

VU Research Portal

Mistaken identity: Paracetamol induces amino acid starvation through mimicry of tyrosine and changes ubiquitin homeostasis

Huseinovic, A.

2019

document version

Publisher's PDF, also known as Version of record

[Link to publication in VU Research Portal](#)

citation for published version (APA)

Huseinovic, A. (2019). *Mistaken identity: Paracetamol induces amino acid starvation through mimicry of tyrosine and changes ubiquitin homeostasis*. [PhD-Thesis - Research and graduation internal, Vrije Universiteit Amsterdam].

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

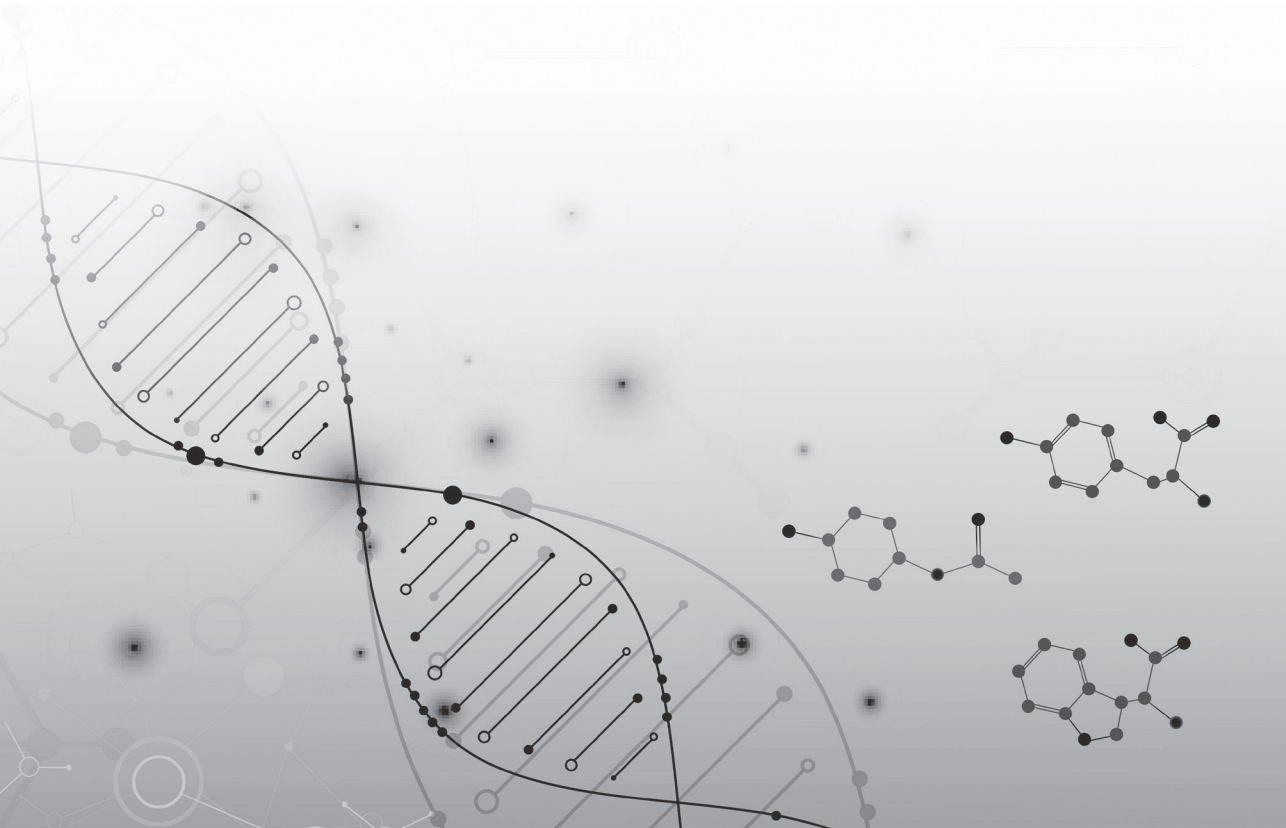
Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

E-mail address:

vuresearchportal.ub@vu.nl

Appendices



Abbreviations

AAP	amino acid permease
ADHD	attention deficit hyperactivity disorder
AIF	apoptosis-inducing factor
AKI	acute kidney injury
ALT	alanine aminotransferase
AMAP	acetyl-meta-aminophenol
APAP	acetyl-para-aminophenol, acetaminophen
APC/C	anaphase-promoting complex or cyclosome
BDNF	brain-derived neurotrophic factor
CHX	cycloheximide
ASK1	apoptosis signal-regulating kinase 1
CP	catalytic particle
CYP	Cytochrome P450
DAmP	Decreased Abundance by mRNA Perturbation
DDR	DNA damage response
DDT	DNA damage tolerance
DEEMM	Diethyl ethoxymethylenemalonate
DMEM	Dulbecco's Modified Eagle's Medium
DSB	double-stranded breaks
DUBs	deubiquitinases
EE	early endosome
ERAD	ER-associated degradation
ETC	electron transport chain
FBS	Fetal Bovine Serum
FTY720	fingolimod
GAAC	general amino acid control
GEF	guanine nucleotide-exchange factor
GO	Gene Ontology
GSH	glutathione
GSK	glycogen synthase kinase
GST	Glutathione S-Transferase
HPLC	high pressure liquid chromatography
HR	homologous recombination
HU	hydroxyurea
IBS	irritable bowel syndrome
JNK	c-jun-N-terminal kinase
LE	late endosome

MJD	Machado-Josephin domain
MMS	methyl methanesulfonate
MoA	Mode of action
MPT	membrane permeability transition
MVB	multivesicular body
NAC	N-acetylcysteine
NAPQI	N-acetyl p-benzoquinoneimine
NCR	nitrogen catabolite repression
NER	nucleotide excision repair
NMD	nonsense-mediated mRNA decay
NSAID	non-steroid anti-inflammatory drug
OTU	ovarian tumor
PBS	phosphate-buffered saline
PCNA	proliferating cell nuclear antigen
PPR	postreplication repair
ROS	reactive oxygen species
RP	regulatory particle
RPN	and regulatory particle non-ATPase
RPT	regulatory particle triple-A (RPT)
RTG	retrograde
SCF	Skp1-Cul1-F-box protein
SD	standard deviation
SGD	Saccharomyces Genome Database
ssDNA	single-stranded DNA
SULTs	sulfotransferases
TCA	tricarboxylic acid
TCR	transcription-coupled repair
TGN	trans-Golgi network
TLS	translesion synthesis
TMPs	transmembrane proteins
TOR	Target of Rapamycin
TORC	TOR-complex
UCH	ubiquitin C-terminal hydrolase
UGTs	UDP-glucuronosyl transferases
USP	ubiquitin specific protease

Curriculum Vitae

Angelina Huseinovic was born in Zenica, Yugoslavia (Bosnia) in 1975. She came to the Netherlands in 1994. In 1996, she started her study of Biology and Medical Laboratory sciences at Hogeschool van Amsterdam and Hogeschool Utrecht specializing in Biotechnology, obtaining her Bachelor of Science degree in 2001. Subsequently, she started working as a Research technician at the Netherlands Cancer Institute at Departments of Experimental Therapy and Structural Biology. In 2007 she started working as Associate scientist at the pharmaceutical company Uniqure, specialized in development of gene therapies for genetic disorders. During that time, she also followed the MSc-program Biomolecular Sciences specializing in Biological Chemistry and Molecular Cell Biology at the Vrije Universiteit Amsterdam, graduating with a MSc-degree in 2012 *cum laude*. In 2012, she started the PhD research described in this thesis in the Division of Molecular and Computational Toxicology under supervision of Prof. Dr. Nico Vermeulen, Dr. Chris Vos and Dr. Jan Kooter. Her PhD project was within the AIMMS institute and designed to bridge between two Divisions: Molecular toxicology and Genetics. As of 2018 she started working as a postdoc on HPV-induced carcinogenesis at Cancer Center Amsterdam (VUmc), Department of Pathology in the group of Dr. Renske Steenbergen.

List of publications

- Huseinovic, A., Dekker, S.J., Boogaard, B., Vermeulen, N.P.E., Kooter, J.M., Vos, J.C., 2018. Acetaminophen reduces the protein levels of high affinity amino acid permeases and causes tryptophan depletion. *Amino Acids* 50, 1377–1390.
- Huseinovic, A., van Dijk, M., Vermeulen, N.P.E., van Leeuwen, F., Kooter, J.M., Vos, J.C., 2017a. Drug toxicity profiling of a *Saccharomyces cerevisiae* deubiquitinase deletion panel shows that acetaminophen mimics tyrosine. *Toxicol. In Vitro* 47, 259–268.
- Huseinovic, A., van Leeuwen, J.S., van Welsem, T., Stulemeijer, I., van Leeuwen, F., Vermeulen, N.P.E., Kooter, J.M., Vos, J.C., 2017b. The effect of acetaminophen on ubiquitin homeostasis in *Saccharomyces cerevisiae*. *PLoS One* 12, e0173573.
- Miniarikova, J., Zanella, I., Huseinovic, A., van der Zon, T., Hanemaaijer, E., Martier, R., Koornneef, A., Southwell, A.L., Hayden, M.R., van Deventer, S.J., Petry, H., Konstantinova, P., 2016. Design, Characterization, and Lead Selection of Therapeutic miRNAs Targeting Huntingtin for Development of Gene Therapy for Huntington's Disease. *Mol. Ther. - Nucleic Acids* 5, e297.
- Mason, M.R., Ehlert, E.M., Eggers, R., Pool, C.W., Hermening, S., Huseinovic, A., Timmermans, E., Blits, B., Verhaagen, J., 2010. Comparison of AAV Serotypes for Gene Delivery to Dorsal Root Ganglion Neurons. *Mol. Ther.* 18, 715–724.
- van de Weerd, B.C.M., Littler, D.R., Klompaker, R., Huseinovic, A., Fish, A., Perrakis, A., Medema, R.H., 2008. Polo-box domains confer target specificity to the Polo-like kinase family. *Biochim. Biophys. Acta - Mol. Cell Res.* 1783, 1015–1022.
- Broeks, A., Braaf, L.M., Huseinovic, A., Schmidt, M.K., Russell, N.S., van Leeuwen, F.E., Hogervorst, F.B.L., Van 't Veer, L.J., 2008. The spectrum of ATM missense variants and their contribution to contralateral breast cancer. *Breast Cancer Res. Treat.* 107, 243–248.
- Broeks, A., Braaf, L.M., Huseinovic, A., Nooijen, A., Urbanus, J., Hogervorst, F.B., Schmidt, M.K., Klijn, J.G., Russell, N.S., Van Leeuwen, F.E., Van 't Veer, L.J., 2007. Identification of women with an increased risk of developing radiation-induced breast cancer: a case only study. *Breast Cancer Res.* 9, R26.
- Broeks, A., de Witte, L., Nooijen, A., Huseinovic, A., Klijn, J.G.M., van Leeuwen, F.E., Russell, N.S., van't Veer, L.J., 2004. Excess risk for contralateral breast cancer in CHEK2*1100delC germline mutation carriers. *Breast Cancer Res. Treat.* 83, 91–3.