



HAL
open science

Parkin acts as a transcription factor modulating presenilin-1 and presenilin-2 promoter transactivations

Eric Duplan, Jean Sévalle, Julien Viotti, Thomas Goiran, Charlotte Bauer,
Paul Renbaum, Ephrat Levy-Lahad, Clément Gautier, Olga Corti, Nathalie
Leroudier, et al.

► **To cite this version:**

Eric Duplan, Jean Sévalle, Julien Viotti, Thomas Goiran, Charlotte Bauer, et al.. Parkin acts as a transcription factor modulating presenilin-1 and presenilin-2 promoter transactivations. *Molecular Neurodegeneration*, 2013, 8 (Suppl 1), pp.P56. inserm-00869879

HAL Id: inserm-00869879

<https://inserm.hal.science/inserm-00869879>

Submitted on 4 Oct 2013

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

POSTER PRESENTATION

Open Access

Parkin acts as a transcription factor modulating presenilin-1 and presenilin-2 promoter transactivations

Eric Duplan^{1*}, Jean Sévalle¹, Julien Viotti¹, Thomas Goiran¹, Charlotte Bauer¹, Paul Renbaum², Ephrat Levy-Lahad², Clément A. Gautier³, Olga Corti³, Nathalie Leroudier¹, Frédéric Checler¹, Cristine Alves da Costa¹

From Molecular Neurodegeneration: Basic biology and disease pathways
Cannes, France. 10-12 September 2013

Background

Parkin is associated to autosomal recessive early-onset Parkinson's disease. Parkin acts as an E3-ubiquitin ligase involved in the proteasome-mediated degradation of various substrates. It has been suggested that pathogenic mutations of parkin, abolishing its ubiquitin-ligase activity, could explain the accumulation of proteins and lead to neuronal death by apoptosis. However, besides this function, additional parkin-dependent cellular pathways exist. We demonstrated that parkin is a direct transcriptional repressor of the tumor suppressor p53 [1]. p53 regulates the expression and functions of presenilin-1 (PS1) and presenilin-2 (PS2), two members of the gamma secretase complex involved in the production of the amyloid β peptide ($A\beta$) and parkin could control the homeostasis of intracellular $A\beta$. These findings prompted us to investigate whether parkin could control presenilins and if so, whether it is via a direct transcriptional control of PS promoters or indirectly, via p53.

Materials and methods

Experiments were conducted on TSM1 neurons, SH-SY5Y human neuroblastoma cells, human embryonic kidney 293 cells, and immortalized mouse embryonic fibroblasts invalidated or not for *parkin*, *presenilin 1* and/or *2*, *p19^{arf}* and both *p19^{arf}* *p53*. We also used primary cultured neurons and brain extract from mouse invalidated or not for *parkin*.

We did Q-PCR, Western-blot, caspases-3 activity measurement and in vitro gamma secretase assays experiments. We document by chromosome immunoprecipitation, gel shift, gene reporter and mutagenesis experiments parkin direct interaction with presenilins promoters.

precipitation, gel shift, gene reporter and mutagenesis experiments parkin direct interaction with presenilins promoters.

Results

Parkin controls presenilin 1 and 2 expressions, promoter activity, and mRNA levels *ex vivo* and in mouse brains. This regulation impacts on PS-dependent γ -secretase activity and presenilin-mediated control of cell death. This control is independent of parkin ubiquitin-ligase activity, does not involve p53 and is not affected by PS1 and PS2 functional interplay. Parkin binds to presenilins promoters via a consensus binding sequence that we identify and validate by functional analysis [2].

Conclusions

This study is a "framework" for the identification of novel transcriptional targets of parkin and for a better comprehension of parkin's functions.

Acknowledgements

This work was supported by the 'Fondation pour la Recherche Médicale', the 'Conseil Général des Alpes Maritimes', and the LABEX (excellence laboratory, program investment for the future) DISTALZ.

Authors' details

¹IPMC-CNRS UMR 7275, Valbonne, France. ²Medical Genetics Institute, Shaare Zedec Medical Center, Hebrew University Medical School, Jerusalem, Israel. ³INSERM U679, Hôpital de la Pitié-Salpêtrière, Paris, France.

Published: 4 October 2013

References

1. da Costa CA, *et al*: Transcriptional repression of p53 by parkin and impairment by mutations associated with autosomal recessive juvenile Parkinson's disease. *Nat Cell Biol* 2009, **11**(11):1370-1375.

¹IPMC-CNRS UMR 7275, Valbonne, France
Full list of author information is available at the end of the article

- Duplan E, *et al*: Parkin differently regulates presenilin-1 and presenilin-2 functions by direct control of their promoter transcription. *J Mol Cell Biol* 2013, **5**(2):132-142.

doi:10.1186/1750-1326-8-S1-P56

Cite this article as: Duplan *et al*: Parkin acts as a transcription factor modulating presenilin-1 and presenilin-2 promoter transactivations. *Molecular Neurodegeneration* 2013 **8**(Suppl 1):P56.

**Submit your next manuscript to BioMed Central
and take full advantage of:**

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit

