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Cancer chess: molecular insights into PARP inhibitor resistance

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Citation
Barazas, M. (2021, December 14). *Cancer chess: molecular insights into PARP inhibitor resistance*. Retrieved from https://hdl.handle.net/1887/3247064

Version:	Publisher's Version
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Downloaded from:	https://hdl.handle.net/1887/3247064

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

List of Publications

1. Tannous BA, Kerami M, Van der Stoop PM, Kwiatkowski N, Wang J, Zhou W, Kessler AF, Lewandrowski G, Hiddingh L, Sol N, Lagerweij T, Wedekind L, Niers JM, **Barazas M**, Nilsson RJ, Geerts D, De Witt Hamer PC, Hagemann C, Vandertop WP, Van Tellingen O, Noske DP, Gray NS, Würdinger T. *'Effects of the selective MPS1 inhibitor MPS1-IN-3 on glioblastoma sensitivity to antimitotic drugs.'* J Natl Cancer Inst. 2013; 105(17): 1322-31.

2. Xu G, Chapman JR, Brandsma I, Yuan J, Mistrik M, Bouwman P, Bartkova J, Gogola E, Warmerdam D, **Barazas M**, Jaspers JE, Watanabe K, Pieterse M, Kersbergen A, Sol W, Celie PHN, Schouten PC, van den Broek B, Salman A, Nieuwland M, de Rink I, de Ronde J, Jalink K, Boulton SJ, Chen J, van Gent DC, Bartek J, Jonkers J, Borst P, Rottenberg S. *'REV7 counteracts DNA double-strand break resection and affects PARP inhibition.'* Nature. 2015; 521(7553): 541-544.

3. Annunziato S, **Barazas M**, Rottenberg S, Jonkers J. *'Genetic Dissection of Cancer Development, Therapy Response, and Resistance in Mouse Models of Breast Cancer.'* Cold Spring Harb Symp Quant Biol. 2016; 81:141-150.

4. Teng J, Hejazi S, Hiddingh L, Carvalho L, de Gooijer MC, Wakimoto H, **Barazas M**, Tannous M, Chi AS, Noske DP, Wesseling P, Wurdinger T, Batchelor TT, Tannous BA. *'Recycling drug screen repurposes hydroxyurea as a sensitizer of glioblastomas to temozolomide targeting de novo DNA synthesis, irrespective of molecular subtype.' Neuro Oncol. 2018; 20(5): 642-654.*

5. Duarte AA, Gogola E, Sachs N, **Barazas M**, Annunziato S, R de Ruiter J, Velds A, Blatter S, Houthuijzen JM, van de Ven M, Clevers H, Borst P, Jonkers J, Rottenberg S. *'BRCA-deficient mouse mammary tumor organoids to study cancer-drug resistance.'* Nat Methods. 2018; 15(2): 134-140.

6. Becker JR, Cuella-Martin R*****, **Barazas M***, Liu R*****, Oliveira C, Oliver AW, Bilham K, Holt AB, Blackford AN, Heierhorst J, Jonkers J, Rottenberg S, Chapman JR. *'The ASCIZ-DYNLL1 axis promotes 53BP1-dependent non-homologous end joining and PARP inhibitor sensitivity.'* Nat Commun. 2018; 9(1): 5406.

7. Gogola E, Duarte AA, de Ruiter JR, Wiegant WW, Schmid JA, de Bruijn R, James DI, Guerrero Llobet S, Vis DJ, Annunziato S, van den Broek B, **Barazas M**, Kersbergen A, van de Ven M, Tarsounas M, Ogilvie DJ, van Vugt M, Wessels LFA, Bartkova J, Gromova I, Andújar-Sánchez M, Bartek J, Lopes M, van Attikum H, Borst P, Jonkers J, Rottenberg S. *'Selective Loss of PARG Restores PARylation and Counteracts PARP Inhibitor-Mediated Synthetic Lethality.'* Cancer Cell. 2018; 33(6): 1078-1093.

8. Noordermeer SM*, Adam S*, Setiaputra D*, **Barazas M**, Pettitt SJ, Ling AK, Olivieri M, Álvarez-Quilón A, Moatti N, Zimmermann M, Annunziato S, Krastev DB, Song F, Brandsma I, Frankum J, Brough R, Sherker A, Landry S, Szilard RK, Munro MM, McEwan A, Goullet de Rugy T, Lin ZY, Hart T, Moffat J, Gingras AC, Martin A, van Attikum H, Jonkers J, Lord CJ, Rottenberg S, Durocher D. *'The shieldin complex mediates 53BP1-dependent DNA repair.'* Nature. 2018; 560(7716): 117-121.

9. **Barazas M**, Annunziato S, Pettitt SJ, de Krijger I, Ghezraoui H, Roobol SJ, Lutz C, Frankum J, Song FF, Brough R, Evers B, Gogola E, Bhin J, van de Ven M, van Gent DC, Jacobs JJL, Chapman R, Lord CJ, Jonkers J, Rottenberg S. *'The CST Complex Mediates End Protection at Double-Strand Breaks and Promotes PARP Inhibitor Sensitivity in BRCA1-Deficient Cells.'* Cell Rep. 2018; 23(7): 2107-2118.

10. **Barazas M**, Gasparini A, Huang Y, Küçükosmanoğlu A, Annunziato S, Bouwman P, Sol W, Kersbergen A, Proost N, de Korte-Grimmerink R, van de Ven M, Jonkers J, Borst GR, Rottenberg S. *'Radiosensitivity Is an Acquired Vulnerability of PARPi-Resistant BRCA1-Deficient Tumors.'* Cancer Res. 2019; 79(3): 452-460.

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Curriculum Vitae

Marco Barazas was born in 1988, Hoorn, the Netherlands. In 2006, he enrolled into the Life Science Bachelor program at Hogeschool Inholland Alkmaar. After receiving his propaedeutic diploma in 2007, he continued his Bachelor program at Hogeschool Leiden. His interest in molecular biology with a translational angle led to his participation in several courses organized by the Molecular Biology and Animal Experimentation programs. He then put this combination in practice during an internship on the DNA repair gene *p53* in the lab of Prof. Dr. Hein te Riele at the Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital (NKI-AVL), which was concluded by a Bachelor thesis and Article 12 of the *Wet op de Dierproeven* (WOD, Experiments on Animals Act) in 2009. Later that year, he started the Master's program Oncology at the VU university. He performed his first internship in the lab of Prof.Dr. Tom Würdinger at the VUmc Cancer Center Amsterdam (CCA), where he worked on the establishment of a mouse model for diffuse intrinsic pontine glioma (DIPG). In 2011, he performed his second internship in the lab of Dr. Bakhos Tannous at the Harvard Medical School/Massachussetts General Hospital (HMS/MGH) in Boston. It was here where he first combined his interest in molecular biology with cancer therapy using high-throughput screening technology in a project aimed to identify sensitizers to temozolomide in glioblastoma. He graduated Cum Laude in December 2012. In February 2013, Marco returned to the NKI-AVL when he joined the lab of Prof.Dr. Sven Rottenberg. During his PhD, he further pursued his interest in combining molecular biology to improve cancer therapy this time with a focus on BRCA1-deficient breast cancer. Here, he could take advantage of his previous experience in the DNA repair field and functional high-throughput screening technology. The major findings of this research are described in this thesis. From January 2019, he holds a post-doc position in the lab of Prof.Dr. Marcel Tijsterman at the Leiden University Medical Center (LUMC).

Acknowledgements

This thesis concludes what has been a great period of my career. Of course, I could not have done the work presented in this thesis if it wasn't for the fantastic support that I received over the years, so to everyone who has been involved in this work – a big thank you, your help has always been greatly appreciated!

In particular I would like to thank:
My promotor, Prof.dr. Jos Jonkers and *co-promotor Prof.dr. Sven Rottenberg*, for allowing me the opportunity to dive into this fascinating subject where I could combine my scientific interests. The move of the *Rottenberg*-lab to Switzerland came as a surprise to me, but I could not have wished for a smoother integration within the *Division of Molecular Pathology* and the *Jonkers*-lab. It later turned out we were ahead of the curve with our online meetings. I have learned a great deal in the lab, have participated in inspiring collaborations and attended (inter)national meetings, and foremost I have been able to develop myself as an independent researcher, all under your guidance. *Dr. Piet Borst*, when it comes to the importance of critical thinking and careful thought about controls, I could not have had a better teacher. Together, *Sven*, *Jos* and *Piet*, you provide a case-in-point of the strength of collaboration and team effort. I would also like to thank my national and international collaborators *Dr. Gerben Borst*, *Dr. Jacqueline Jacobs, Dr. Dik van Gent, Dr. Ross Chapman*, *Prof. Dr. Daniel Durocher* and *Prof. Dr. Chris Lord* for their valuable feedback, supportive attitude and fruitful collaborations.

All members of the *Rottenberg*-lab, although it hasn't always been easy to stay connected between the two locations, I have enjoyed our shared meetings and Lab outings. *Ewa,* we both started and ended our work at the NKI around the same time. While we have had our challenges, your passion for science cannot be denied and I wish you great success.

All colleagues of the *Division of Molecular Pathology*, I have enjoyed the atmosphere in the department. *Stefano*, it has been a real pleasure to collaborate with you on many projects. Your can-do and let's-do work ethos has stimulated many experiments. I cannot thank you, and *Sjors, Koen, Chiara, Julian, Anne Paulien, Arne, Ellen, Ingrid, Hanneke, Peter, Catrin, Guotai, Asli, Hanneke, Wendy, Sohvi, Nora, Inge and my students Yike and Julia* enough for the positive environment we created and that always made work enjoyable.

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All the *facilities of the NKI*, although you may not always end up in the spot lights there is no question about the importance of your contributions. Your expert knowledge and collaborative attitude forms the foundation of many complex experiments. A special thanks to the colleagues of the *Mouse Cancer Clinic Amsterdam (MCCA) Preclinical Intervention Unit* (*Marieke* and the team). I have experienced the time "without" and "with" the MCCA, and can only conclude that you have transformed the way of doing mouse experiments for researchers. It has been great working together with you.

Papa, Mama, Familie, Vrienden en natuurlijk *Tessa*, bedankt voor alle steun. Mijn nieuwsgierigheid is van jongs af aan al gestimuleerd en daar ben ik dankbaar voor. Jullie hebben mij altijd aangemoedigd om het beste uit mezelf te halen en dit heeft ontegenzeggelijk bijgedragen aan de totstandkoming van dit proefschrift.