

Curriculum Vitae

Name: Jeroen den Hertog
Date of birth: 20 September 1965
Nationality: Netherlands

Education/positions

1983 - 1988 MSc, Utrecht University, Chemistry
1988 - 1992 PhD graduate student. Thesis: "Phosphotyrosine and neuronal differentiation. Of kinases and phosphatases". supervisors: Prof. Dr. S.W. de Laat and Dr. W. Kruijer, Utrecht University
1992 - 1994 Postdoc at the Salk Institute, La Jolla, CA in the lab of Tony Hunter
1994 - 1997 Project leader, Hubrecht Laboratory, Utrecht, the Netherlands
1997 - Group leader, Hubrecht Laboratory/Institute, Utrecht, the Netherlands
2008 - Deputy director research, Hubrecht Institute, Utrecht, the Netherlands
2008 - Professor of Molecular Developmental Zoology, Leiden University, the Netherlands

Memberships

1991 - present Nederlandse Vereniging voor Biochemie en Moleculaire Biologie
2003 - present American Society for Biochemistry and Molecular Biology
2014 - present Founding member of the Zebrafish Disease Models Society

Awards

1992 Fellowship, Dutch Cancer Society "Role of Protein-Tyrosine Phosphatases in carcinogenesis; regulation of enzymatic activity"

Other activities

2002, 2003, 2008 Co-organizer of the Dutch zebrafish meetings at the Hubrecht Institute
2014 Co-organizer of the meeting "Zebrafish: from fundamental research to industry", Leiden, the Netherlands
2007 Co-organizer of the Europhosphatases meeting in Aveiro, Portugal
2007 Co-organizer of the 5th European Zebrafish Genetics and Development Meeting in Amsterdam
2009 Organizer of the Europhosphatases meeting in Egmond aan Zee, the Netherlands
2011 Co-organizer of the Europhosphatases meeting in Baden near Vienna, Austria

Thesis advisor for

- Andre van Puijenbroek (1997): "Signal transduction by distinct neurotrophic receptors"
- Wouter van Inzen (1997): "Receptor Protein Tyrosine Phosphatase alpha and neuronal differentiation"
- Arjan Buist (1999): "Characterization of Receptor Protein-Tyrosine Phosphatase alpha"
- Christophe Blanchetot (2000): "Dimerization of receptor protein-tyrosine phosphatases. Characterization of RPTPalpha interacting proteins"
- Astrid van der Sar (2001): "Protein-tyrosine phosphatases in zebrafish development"
- Robert Bink (2002): "Embryonic development of the zebrafish central nervous system"
- Arnoud Groen (2006): "Redox regulation of receptor protein-tyrosine phosphatases"
- Chris Jopling (2006): "Gastrulation Signaling makes the round go long"
- Fiona Rodriguez (2007): "Functional characterization of the RPTP Dep1 in the zebrafish"
- Simone Lemeer (2008): "Mapping protein phosphorylation in zebrafish development"
- Andrei Vacaru (2010): "RPTP α -mediated activation of Src"
- Mark J.L. van Eekelen (2011): "Protein-tyrosine phosphatases in zebrafish gastrulation"
- Vincent J. Runtuwene (2012): "Functional characterization of protein-tyrosine phosphatases in zebrafish development using image analysis"
- Monica Bonetti and Jeroen Paardekooper Overman (2014): "Noonan and LEOPARD Syndrome in Zebrafish: Molecular Mechanisms and Cardiac Development"
- Miriam Stumpf (2016): "Interplay of PTEN subcellular localization and catalytic activities in vivo"

Invited speaker on meetings (2010-2016)

2010 Cancer Genomics Center annual meeting, Utrecht
2010 Disease Modeling in Zebrafish meeting, Boston, MA, USA
2010 FASEB meeting "Protein Phosphatases" Steamboat Springs, CO, USA
2010 Protein Phosphorylation, The Salk Institute, La Jolla, CA, USA
2010 ZF-CANCER meeting, San Sebastian, Spain
2011 PTPNET, Rehovot, Israel
2011 4th Strategic conference of zebrafish investigators, Asilomar, CA, USA
2011 4th Zebrafish disease models meeting, Edinburgh, UK
2011 Europhosphatases, Baden bei Wien, Austria
2012 Phosphatases in human disease, Melbourne, Australia
2012 Zebrafish 2012, 13th Australia and New Zealand workshop
2012 Fishing for answers: Zebrafish models of human development & disease, Cold Spring Harbor Asia Conference, Suzhou, China
2012 Cellular Signaling & Molecular Medicine, Cavtat-Dubrovnik, Croatia
2012 FASEB Meeting "Protein Phosphatases", Snowmass, CO, USA
2013 5th Strategic conference of zebrafish investigators, Asilomar, CA, USA
2013 Aarhus University, Denmark; host: Claus Oxvig
2013 Europhosphatases 2013, Rehovot, Israel
2014 Yale University, host: Anton M. Bennett
2014 3rd European Zebrafish PI Meeting, Ein-Gedi, Israel
2014 7th Zebrafish disease models conference, Madison, WI, USA
2014 FASEB meeting on Protein Phosphatases, Nassau, the Bahamas
2015 Invited talk at UC Davis, Davis, CA, USA; host: Fawaz Haj
2015 6th Strategic Zebrafish PI meeting, Asilomar, CA, USA
2015 Europhosphatases, Turku, Finland
2015 Zebrafish Disease Models 8, Boston, MA, USA
2016 4th European Zebrafish PI meeting, Lisbon, Portugal
2016 FASEB meeting on Protein Phosphatases, Steamboat Springs, CO, USA
2016 Zebrafish Disease Models 9, Singapore

Grants (2010-2016)

2010 Cancer Genomics Center "Anti-cancer activity of fungal secondary metabolites"
2012 ZonMw 205200001-1 "Bioprospecting for novel antibiotics"
2012 Yale/ Subward No. M12A11433 (NIH-grant) "Signaling by gain-of-function Shp-2 mutants in Noonan syndrome" (project leader: Anton M. Bennett)
2016 Horizon 2020 ERARE project NSEuroNET (project leader: Marco Tartaglia)

Patents etc. (2008-2014)

Patent application "Novel antibiotic" submitted on 30 July 2014

Publications in refereed journals (*complete*)

- de Groot, R.P., Rijken, P.J., den Hertog, J., Boonstra, J., Verkleij, A.J., de Laat, S.W., Kruijer, W. (1990) Microgravity decreases c-fos induction and serum response element activity. *J. Cell Sci.* 97: 33-38.
- de Groot, R.P., Rijken, P.J., den Hertog, J., Boonstra, J., Verkleij, A.J., de Laat, S.W., Kruijer, W. (1991) Nuclear responses to protein kinase C signal transduction are sensitive to gravity changes. *Exp. Cell Res.* 197: 87-90.
- den Hertog, J., de Laat, S.W., Schlessinger, J., Kruijer, W. (1991) Neuronal differentiation in response to epidermal growth factor of transfected murine P19 embryonal carcinoma cells expressing human epidermal growth factor receptors. *Cell Growth Differ.* 2: 155-164.
- den Hertog, J., Eman, R., Tertoolen, L.G., de Laat, S.W., Kruijer, W. (1991) Characterization of a tyrosine kinase signaling pathway in undifferentiated P19 embryonal carcinoma cells. *Exp. Cell Res.* 196: 226-232.
- Shen, S., Kruyt, F.A., den Hertog, J., van der Saag, P.T., Kruijer, W. (1991) Mouse and human retinoic acid receptor beta 2 promoters: sequence comparison and localization of retinoic acid responsiveness. *DNA Seq.* 2: 111-119.
- de Laat, S.W., de Groot, R.P., den Hertog, J., Rijken, P.J., Verkleij, A.J., Kruijer, W., Boonstra, J. (1992) Epidermal growth factor induced signal transduction in A431 cells is influenced by altered gravity conditions. *Physiologist* 35: S19-S22.
- den Hertog, J., de Groot, R.P., de Laat, S.W., Kruijer, W. (1992) EGF-induced jun B-expression in transfected P19 embryonal carcinoma cells expressing EGF-receptors is dependent on Jun D. *Nucleic Acids Res.* 20: 125-130.
- den Hertog, J., Pals, C.E., Jonk, L.J., Kruijer, W. (1992) Differential expression of a novel murine non-receptor protein tyrosine phosphatase during differentiation of P19 embryonal carcinoma cells. *Biochem. Biophys. Res. Commun.* 184: 1241-1249.
- Peppelenbosch, M.P., Tertoolen, L.G., den Hertog, J., de Laat, S.W. (1992) Epidermal growth factor activates calcium channels by phospholipase A2/5-lipoxygenase-mediated leukotriene C4 production. *Cell* 69: 295-303.
- de Groot, R.P., den Hertog, J., Vandenheede, J.R., Goris, J., Sassone-Corsi, P. (1993) Multiple and cooperative phosphorylation events regulate the CREM activator function. *EMBO J.* 12: 3903-3911.
- den Hertog, J., Pals, C.E., Peppelenbosch, M.P., Tertoolen, L.G., de Laat, S.W., Kruijer, W. (1993) Receptor protein tyrosine phosphatase alpha activates pp60c-src and is involved in neuronal differentiation. *EMBO J.* 12: 3789-3798.
- den Hertog, J., Tracy, S., Hunter, T. (1994) Phosphorylation of receptor protein-tyrosine phosphatase alpha on Tyr789, a binding site for the SH3-SH2-SH3 adaptor protein GRB-2 in vivo. *EMBO J.* 13: 3020-3032.
- den Hertog, J., Kruijer, W. (1994) Receptor protein-tyrosine phosphatase alpha: regulation by phosphorylation and involvement in neuronal differentiation. *Adv. Prot. Phosphat.* 8: 311-324.
- Chen, L., Wu, L., Otaka, A., Smyth, M.S., Roller, P.P., Burke, T.R.J., den Hertog, J., Zhang, Z.Y. (1995) Why is phosphonodifluoromethyl phenylalanine a more potent inhibitory moiety than phosphonomethyl phenylalanine toward protein-tyrosine phosphatases? *Biochem. Biophys. Res. Commun.* 216: 976-984.
- den Hertog, J., Sap, J., Pals, C.E., Schlessinger, J., Kruijer, W. (1995) Stimulation of receptor protein-tyrosine phosphatase alpha activity and phosphorylation by phorbol ester. *Cell Growth Differ.* 6: 303-307.
- Ameerun, R.F., de Winter, J.P., van den Eijnden-van Raaij, A.J., den Hertog, J., de Laat, S.W., Tertoolen, L.G. (1996) Activin and basic fibroblast growth factor regulate neurogenesis of murine embryonal carcinoma cells. *Cell Growth Differ.* 7: 1679-1688.
- Bilwes, A.M., den Hertog, J., Hunter, T., Noel, J.P. (1996) Structural basis for inhibition of receptor protein-tyrosine phosphatase-alpha by dimerization. *Nature* 382: 555-559.
- den Hertog, J., Hunter, T. (1996) Tight association of GRB2 with receptor protein-tyrosine phosphatase alpha is mediated by the SH2 and C-terminal SH3 domains. *EMBO J.* 15: 3016-3027.
- den Hertog, J., Overvoorde, J., de Laat, S.W. (1996) Expression of receptor protein-tyrosine phosphatase alpha mRNA and protein during mouse embryogenesis. *Mech. Dev.* 58: 89-101.
- van Puijenbroek, A.A., van Weering, D.H., van den Brink, C.E., Bos, J.L., van der Saag, P.T., de Laat, S.W., den Hertog, J. (1997) Cell scattering of SK-N-MC neuroepithelioma cells in response to Ret and FGF receptor tyrosine kinase activation is correlated with sustained ERK2 activation. *Oncogene* 14: 1147-1157.

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- Buist, A., Tertoolen, L.G., den Hertog, J. (1998) Potentiation of G-protein-coupled receptor-induced MAP kinase activation by exogenous EGF receptors in SK-N-MC neuroepithelioma cells. *Biochem. Biophys. Res. Commun.* 251: 6-10.
- Buist, A., Zhang, Y.L., Keng, Y.F., Wu, L., Zhang, Z.Y., den Hertog, J. (1999) Restoration of potent protein-tyrosine phosphatase activity into the membrane-distal domain of receptor protein-tyrosine phosphatase alpha. *Biochemistry* 38: 914-922.
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- den Hertog, J. (1999) Protein-tyrosine phosphatases in development. *Mech. Dev.* 85: 3-14.
- den Hertog, J., Blanchetot, C., Buist, A., Overvoorde, J., van der Sar, A., Tertoolen, L.G. (1999) Receptor protein-tyrosine phosphatase signalling in development. *Int. J. Dev. Biol.* 43: 723-733.
- Jiang, G., den Hertog, J., Su, J., Noel, J., Sap, J., Hunter, T. (1999) Dimerization inhibits the activity of receptor-like protein-tyrosine phosphatase-alpha. *Nature* 401: 606-610.
- Kester, H.A., Blanchetot, C., den Hertog, J., van der Saag, P.T., van der Burg, B. (1999) Transforming growth factor-beta-stimulated clone-22 is a member of a family of leucine zipper proteins that can homo- and heterodimerize and has transcriptional repressor activity. *J. Biol. Chem.* 274: 27439-27447.
- van der Sar, A.M., de Fockert, J., Betist, M., Zivkovic, D., den Hertog, J. (1999) Pleiotropic effects of zebrafish protein-tyrosine phosphatase-1B on early embryonic development. *Int. J. Dev. Biol.* 43: 785-794.
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- Blanchetot, C., den Hertog, J. (2000) Multiple interactions between receptor protein-tyrosine phosphatase (RPTP) alpha and membrane-distal protein-tyrosine phosphatase domains of various RPTPs. *J. Biol. Chem.* 275: 12446-12452.
- Buist, A., Blanchetot, C., den Hertog, J. (2000) Involvement of the membrane distal catalytic domain in pervanadate-induced tyrosine phosphorylation of receptor protein-tyrosine phosphatase alpha. *Biochem. Biophys. Res. Commun.* 267: 96-102.
- Buist, A., Blanchetot, C., Tertoolen, L.G., den Hertog, J. (2000) Identification of p130cas as an in vivo substrate of receptor protein-tyrosine phosphatase alpha. *J. Biol. Chem.* 275: 20754-20761.
- Jiang, G., den Hertog, J., Hunter, T. (2000) Receptor-like protein tyrosine phosphatase alpha homodimerizes on the cell surface. *Mol. Cell. Biol.* 20: 5917-5929.
- Tertoolen, L.G., Blanchetot, C., Jiang, G., Overvoorde, J., Gadella, T.W.J., Hunter, T., den Hertog, J. (2001) Dimerization of Receptor Protein-Tyrosine Phosphatase alpha in living cells. *BMC Cell Biol.* 2: 8.
- van der Sar, A., Betist, M., de Fockert, J., Overvoorde, J., Zivkovic, D., den Hertog, J. (2001) Expression of receptor protein-tyrosine phosphatase alpha, sigma and LAR during development of the zebrafish embryo. *Mech. Dev.* 109: 423-426.
- Blanchetot, C., Tertoolen, L.G., den Hertog, J. (2002) Regulation of Receptor Protein Tyrosine Phosphatase alpha by oxidative stress. *EMBO J.* 21: 493-503.
- van der Sar, A., Zivkovic, D., den Hertog, J. (2002) Eye defects in receptor protein-tyrosine phosphatase alpha knock-down zebrafish. *Dev. Dyn.* 223: 292-297.
- Blanchetot, C., Tertoolen, L.G., Overvoorde, J., den Hertog, J. (2002) Intra- and inter-molecular interactions between intracellular domains of Receptor Protein-Tyrosine Phosphatases. *J. Biol. Chem.* 277: 47263-47269.
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- van der Wijk, T., Overvoorde, J., den Hertog, J. (2004) H₂O₂ induced intermolecular disulfide bond formation between Receptor Protein-Tyrosine Phosphatases. *J. Biol. Chem.* 279: 44355-44361.
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- Jopling, C., den Hertog, J. (2005) Fyn/Yes and non-canonical Wnt signaling converge on RhoA in vertebrate gastrulation cell movements. *EMBO Rep.* 6: 426-431.
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- den Hertog, J., Groen, A., van der Wijk, T. (2005) Redox regulation of protein-tyrosine phosphatases. *Arch. Biochem. Biophys.* 434: 11-15.
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- van der Wijk, T., Blanchetot, C., den Hertog, J. (2005) Regulation of Receptor Protein-Tyrosine Phosphatase dimerization. *Methods* 35: 73-79.
- Diks, S.H., Bink, R.J., van de Water, S., Joore, J., van Rooijen, C., Verbeek, F.J., den Hertog, J., Peppelenbosch, M.P., Zivkovic, D. (2006) The novel gene *asb11*: a regulator of the size of the neural progenitor compartment. *J. Cell Biol.* 174: 581-592.
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- Jopling, C., van Geemen, D., den Hertog, J. (2007) Shp2 knock down and Noonan/LEOPARD mutant Shp2 induced gastrulation cell movement defects in zebrafish. *PLoS Genet.* 3: e225.
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- Lemeer, S., Jopling, C., Naji, F., Ruijtenbeek, R., Slijper, M., Heck, A.J.R., den Hertog, J. (2007) Protein-tyrosine kinase activity profiling in knock down zebrafish embryos. *PLoS One* 2: e581.
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