given compound is a good predictive value for their toxicity, allowing the development of highly cytotoxic compounds using quick evaluations of the effect of chemical modifications in the drug structure. The methods are widely used for the evaluation of novel synthesized or discovered tubulin targeting agents.

4.- Strategies of optimization of drugs able to overcome resistance/avoid toxicity to chemotherapy.
The development of a safe microtubule modulators able to overcome resistance to chemotherapy and to minimize the undesired secondary effects are the final objective of my research. The technology developed to evaluate the binding affinity of paclitaxel site ligands have been employed to develop a super taxane, with more than 500 times the binding affinity of the parent compound paclitaxel, the compound is highly effective in all kind of tumoural cells resistant to paclitaxel chemotherapy. The same kind of approach has been used with the company Pharmamar S.A. to select a compound with high affinity targeting the newly discovered Maytansine site. The compound is effective in tumours resistant to chemotherapy and has entered clinical Phase II in Spain and USA. We are now developing drugs able to stabilize microtubules without altering their structure and chemical transport properties, therefore with the potential to show less peripheral neurotoxicity (the main toxical secondary effect), with possible use to stabilize microtubules in neurodegenerative taupaties.

Part C. Relevant accomplishments

C.1. Publications

Ten more relevant articles since 2011.

1.- Canales, A., Salarichs, J.R. ,Trigili, C., Nieto, L., Coderch, C, Andreu, J.M., Paterson, I., Jimenez-Barbero, J., and Díaz, J.F. Insights into the interaction of discodermolide and docetaxel with tubulin. Mapping the binding sites of microtubule-stabilizing agents by using an integrated NMR and computational approach. ACS Chemical Biology (2011) 6; 8, 789-799. Corresponding author.

2.-Field, J.J., Pera, B.*, Calvo, E*, Canales, A., Zurwerra, D., Trigili, C, Rodríguez-Salarichs, J., Matesanz, R., Kanakkanthara, A., Wakefield, S., Singh, A.J., Jiménez-Barbero, J., Northcote, P., Miller, J.H., López, J.A., Hamel, E., Barasoain, I., Altmann, K.H. and Díaz, J.F. (2012) Zampanolide, a potent new microtubule stabilizing agent, covalently reacts with the taxane luminal site in both tubulin α,β-heterodimers and microtubules. Chemistry and Biology. 19, 686–698. Corresponding author.

3.- Prota, A.E., Bargsten, K., Zurwerra, D., Field,J.J., Díaz, J.F. Altmann, K.H. and Steinmetz, M.O. Molecular Mechanism of Action of Microtubule-Stabilizing Anticancer Agents, Science (2013) 339, (6119) 587-590

4.- Prota, A.E., Bargsten, K., Northcote, P.T., Marsh, M, Altmann, K.H., Miller, J.H., Díaz, J.F. and Steinmetz, M.O. Structural Basis of Microtubule Stabilization by Laulimalide and Peloruside A (2014) Angew. Chem. Int. Ed., 53, 1621-1625.

5.-Prota A.E., Bargsten, K., Díaz, J.F., Marsh, M., Cuevas C., Liniger, M., Neuhaus, C., Andreu, J.M. Altmann, K.-H. and Steinmetz M.O. A new tubulin-binding site and pharmacophore for microtubule-destabilizing anticancer drugs. (2014) PNAS 111, 38, 13817-13821.

6.- Sáez-Calvo, G.; Sharma, A.; Balaguer, F.; Barasoain, I.; Rodríguez-Salarichs, J. Olieric, N.; Muñoz-Hernández, H; Berbís, M.A.; Wendeborn, S.; Peñalva, M.A.; Matesanz, R. Canales, A.; Prota, A.E.; Jímenez-Barbero, J.; Andreu, J.M.; Lamberth, C.; Steinmetz, M.O. and Díaz, J.F. Triazolopyrimidines Are Microtubule-Stabilizing Agents that Bind the Vinca Inhibitor Site of Tubulin. (2017) Cell Chemical Biology, 24 (6), 737-750. Corresponding author.

7.- Field, J.J.; Pera, B.; Estévez-Gallego, J.; Calvo, E.; Rodríguez-Salarichs, J.; Sáez-Calvo, G.; Zuwerra, D.; Jordi, M.; Andreu, J.M.; Prota, A.E.; Ménchon, G.; Miller, J.H.; Altmann; K.H. and Díaz, J.F. Zampanolide binding to tubulin indicates crosstalk of taxane site with colchicine and nucleotide sites. J. Nat. Prod. (2018) 81, 3, 494-505. Corresponding author.

8.-Estévez-Gallego, J.; Josa-Prado, F.; Ku, S.; Buey, R.M.; Balaguer, F.A., Prota, A.E.; Lucena-Agell, D.; Kamma-Lorger,C.; Steinmetz, M.O.; Barasoain,I.; Chrétien, D.; Kamimura, S.; Díaz, J.F.; Oliva, M.A. Structural model for differential cap maturation at growing microtubule ends (2020) eLife 2020, 9, e50155. DOI: https://doi.org/10.7554/eLife.50155

9.- Oliva, M.A.; Prota, A.E.; Rodríguez-Salarichs, J.; Gu, W.; Bennani, Y.L.; Jiménez-Barbero, J.; Bargsten, K.; Canales, A.; Steinmetz, M.O.; Díaz, J.F.; Structural basis of noscapine activation for tubulin binding (2020) J. Med. Chem 63, 15, 8495–8501 https://doi.org/10.1021/acs.jmedchem.0c00855 Corresponding author.

10.- Matthew, S.; Chen, Q.Y.; Ratnayake, R.; Fermaintt, C.S.; Lucena-Agell, D.; Bonato, F.; Prota, A.E.; Lim, S.T.; Wang, X.; Díaz, J.F.; Risinger, A.L.; Paul, V.J.; Oliva, M.A., Luesch, H. Gatorbulin-1, a distinct cyclodepsipeptide chemotype, targets a seventh tubulin pharmacological site. (2021) PNAS Vol. 118 No. 9 e2021847118 10.1073/pnas.2021847118

C.2. Research Projects and Grants

Since 2011

1.-Diseño y evaluacion de agentes antitumorales dirigidos contra tubulina en sitios alternativos. 257100 € Ministerio de Ciencia e Innovación. BIO2010-16351 2011-2013 IP: J.F. Díaz

2.-Determinación de la estructura de los complejos entre agentes moduladores de microtúbulos y su diana utilizando téncicas de RMN y biofísicas avanzadas. 2011CU0006 58200 € IP: J.F. Díaz

3.-Bioinformatics Integrative Platform for Estructure Based Drug Discovery II 1.000.000 € Comunidad Autónoma de Madrid 2012-2015, BIPPEDII CAM S2010/BMD-2457. Coordinador F. Gago (U. Alcalá) I.P.:José Fernando Díaz

4.- Diseño de compuestos activos contra tumores resistentes a farmacos dirigidos contra tubulina. 260.000,00 € Ministerio de Ciencia y Competitividad. (2014-2016) BIO2013-42984-R IP: José Fernando Díaz

5.- Challenging organic syntheses inspired by nature: from natural products chemistry to drug Discovery. COST Action number: CM1407. Main Proposer:Bruno Botta Participant:José Fernando Díaz

6.- Purifícacion de proteínas de citoesqueleto a partir de diversos organismos y evaluación de compuestos con actividad biológica frente a ellas. 21.000 € Proyecto Intramural CSIC, 201620E051. IP: José Fernando Díaz

7.-Diseño de antitumorales inhibidores de los procesos metastáticos y eficaces en celulas cancerigenas resistentes a quimioterapia. 160.000 € Ministerio de Economía y Competitividad (2017-2019) BFU2016-75319-R I.P. José Fernando Díaz

8.- Tuning Tubulin Dynamics and Interactions to Face Neurotoxicity: a Multidisciplinary Approach for Training and Research H2020 MARIE SKLODOWSKA-CURIE ACTIONS UE/TUBINTRAIN (H2020-MSCA-ITN-ETN/0582). 250.904,88 € Main Proposer Daniele Passarella I.P. CSIC. José Fernando Díaz

9.-Analisis estructural de la interacción de compuestos antitumorales con tubulina y microtubulos. 37484.46 € Proyecto Intramural CSIC, 201920E111 IP: José Fernando Díaz

10.-Interrupción de los procesos virales de transporte mediados por microtúbulos. 70.000 € COV20/01007 ISCIII, FIS. IP: José Fernando Díaz Pereira. (Marzo 2020 Diciembre 2020)

11.-Bases estructurales de la neurotoxicidad por antitumorales dirigidos contra tubulina: hacia mejores moduladores de microtubulos contra cancer y enfermedades neurodegenerativas 160.000 € Ministerio de Ciencia e Innovación PID2019-104545RB-I00 (2020-2023) IP: José Fernando Díaz.

12.-Bases moleculares de la regulación de microtúbulos y sus implicaciones en la neurotoxicidad producida por fármacos: Fundación TATIANA 92.400 € IP: José Fernando Díaz Pereira y Juan Francisco Giménez Abian. (Diciembre 2020 Diciembre 2023)

13.-Interrupción de los procesos virales de transporte mediados por microtúbulos. 45.000 € 20202020E301 CSIC. IP: José Fernando Díaz Pereira. (Diciembre 2020 Diciembre 2021)

C.3. Contracts

1.-Estudio del modo de acción de Plocabulina y análogos. Optimización de sus propiedades bioquímicas y estructurales. Pharmamar 2012-2013 175.265,97 €
2.- Technological support Contract Paul Scherrer Institut 2015.Villingen Switzerland 8.000 €
3.- Technological support Contract Paul Scherrer Institut 2016.Villingen Switzerland 15.000 €
4.- Paul Scherrer Institut 2018. Villingen Switzerland 7.500 €
5.- Contract License / PURSOLUTION LLC Memphis, Tennessee, USA 2016-2023 20.000 €
6.-Technological support Contract Pharmamar 2018. 15000 €
7.- Paul Scherrer Institut 2018. Villingen Switzerland 22.000 €
8.- Technological support Contract. Pharmamar Jan 2019. 13000 €
9.- Paul Scherrer Institut 2019. Villingen Switzerland 22.000 €
10.- Technological support Contract. Pharmamar Oct 2019-June 2020. 12000 €
11.- Technological support Contract. Pharmamar Jan 2021-March 2022. 12000 €
12.- Paul Scherrer Institut 2021. Villingen Switzerland 22.000 €

C.4. Patents and other IPR

Andreu, J.M., Díaz J.F., Barasoain I. Método de detección y evaluación de compuestos miméticos de paclitaxel N. de solicitud: 200101710 País de prioridad: ES

Andreu, J.M., Díaz J.F., Barasoain I. Redondo-Horcajo, M. Metodo para la producción y liofilización de tubulina purificada. Secreto Industrial registrado. 2016 Licenciado a PURSOLUTION LLC Memphis, Tennessee, USA.

C.5, C.6, C.7… Other

Head of the Evaluation Panel for Biological Sciences of ALBA synchrotron (2014-2019).