The role of the proteasome in Huntington's disease
Krom, Sabine

Citation for published version (APA):
Krom, S. (2013). The role of the proteasome in Huntington’s disease

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

Download date: 15 Mar 2019
THE ROLE OF THE PROTEASOME IN HUNTINGTON’S DISEASE

Sabine Schipper-Krom

“A man who dares to waste one hour of time has not discovered the value of life”
Charles R. Darwin (1809-1882)
The studies described in this thesis were performed at the Department of Cell Biology and Histology of the Academic Medical Center, University of Amsterdam, The Netherlands. The production of this thesis was financially supported by the University of Amsterdam.

Design and lay-out: Sixtyseven Communicatie BV - www.sixtyseven.com
Production: Gildeprint Drukkerijen - www.gildeprint.nl
Publisher: S. Schipper-Krom
Cover picture: Living cells expressing mHtt(Q103)-GFP in blue and in white labeling with activity based probe for active proteasome visualization

Copyright © 2013 by S. Schipper-Krom
All rights reserved.
No part of this publication may be reproduced, stored or transmitted in any way without prior permission from the author

THE ROLE OF THE PROTEASOME IN HUNTINGTON'S DISEASE

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad van doctor aan de Universiteit van Amsterdam
op gezag van de Rector Magnificus
prof. dr. D.C. van den Boom
ten overstaan van een door het college voor promoties ingestelde commissie, in het openbaar te verdedigen in de Agnietenkapel
op woensdag 18 december 2013, te 12:00 uur

door

Sabine Krom
geboren te Beverwijk
TABLE OF CONTENTS

1 Short introduction and outline of the thesis 6
2 The ubiquitin-proteasome system in huntington’s disease 13
3 Mimicking proteasomal release of polyglutamine peptides initiates aggregation and toxicity 36
4 The DNAJB6 and DNAJB8 chaperones prevent intracellular aggregation of polyglutamine peptides 60
5 Expanded polyglutamine-containing N-terminal huntingtin fragments are entirely degraded by mammalian proteasomes 82
6 Enlightening proteasomes: methods to visualize their intracellular distribution, activity and interactions 114
7 Dynamic recruitment of active proteasomes into polyglutamine initiated inclusion bodies 146
8 Modulating proteasome activity in huntington’s disease 162
9 Summary and conclusion 190
& Addendum 196