Curricula vitae

Monica Bonetti was born the 7th of October 1984 in Italy (RC), where she got her secondary education diploma at the Scientific Liceum, in 2002. From there she went to the University of Messina for her B.Sc in Biology. Her interest in Molecular Biology led her to choose the specialization in Genetics and Molecular Biology in Rome (Università La Sapienza). She got her M.Sc degree *cum laude* in March 2008. In May 2008 she started to work at the CSS-Mendel Institute (Rome) in the Neurogenetics team of Prof. Enza Maria Valente and Prof. Bruno Dallapiccola, where she focused on the correlation between movement disorders and human genetic variations. She started her Ph.D at the Hubrecht Institute (Utrecht) in 2010, under the supervision of Prof. Jeroen den Hertog. The research topic was focus on the characterization of cardiac defects of Noonan and LEOPARD patients, using zebrafish as animal model. The results of these studies are described in this thesis.

List of Publications

1) M Bonetti, A Ferraris, M Petracca, A R Bentivoglio, B Dallapiccola, E M Valente. (2009). GIGYF2 variants are not associated with Parkinson's disease in Italy. *Mov Disord*. 24(12):1867-8

2) M Bonetti*, C Barzaghi*, F Brancati, A Ferraris, E Bellacchio, A Giovanetti,T Ialongo, G Zorzi, C Piano, M Petracca, A Albanese, N Nardocci, B Dallapiccola, A R Bentivoglio, B Garavaglia# and E M Valente#.(2009). Mutation Screening of the DYT6/THAP1 Gene in Italy. *Mov Disord.* 24(16):2424-7

3) M Carecchio, M Magliozzi, M Copetti, A Ferraris, L Bernardini, M Bonetti, G Defazio, M J Edwards, I Torrente, F Pellegrini, C Comi, K P Bhatia, E M Valente. (2013). Defining the Epsilon-Sarcoglycan (SGCE) Gene Phenotypic Signature in Myoclonus-Dystonia: A Reappraisal of Genetic Testing Criteria. *Mov Disord*. 28(6):787-94

4) V Guida*, R Ferese*, M Rocchetti, M Bonetti, A Sarkozy, S Cecchetti, V Gelmetti, F Lepri, M Copetti, G Lamorte, C Digilio, B Marino, A Zaza, J den Hertog, B Dallapiccola, A De Luca. (2013). A variant in the carboxyl-terminus of connexin 40 alters GAP junctions and increases risk for tetralogy of Fallot. *Eur J Hum Genet*. 21(1):69-75

5) M Bonetti, J Paardekooper Overman, F Tessadori, E Noël, J Bakkers, J den Hertog. (2014). Noonan- and Leopard-syndrome Shp2 variants induce cilia-related laterality defects in Zebrafish. *Development*. 141(9):1961-70

6) M Bonetti, V Rodriguez Martinez, J Paardekooper Overman, J Overvoorde, M van Eekelen, C Jopling, J den Hertog. (2014). Distinct and overlapping functions of ptpn11 genes in zebrafish development. *PLoS One*. 9(4):e94884

7) L E L M Vissers*, M Bonetti*, J Paardekooper Overman*, W M Nillesen, S G M Frints, J de Ligt, G Zampino, M Schepens, H G Brunner, J A Veltman, H Scheffer, P Gros, J L Costa, Ma Tartaglia, I van der Burgt, H G Yntema# and J den Hertog#.(2014). Heterozygous germline mutations in A2ML1, encoding the secreted protease Inhibitor Alpha-2-Macroglobulin-Like-1, cause Noonan-like syndrome. *Eur J Hum Genet*. doi: 10.1038

8) J Paardekooper Overman*, J S Yi*, M Bonetti, M Soulsby, C Preisinger, M Stokes , L Hui, J Silva, A J R Heck, M I Kontaridis, J den Hertog# and A M Bennett#.(2014). PZR coordinates Shp2 phosphatase independent Noonan and LEOPARD syndrome signaling in zebrafish and mice. *Mol Cell Biol* 34(15):2874-89

9) J Paardekooper Overman, C Preisinger, K Prummel, M Bonetti, P Giansanti, J Overvoorde, A Heck, J den Hertog. (2014). A role for Fer kinase in the pathogenesis of Noonan and LEOPARD syndrome. *PlosOne*, Accepted

* equal contribution
# These authors jointly directed this work

Jeroen Paardekooper Overman was born on April 13th in Hoorn, the Netherlands. After obtaining his Athenaeum diploma from the Schoter Scholengemeenschap in Haarlem in 2002 he went to the Vrije Universiteit Amsterdam where he studied Biomedical Sciences. After doing his internship at the Molecular and Cellular Neurosciences group he obtained his B.Sc. degree in 2008. During his M.Sc. Biomolecular Sciences at the Vrije Universiteit he studied the role of Notch1 in cervical cancer at the VU Medical center and researched mitchondrial mutations using mass spectrometry at the Leiden University Medical Center. His thesis on microRNAs in the brain was performed in collaboration with the Hubrecht Institute. After obtaining his M.Sc. in 2009, Jeroen started his Ph.D. studies at the Hubrecht Institute under the supervision of Prof. Dr. Jeroen den Hertog. The aim was to study the role of Shp2 and potential downstream factors in Noonan and LEOPARD syndrome using zebrafish and mass spectrometry. The results are described in this thesis. He is currently working as a scientific information specialist at Elsevier in Amsterdam.

List of Publications

1) J Paardekooper Overman, J den Hertog. (2014). Zebrafish as a model to study PTPs during development. *Methods*. 15;65(2):247-53

2) M Bonetti, J Paardekooper Overman, F Tessadori, E Noël, J Bakkers, J den Hertog. (2014). Noonan and Leopard-syndrome Shp2 variants induce cilia-related laterality defects in Zebrafish. *Development.* 141(9):1961-70

3) M Bonetti, V Rodriguez Martinez, J Paardekooper Overman, J Overvoorde, M van Eekelen, C Jopling, J den Hertog. (2014). Distinct and overlapping functions of ptpn11 genes in zebrafish development. *PLoS One*. 9(4):e94884

4) L E L M Vissers*, M Bonetti*, J Paardekooper Overman*, W M Nillesen, S G M Frints, J de Ligt, G Zampino, M Schepens, H G Brunner, J A Veltman, H Scheffer, P Gros, J L Costa, Ma Tartaglia, I van der Burgt, H G Yntema# and J den Hertog#.(2014). Heterozygous germline mutations in A2ML1, encoding the secreted protease Inhibitor Alpha-2-Macroglobulin-Like-1, cause Noonan-like syndrome. *Eur J Hum Genet*. doi: 10.1038

5) J Paardekooper Overman*, J S Yi*, M Bonetti, M Soulsby, C Preisinger, M Stokes , L Hui, J Silva, A J R Heck, M I Kontaridis, J den Hertog# and A M Bennett#.(2014). PZR coordinates Shp2 phosphatase independent Noonan and LEOPARD syndrome signaling in zebrafish and mice. *Mol Cell Biol* 34(15):2874-89

6) J Paardekooper Overman, C Preisinger, K Prummel, M Bonetti, P Giansanti, J Overvoorde, A Heck, J den Hertog. A role for Fer kinase in the pathogenesis of Noonan and LEOPARD syndrome. *PLoS One*, Accepted.

* equal contribution
# These authors jointly directed this work

Abbreviation list

A2ML1	Alpha 2 Macroglobulin like 1
C&E	Convergence and Extension
CRISPR	Clustered Regularly Interspaced Short Palindromic Repeat
DFC	Dorsal Forerunner Cell
DORV	Double Outlet Right Ventricle
DPF	Days Post Fertilization
ECM	Extracellular Matrix
ENU	N-ethyl-N-nitrosourea
EVL	Enveloping Layer Cells
FER	Fps/Fes related
HCM	Hypertrophic Cardiomyopathy
HPF	Hours Post Fertilization
ISH	In Situ Hybridization
ITIM	Immunoreceptor Tyrosine-based Inhibitory Motif
KV	Kupffer's Vesicle
LEOPARD	Lentigines, Electrocardiographic conduction abnormalities, Ocular hypertelorism, Pulmonary stenosis, Abnormal genitalia, Retarded growth, Deafness: Sensorineural
LPM	Lateral Plate Mesoderm
LS	LEOPARD Syndrome
MO	Morpholino
MPZL1	Myelin Protein Zero Like 1
MS	Mass Spectrometry
NIC	Non Injected Control
NS	Noonan Syndrome
PS	Pulmonary Stenosis
PRR	Proline Rich Region
PTK	Protein Tyrosine Kinase
PTP	Protein Tyrosine Phosphatase
PTPN11	Tyrosine-protein phosphatase non-receptor type 11
PZR	Protein Zero Related
RTK	Receptor Tyrosine Kinase
SFK	Src Family Kinase
SH2	Src Homology 2
SHP2	Src Homology 2-containing protein-tyrosine-phosphatase 2
Spaw	Southpaw
TALEN	Transcription Activator Like Effector Nuclease
TSGI	Target Selected Gene Inactivation
VSD	Ventricle Septal Defect
YSL	Yolk Syncytial Layer
ZFN	Zinc Finger Nuclease