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Using functional genetic screens to understand and overcome PARP inhibitor resistance

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Citation

Paes Lobo Lopes Dias, M. (2023, January 18). *Using functional genetic screens to understand and overcome PARP inhibitor resistance*. Retrieved from <https://hdl.handle.net/1887/3512289>

Version: Publisher's Version

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Note: To cite this publication please use the final published version (if applicable).

CURRICULUM VITAE

Mariana Paes Lobo Lopes Dias was born on August 29th, 1994 in Faro, Portugal. She graduated high school in 2012 to start her bachelor's degree in Cell and Molecular Biology at the NOVA University (Lisbon, Portugal). During her bachelor's, she performed internships at the Molecular Genetics Unit of the National Health Institute Doutor Ricardo (Lisbon, Portugal), learning about different molecular techniques used in molecular diagnosis of various genetic hereditary diseases; and at the lab of Prof. José António Belo at the Chronic Diseases Research Center (CEDOC) (Lisbon, Portugal), where she had her first experience in a research lab. After obtaining her degree in 2015, Mariana enrolled into the Molecular Medicine and Oncology master's degree programme of the University of Porto (Porto, Portugal). During the first year of her master's, she joined the lab of Prof. José Carlos Machado at the Instituto de Investigação e Inovação em Saúde (i3S) (Porto, Portugal) where she participated in a project aimed at studying the influence of somatic mutations on immune surveillance in colorectal cancer. She was then awarded an Erasmus+ fellowship which allowed her to join the lab of Dr. Jacqueline Jacobs at the Netherlands Cancer Institute (NKI) (Amsterdam, the Netherlands) to develop her master's degree dissertation project on the role of BRCA1-A and BRCA1-B complexes in DNA repair pathway choice, replication stress and PARPi response. She successfully defended her dissertation and graduated from her master's degree in 2017. During her last internship, Mariana became very interested in the study of DNA repair pathways and in the biological mechanisms behind the anti-cancer activity of PARPi. That is why in 2017 she started her PhD at the lab of Prof. Jos Jonkers at the Netherlands Cancer Institute (NKI) (Amsterdam, the Netherlands) where she could follow her interest in the study of PARPi response by conducting several functional genetic screens to identify mechanisms of PARPi resistance and to find potential therapeutic targets that could be exploited to improve response to PARPi treatment. The results of her work are presented in this thesis.

LIST OF PUBLICATIONS AND PREPRINTS

Multi-omics analysis reveals distinct non-reversion mechanisms of PARPi resistance in BRCA1- versus BRCA2-deficient mammary tumors

Jinhyuk Bhin*, [Mariana Paes Dias](#)*, Ewa Gogola*, Frank Rolfs, Sander R. Piersma, Roebi de Bruijn, Julian R. de Ruiter, Bram van den Broek, Alexandra A. Duarte, Wendy Sol, Ingrid van der Heijden, Lara Bakker, Taina S. Kaiponen, Cor Liefink, Ben Morris, Roderick L. Beijersbergen, Marieke van de Ven, Connie R. Jimenez, Lodewyk F. A. Wessels, Sven Rottenberg and Jos Jonkers

BioRxiv, 2022; 2022.09.07.506927, doi:10.1101/2022.09.07.506927.

Functional genetic dropout screens and *in vivo* validation of candidate therapeutic targets using mouse mammary tumoroids

[Mariana Paes Dias](#), Sven Rottenberg, Jos Jonkers

STAR Protoc., 2022; 3(1):101132, doi:10.1016/j.xpro.2022.101132.

Filling in the gaps in PARP inhibitor-induced synthetic lethality

[Mariana Paes Dias](#) and Jos Jonkers

Mol. Cell Oncol., 2021; 8(6): 2010512, doi:10.1080/23723556.2021.2010512.

Loss of nuclear DNA ligase III reverts PARP inhibitor resistance in BRCA1/53BP1 double-deficient cells by exposing ssDNA gaps

[Mariana Paes Dias](#)*, Vivek Tripathi*, Ingrid van der Heijden, Ke Cong, Eleni-Maria Manolika, Jinhyuk Bhin, Ewa Gogola, Panagiotis Galanos, Stefano Annunziato, Cor Liefink, Miguel Andujar-Sanchez, Sanjiban Chakrabarty, Graeme C.M. Smith, Marieke van de Ven, Roderick L. Beijersbergen, Jirina Bartkova, Sven Rottenberg, Sharon Cantor, Jiri Bartek, Arnab Ray Chaudhuri, and Jos Jonkers

Mol. Cell, 2021; 81, 4692-4708.e9, doi:10.1016/J.MOLCEL.2021.09.005.

Understanding and overcoming resistance to PARP inhibitors in cancer therapy

[Mariana Paes Dias](#)*, Sarah C. Moser*, Shridar Ganesan and Jos Jonkers

Nat. Rev. Clin. Oncol., 2021; 18,773–791, doi:10.1038/s41571-021-00532-x.

Feasibility of phosphoproteomics on leftover samples after RNA extraction with guanidinium thiocyanate

Frank Rolfs, Sander R. Piersma, [Mariana Paes Dias](#), Jos Jonkers, Connie R. Jimenez

Mol. Cell Proteomics, 2021; 20:100078, doi:10.1016/j.mcpro.2021.100078.

SMARCAD1-mediated active replication fork stability maintains genome integrity

Calvin Shun Yu Lo, Marvin van Toorn, Vincent Gaggioli, [Mariana Paes Dias](#), Yifan Zhu, Eleni

Maria Manolika, Wei Zhao, Marit van der Does, Chirantani Mukherjee, João G S C Souto Gonçalves, Martin E van Royen, Pim J French, Jeroen Demmers, Ihor Smal, Hannes Lans, David Wheeler, Jos Jonkers, Arnab Ray Chaudhuri , Jurgén A Martéijn, Nitika Taneja
Sci. Adv., 2021; 7(19):eabe7804, doi:10.1126/sciadv.abe7804.