biology and life sciences forum

MDPI

Abstract

New Insights on Signaling Pathways Deregulated in LAP1-Deficient Cells: A Proteomics Study †

Cátia D. Pereira [1], Guadalupe Espadas [2,3], Filipa Martins [1], Anne T. Bertrand [4], Laurent Servais [5,6], Eduard Sabidó [2,3], Odete A. B. da Cruz e Silva [1] and Sandra Rebelo [1,*]

1 Department of Medical Sciences, Institute of Biomedicine (iBiMED), University of Aveiro, 3810-193 Aveiro, Portugal; daniela.pereira@ua.pt (C.D.P.); samartins@ua.pt (F.M.); odetecs@ua.pt (O.A.B.d.C.e.S.)
2 Centre de Regulació Genòmica (CRG), Barcelona Institute of Science and Technology (BIST), 08003 Barcelona, Spain; guadalupe.espadas@crg.eu (G.E.); eduard.sabido@crg.eu (E.S.)
3 Department of Medicine and Life Sciences, Universitat Pompeu Fabra (UPF), 08003 Barcelona, Spain
4 Institut de Myologie, Center of Research in Myology, INSERM UMRS 974, Medicine Faculty—Sorbonne Université, 75013 Paris, France; a.bertrand@institut-myologie.org
5 MDUK Oxford Neuromuscular Center, Department of Paediatrics, University of Oxford and NIHR Oxford Biomedical Research Center, Oxford OX3 9DU, UK; laurent.servais@paediatrics.ox.ac.uk
6 Neuromuscular Center, Division of Paediatrics, University Hospital of Liège and University of Liège, 4000 Liège, Belgium
* Correspondence: srebelo@ua.pt; Tel.: +351-924-406-306
† Presented at Cells, Cells and Nothing but Cells: Discoveries, Challenges and Directions, 6–8 March 2023; Available online: https://cells2023.sciforum.net/.

Abstract: Mutations in genes encoding nuclear envelope (NE) proteins, despite being rare, represent a major threat to cell homeostasis by compromising nuclear integrity and function as well as nucleo-cytoplasmic communication. In the last decade, several diseases have been associated to mutations in the *TOR1AIP1* gene that codes for lamina-associated polypeptide 1 (LAP1), a NE protein ubiquitously expressed in human tissues. Although this is suggestive of an important physiological role of LAP1, it remains unclear which cellular activities are regulated by this protein. To address this, we investigated the molecular repercussions of its deficiency in patient-derived skin fibroblasts carrying a pathological LAP1 mutation (p.E482A), previously reported in a case of severe dystonia, cerebellar atrophy and cardiomyopathy. Using liquid chromatography with tandem mass spectrometry (LC–MS/MS), a quantitative proteome analysis was performed to identify up-/downregulated proteins in LAP1 E482A fibroblasts relative to age-matched control fibroblasts. A subsequent functional characterization of the LC–MS/MS-identified differentially expressed proteins using bioinformatics tools unraveled various signaling pathways/biological processes potentially deregulated in LAP1 E482A fibroblasts, such as DNA repair, neurodevelopment and myogenesis, among others. This work sheds light on dysfunctional molecular mechanisms in LAP1-deficient cells, which will contribute to a better understanding of LAP1's physiological relevance for the maintenance of cell homeostasis and, hopefully, allow the identification of potential therapeutic targets for LAP1-associated pathologies.

Keywords: LAP1; DNA repair; neurodevelopment; myogenesis

check for updates

Citation: Pereira, C.D.; Espadas, G.; Martins, F.; Bertrand, A.T.; Servais, L.; Sabidó, E.; da Cruz e Silva, O.A.B.; Rebelo, S. New Insights on Signaling Pathways Deregulated in LAP1-Deficient Cells: A Proteomics Study. *Biol. Life Sci. Forum* **2023**, *21*, 25. https://doi.org/10.3390/blsf2023021025

Academic Editor: Alexander E. Kalyuzhny

Published: 24 March 2023

Copyright: © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

Author Contributions: C.D.P., F.M. and S.R. conceived and designed the experiments; C.D.P. and G.E. performed the experimental work and analysis of the results; A.T.B. and L.S. established and provided the human fibroblast cell lines; E.S., O.A.B.d.C.e.S. and S.R. provided the reagents/materials/analysis tools; C.D.P. wrote the original draft of the manuscript; C.D.P., G.E., F.M., E.S., O.A.B.d.C.e.S. and S.R. critically revised the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: This work was financed by the Institute of Biomedicine (iBiMED)—UIDP/04501/2020 and UIDB/04501/2020—and the Fundação para a Ciência e a Tecnologia (FCT) of the Ministério da

Ciência, Tecnologia e Ensino Superior, the COMPETE 2020 Program, the QREN and the European Union (Fundo Europeu de Desenvolvimento Regional). Authors acknowledge support from EPIC-XS, project number 823839, funded by the Horizon 2020 Program of the European Union. The proteomics analyses were performed in the Proteomics Unit from the Centre de Regulació Genòmica (CRG) and Universitat Pompeu Fabra (UPF). The CRG/UPF Proteomics Unit is part of the Spanish National Infrastructure for Omics Sciences (ICTS OmicsTech). Cátia D. Pereira is the recipient of a PhD fellowship (SFRH/BD/140310/2018 and COVID/BD/152982/2023) co-funded by FCT of the Ministério da Ciência, Tecnologia e Ensino Superior, the Centro 2020 Program and the European Union (Fundo Social Europeu).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data will be available upon the full length manuscript acceptance.

Acknowledgments: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.