Identification and Characterization of Aberrant Splicing in Pompe Disease Using a Generic Approach

Atze J. Bergsma1–3, Marian Kroos1–3, Marianne Hoogeveen-Westerveld1–3, Dicky Halley4, Ans T. van der Ploeg2,3 and W.W.M. Pim Pijnappel1–3,*

1Molecular Stem Cell Biology, Department of Clinical Genetics, Erasmus MC University Medical Center, Rotterdam, Netherlands
2Department of Pediatrics, Erasmus MC University Medical Center, Rotterdam, Netherlands
3Center for Lysosomal and Metabolic Diseases, Erasmus MC University Medical Center, Rotterdam, Netherlands
4Molecular Diagnostics, Department of Clinical Genetics, Erasmus MC University Medical Center, Rotterdam, Netherlands

RESULTS

Application of this approach to six previously published and one novel variant(s) in the acid alpha-glucosidase gene causing Pompe disease enabled detection of a total of 11 novel splicing events. Aberrant splicing included cryptic splice site usage, intron retention, and exon skipping. Importantly, the extent of leaky wild-type splicing correlated with disease onset and severity.

CONCLUSION

These results indicate that this approach enables sensitive detection and in-depth characterization of variants affecting splicing, many of which are still unrecognized or poorly understood. The approach is generic and should be adaptable for application to other monogenic diseases to aid in improved diagnostics.

*Correspondence to: W.W.M. Pim Pijnappel, Department of Clinical Genetics, Erasmus MC University Medical Center, Faculty building, Room Ee-916a, P.O. Box 2040, 3000 CA Rotterdam, Netherlands. E-mail: w.pijnappel@erasmusmc.nl

Contract grant sponsors: Sophia Children’s Hospital Foundation (SSWO), grant S-687.

ISSN 2214-3599/15/$27.50 © 2015 – IOS Press and the authors. All rights reserved
This article is published online with Open Access and distributed under the terms of the Creative Commons Attribution Non-Commercial License.