

## *Curriculum vitae*

### **Mart Saarma**

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### **Education and Training**

- Tartu University, Estonia, MSc, biochemistry and molecular biology 1972
- Tartu University, Estonia, PhD, biochemistry and molecular biology 1975

### **Postdoctoral research**

- Friedrich Miescher Institute, Basel, Switzerland, postdoctoral fellow 1982
- Institute of Molecular Biology, Russian Academy of Sci., Dr. Habil 1986

**Current position:** Professor of Biotechnology, Director of the Laboratory of Molecular Neuroscience, Institute of Biotechnology, University of Helsinki, Finland

### **Positions and Employment**

- *Research assistant & junior researcher*, Department of Biochemistry, Medical Faculty, Tartu University 1971-1977
- *Head of the Laboratory of Molecular Genetics*, Institute of Physics, Estonian Academy of Sciences, Tartu 1977-1980
- *Head of the Department of Molecular Genetics*, Institute of CPB, Estonian Academy of Sciences, Tartu, Tallinn 1980-1990
- *Professor*, Tallinn Technical University (part time) 1986-2015
- *Director, Professor*, Institute of Biotechnology, Univ. of Helsinki 1990-2008
- *Director*, Biocenter Finland 2008-2009
- *Director*, Centre of Excellence in Molecular and Integrated Neuroscience Research 2008-2013
- *Academy Professor*, Institute of Biotechnology 2009-2013
- *Professor of Biotechnology*, Institute of Biotechnology 2014-

### **Other Experience and Professional Memberships**

- Founder and member Board of the Directors of the Mobidiag Ltd., Finland  
-Member of the board 2000-2010
- Board of the Directors of the Finnish Genome Centre, Chairman of the board 2004-2007
- Estonian Prime Minister's Council for Science and Technology  
-Member of the Council 2001-
- Scientific Advisory Board of the Heidelberg Neuroscience Center  
-Chairman of the board 2002-
- Scientific Advisory Board of the Göttingen Neuroscience Center, member 2003-
- Journal Experimental Neurology- Member of the editorial board 2003-
- Scientific Board of the Helsinki Institute of Information Technology  
Member of the SAB 2009-



degree. Fifteen of Dr. Saarma's former PhD students or post-docs have become group leaders and received professorships.

### **Recent Research Funding**

1. Academy professor, 2011-2013, 300,000 €/year
2. Centre of Excellence in Neuroscience, Academy of Finland, 2011-2013, 200,000 €/year
3. MJFF for Parkinson's Research, USA, "Methods for CDNF delivery" 2011-2014, 220,000 €/year
4. Neurotrophics Inc., USA, 2011-2013, Research contract on NRTN mutants, 120,000 €/year
5. Sigrid Jusélius Medical Research Foundation, "Novel NTFs", 2013-2019, 110,000 €/year.
6. MFJJ for Parkinson's Research, "CDNF and  $\alpha$ -synuclein model of PD", 2014-2015, 75,000 €/year.
7. Academy of Finland grant "Novel neurotrophic factors". 2012-2016, 150,000 €/year).
8. European Union FP7, "New drugs for pain", 2013-2017, 120,000 €/year,
9. European Union Marie Curie IAAP project, "GDNF mimetics", 2013-2017, 140,000 €/year.
10. Juvenile Diabetes Research Foundation, USA, "MANF & diabetes, 2013-2016, 140,000 €/year.
11. Juvenile Diabetes Research Foundation, USA, "MANF receptors", 2014-2015, 50,000 €/year.
12. GeneCode-Orion Pharma collaboration, "GDNF mimetics", 2013-2015, 75,000€/year.
13. Herantis Pharma Ltd. collaboration, "CDNF for Parkinson's", 2013-2015, 50,000€/year.
14. Parkinson's UK, "GDNF mimetics for PD", 2014-2015, 45,000€total.
15. Jane and Aatos Erkkö Foundation, "CDNF for Parkinson's disease", 2014-2019, 3.100,000 €total
16. European Union H2020 grant, "TreatER- CDNF clinical trials in Parkinson's disease", 2017-2019, 600,000€total
18. Department of Defense grant, USA. "CDNF for the Treatment of Amyotrophic Lateral Sclerosis", 2017-2018, 500,000 USD total
19. USA ALS Association ALSA grant, "CDNF and C-CDNF variants": new therapy for ALS, 2018-2019, 300,000 USD
20. Juvenile Diabetes Res. Found., USA, "Therapeutic Potential of MANF for T1D", 2017-2019, 500,000 USD.

### **Selected peer-reviewed publications (in chronological order).**

1. Pirvola, U., Palgi, J., Ylikoski, J., Lehtonen, E. Arumäe, U. & Saarma, M. (1992) Brain-derived neurotrophic factor and neurotrophin 3 in the peripheral target fields of developing inner ear ganglia. **Proc. Natl. Acad. Sci.**, USA, 89, 9915-9919.
2. Trupp, M., Arenas, E., et al. Saarma, M. & Ibañez, C.F. (1996) Functional receptor for GDNF encoded by the *c-ret* proto-oncogene. **Nature**, 381, 785-789.
3. Rivera, C., Voipio, J., Payne, J.A., Ruusuvuori, E., Lahtinen, H., Lamsa, K., Pirvola, U., Saarma, M. & Kaila, K. (1999) A  $K^+$ /Cl<sup>-</sup> co-transporter KCC2 renders GABA hyperpolarizing during neuronal maturation. **Nature** 397, 251-255.
4. Rossi, J., Luukko, K. et al. Saarma, M. & Airaksinen, M.S. (1999) Retarded growth and deficits in the enteric and parasympathetic nervous system in mice lacking GFRa2, a functional neurturin receptor. **Neuron** 22, 243-252.
5. Meng, X., Lindahl, M., Hyvönen, M. E., Parvinen, M., de Rooij, D. G., Hess, M. W., Raatikainen-Ahokas, A., Sainio, K., Rauvala, H., Lakso, M., Pichel, J. G., Westphal, H., Saarma, M. & Sariola, H. (2000) Regulation of cell fate decision of undifferentiated spermatogonia by GDNF. **Science**, 287, 1489-1493.
6. Airaksinen, M. S. & Saarma, M. (2002) GDNF family neurotrophic factors: receptor mechanisms, biological functions and therapeutic utility. **Nature Rev. Neurosci.**, 3, 383-394.
7. Rivera, C., Hong Li, Thomas-Crusells, J., Lahtinen, H., Viitanen, T., Nanobashvili, A., Kokaia, Z., Airaksinen, M. S., Voipio, J., Kaila, K. & Saarma, M. (2002). BDNF-induced TrkB activation down-regulates the  $K^+$ -Cl<sup>-</sup> cotransporter KCC2 and impairs neuronal Cl<sup>-</sup> extrusion. **J. Cell Biol.**, 159: 747-752.
8. Lindholm, P., Voutilainen, M et al. and Saarma, M. (2007) Novel neurotrophic factor CDNF protects and rescues midbrain dopaminergic neurons *in vivo*. **Nature**, 448, 73-77.

9. Parkash, V., Leppänen, V-M., Virtanen, H., Jurvansuu, J. M., Bespalov, M. M., Sidorova, Y. A., Runeberg-Roos, P., Saarma, M. and Goldman, A. (2008) The Structure of the glial cell line-derived neurotrophic factor-coreceptor complex. Insights into RET signalling and heparin binding. **J. Biol. Chem.**, 283, (50), 35164-35172.
10. Mijatovic J, Airavaara M, Planken A, Auvinen P, Raasmaja A, Piepponen TP, Costantini F, Ahtee L, Saarma M (2007) Constitutive Ret activity in knock-in multiple endocrine neoplasia type B mice induces profound elevation of brain dopamine concentration via enhanced synthesis and increases the number of TH-positive cells in the substantia nigra. **J Neurosci** 27: 4799-4809.
11. Li H, Khirug S, Cai C, Ludwig A, Blaesse P, Kolikova J, Afzalov R, Coleman S K, Lauri S, Airaksinen M S, Keinänen K, Khiroug L, Saarma M, Kaila K and Rivera C. (2007) KCC2 interacts with the dendritic cytoskeleton to promote spine development. **Neuron** 56(6), 1019-1033.
12. Parkash V, Leppanen VM, Virtanen H, Jurvansuu JM, Bespalov MM, Sidorova YA, Runeberg-Roos P, Saarma M, Goldman A (2008) The structure of the glial cell line-derived neurotrophic factor-coreceptor complex: insights into RET signaling and heparin binding. **J Biol Chem** 283: 35164-35172.
13. Palgi M, Lindström R, Peränen J, Piepponen TP, Saarma M, Heino TI. (2009) Evidence that DmMANF is an invertebrate neurotrophic factor supporting dopaminergic neurons. **Proc. Natl. Acad. Sci. U S A.**, 106 (7): 2429-2434.
14. Voutilainen, M.H., Bäck, S., Pörsti, E., Toppinen, L., Lindgren, L., Lindholm, P., Peränen, J., Saarma, M\*. and Tuominen, R. K. (2009) Neurotrophic factor MANF is neurorestorative in rat model of Parkinson's disease . **J. Neurosci**, 29(30):9651-9659. \*Corresponding author.
15. Lonka-Nevalaita L, Lume M, Leppänen S, Jokitalo E, Peränen J and Saarma M. (2010) Characterization of the intracellular localization, processing and secretion of two GDNF splice isoforms. **J. Neurosci.** , 30(34):11403-11413.
16. Bespalov MM, Sidorova Y A, et al. and Saarma M. (2011) Heparan sulfate proteoglycan syndecan-3 is a novel receptor for GDNF, neurturin and artemin **J. Cell Biol.**, 192(1), 153-169.
17. Hellman M, Arumäe U, Yu LY, Lindholm P, Peränen J, Saarma M\*, Permi P\* (2011) Mesencephalic Astrocyte-derived Neurotrophic Factor (MANF) Has a Unique Mechanism to Rescue Apoptotic Neurons. **J Biol Chem** 286: 2675-2680. \*Equal contribution.
18. Glerup S, Lume M et al. Saarma M, Nykjaer A and Petersen CM. (2013) SorLA controls neurotrophic activity through sorting of GDNF and its receptors GFR $\alpha$ 1 and RET. **Cell Reports** 3(1):186-199.
19. Lindahl M, Danilova T, Palm E, Pulkila P, Voikar V, Hakonen E, Ustinov J, Andressoo J-O, Harvery B, Otonkoski T, Rossi J and Saarma M. (2014). MANF is indispensable for the proliferation and survival of pancreatic  $\beta$ -cells. **Cell Reports**, 7(2):366-75. doi: 10.1016/j.celrep.2014.03.023. Epub 2014 Apr 13
20. Kopra J, Vilenius C et al. Saarma M\*, Andressoo J-O\* (2015) GDNF is not required for catecholaminergic neuron survival in vivo. **Nature Neurosci.** 18(3):319-22. doi: 10.1038/nn.3941. \*equal contribution.
21. Kumar A, Kopra J et al. Saarma M\*, Andressoo JO\* (2015) GDNF Overexpression from the Native Locus Reveals its Role in the Nigrostriatal Dopaminergic System Function. **PLoS Genet.** Dec 17;11(12):e1005710. doi: 10.1371/journal.pgen.1005710. \*Equal contribution.
22. Sidorova YA, Bespalov et al. and Saarma M (2017) A Novel Small Molecule GDNF Receptor RET Agonist, BT13, Promotes Neurite Growth from Sensory Neurons In vitro and Attenuates Experimental Neuropathy in the Rat. **Front. Pharmacol.** published: 21 June 2017 doi: 10.3389/fphar.2017.00365
23. Runeberg-Roos P, Piccinini E, et al. Penn R, Saarma M. (2016) Developing therapeutically more efficient Neurturin variants for treatment of Parkinson's disease. **Neurobiology of Disease.** 96:335-345. doi: 10.1016/j.nbd.2016.07.008.
24. Saarma M, Goldman A. (2017) Obesity: Receptors identified for a weight regulator. **Nature** 550 (7675):195-197. doi: 10.1038/nature24143. Epub 2017 Sep 27
25. Lindahl M, Saarma M, Lindholm P (2016) Unconventional neurotrophic factors CDNF and MANF: structure, physiological functions and therapeutic potential. **Neurobiology of Disease**, 2016 Jul 14. pii: S0969-9961(16)30171-1. doi: 10.1016/j.nbd.2016.07.009. [Epub ahead of print]