

# Curriculum Vitae Marten Smidt

May 7, 2014

## Contents

<b>1</b>	<b>Personal details</b>	<b>2</b>
<b>2</b>	<b>Education</b>	<b>2</b>
<b>3</b>	<b>Civil service</b>	<b>2</b>
<b>4</b>	<b>Professional experience</b>	<b>2</b>
<b>5</b>	<b>Professional activities</b>	<b>3</b>
5.1	Grant support . . . . .	3
5.2	Reviewing/editorial activities . . . . .	3
5.3	Brief summary of research . . . . .	4
5.4	Trainees . . . . .	5
5.4.1	PhD students: . . . . .	5
5.4.2	(co-)Promoter: . . . . .	6
5.4.3	Master Students: . . . . .	6
5.4.4	Other trainees . . . . .	7
5.5	Selection of invited lectures . . . . .	7
5.6	Selection of current and past collaborations with (foreign) academic groups . . . . .	9
5.7	Selection of management activities . . . . .	9
5.7.1	Research management . . . . .	9
5.7.2	IT management . . . . .	10
5.7.3	Managment trainings/activities . . . . .	10
5.7.4	Personal management . . . . .	10
<b>6</b>	<b>Educational experience</b>	<b>11</b>
<b>7</b>	<b>Selected honors</b>	<b>12</b>
<b>8</b>	<b>List of publications, books and patent applications</b>	<b>12</b>
8.1	Peer refereed international journals (impact factors (IF) are listed) . . . . .	12
8.2	Patent applications: . . . . .	17
8.3	Books (chapters) . . . . .	17
8.4	Manuscripts (soon to be) submitted . . . . .	17
8.5	Other scientific contributions . . . . .	17
<b>9</b>	<b>Citation information</b>	<b>17</b>

## 1 Personal details

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## 2 Education

- Higher Laboratory Education: September 1981-August, 1984, Main subject :Medical Microbiology
- Biology, University of Groningen: September 1986- March 1991, Main Subject :Biochemistry/Microbial-Physiology
- Doctorate at University of Groningen: June 1991- May 1996, Title of thesis :Two DNA-binding proteins recognizing the apo-VLDL-II gene cis-regulatory element D.

## 3 Civil service

- 1984-1986: Staff member in the division hospital in the Seedorf Facility, Germany

## 4 Professional experience

- 1986: Technician at the special blood bank facility as part of "Eurotransplant", Academic Hospital Groningen, The Netherlands
- 1991-1995: PhD in the group of Dr. Geert AB: Analysis of the involvement of liver specific or enriched transcription factors on the liver specific and estradiol inducible apoVLDL II gene, University of Groningen, The Netherlands.
- 1995-1999: Postdoc at the Rudolf Magnus Institute for Neuroscience in the lab of Prof Dr. J.P.H. Burbach: Study of brain development in relation to mental disorders and cloning of specific transcription factors which are involved in that process, University of Utrecht, The Netherlands.
- 2000- 2006: Assistant professor at the Department of Neuroscience and Pharmacology, Rudolf Magnus Institute of Neuroscience, University Medical Center, Utrecht, The Netherlands.
- 2001-2011: Team leader of the midbrain dopaminergic system research team at the Department of Neuroscience and Pharmacology, Rudolf Magnus Institute of Neuroscience, University Medical Center, Utrecht, The Netherlands.
- 2002-2011: Coordinator Section Developmental Neuroscience of the Rudolf Magnus Institute of Neuroscience, University Medical Center, Utrecht, The Netherlands
- 2006-2009: Associate professor in the department Neuroscience and Pharmacology, University Medical Center, Utrecht, The Netherlands.
- 2008-2011: Head of the research platform Neurodevelopment, department Neuroscience and Pharmacology, University Medical Center, Utrecht, The Netherlands.
- 2009-2011; Full Professor, chair: Developmental Neurobiology, department Neuroscience and Pharmacology, University Medical Center, Utrecht, The Netherlands.
- 2011-present: Full Professor, Molecular Neuroscience, Center for Neuroscience, Swammerdam Institute for Life Sciences, University of Amsterdam, Amsterdam, The Netherlands

## 5 Professional activities

### 5.1 Grant support

1. 1998-2001: National Parkinson Foundation Research Grant: Involvement of the homeobox gene Pitx3 in development and maintenance of mesDA neurons. (PI)
2. 1999-2001: NWO-MW Fellowship: The role of the novel homeodomain Pitx3 in molecular cascades of development and maintenance of the mesencephalic dopaminergic system. (PI)
3. 1999-2002: Korczak Foundation Fellowship: Molecular processes in brain development, Postdoc 3 years. (PI) (With co-PI JPH burbach)
4. 2000-2004: Korczak Foundation Project: Molecular processes in brain development, PhD 4 years, (PI) (With co-PI JPH burbach)
5. 1999-2001: Industrial project with Solvay Pharmaceuticals: Pitx3 function and development of model systems with disturbed mesencephalic dopamine systems . Postdoc (PI) (With co-PI JPH burbach)
6. 2000-2002: NWO-MW grant: Genetic and epigenetic control of mesencephalic dopamine system development, Framework of scientific cooperation between The Netherlands and the Russian Federation. (PI with co-PI WH Gispen )
7. 2003-2007: NWO-ALW grant: The Pitx3 homeobox gene cascade and dysfunction of the midbrain dopamine system. (PI) (with co-PI JPH burbach)
8. 2004-2009: Hypotential program of the University of Utrecht: BAMI: Brain Analysis through Molecular Imaging (PI) (With co-PI Freek Beekman)
9. 2004: Brain Foundation in The Netherlands (Hersenstichting Nederland) research grant. (PI)
10. 2006-2010: NWO-ALW research grant: Identification of Pitx3 regulated genes in midbrain dopamine neurons (PI)
11. 2007-2011: TI-Farma initiative, The Netherlands: 2 PhD and 1 PD position (PI with co PI J Pasterkamp and JPH Burbach))
12. 2007: Brain Foundation in The Netherlands (Hersenstichting Nederland) research grant. (PI)
13. 2009-2012: FP7 EU-grant proposal/project, medium sized EU-research project (coordinator and PI)
14. 2009-2014: NWO-ALW VICI grant (PI)
15. 2009-2013: NWO-ALW program grant (PI)
16. 1009: ZonMw (NWO) ZonMw-networkgrant (for FP-7 meeting).
17. 2012-2013: 4\* publication grants (NWO) open acces publications.
18. MRA-cluster grant “Impact” 2013-2015. (co-PI with “Innosser” (company)).

### 5.2 Reviewing/editorial activities

- Reviewer for Science, Trend in Cell Science, Journal of Neurochemistry, Neuroscience, European Journal of Neuroscience, European Journal of Pharmacology, Journal of Biochemistry, Gene, Pharmacology Biochemistry and Behavior, Cell, Trends in Pharmacological sciences, PNAS and Development.
- Grant reviewer for the Netherlands and Israel organizations for scientific research.
- Member of the grant evaluation board of NWO-ALW(2005-2009).
- Chairman of the grant evaluation board for NWO-ALW-VENI (2009-2011).
- Member of the French National Research Agency (ANR) reviewing board (2008-current).
- Member of the Reviewing board of Frontiers in Neuroanatomy and 2008-current).
- Editorial Board Member of Stem Cell Review Letters (2009-present).
- Member of the NWO-domain grant evaluation board (2009-2012).

- Member of the French National Research Agency (ANR) non-thematic programme reviewing board (Neuroscience, 2010-current).
- Editorial Board member of *ISRN Developmental Biology* (2012-current).
- Member of the EU Marie Curie program Evaluation board (2010, 2011, 2013).
- Chairman of the NWO-ALW-VIDI board (2012-current).

### 5.3 Brief summary of research

My main interest is molecular programming during development of the central nervous system. Since at that time almost nothing was known on the subject, I started on a cloning effort to identify transcription factors that play a role during CNS development. From this work three major breakthroughs were established:

1. The cloning, identification and characterization of the homeobox gene *Pitx3* (publication 79). This gene was found to be exclusively expressed in the substantia nigra (SNc) and ventral tegmental area (VTA) forming the midbrain dopamine system, essential for mood and movement regulation in mammals. The real impact of the work was that this factor is exclusively expressed in these neurons and this formed the first step in the understanding of molecular programming of midbrain dopamine neurons.
2. The identification of the role of the orphan nuclear hormone receptor *Nurr1* (publication 78). It was shown by us and others that *Nurr1* is essential for the development of fully differentiated midbrain dopamine neurons. This was the second factor identified to be involved in midbrain dopamine neurodevelopment.
3. The identification of *Lmx1b* (publication 75). We showed that the early specification of the midbrain by *Lmx1b* is essential for the formation of midbrain dopaminergic neurons. Moreover, we showed that TH expression was possible in early DA neurons without the expression of *Pitx3*, indicating that *Pitx3* might be involved in molecular processes other than transmitter phenotype.

After this cloning and descriptive phase I was interested to go into depth into the role of *Pitx3* (as an NWO fellow) in the neurodevelopment of midbrain dopamine neurons and to broaden my view on molecular signaling events in neuronal cells. This was accomplished by the start of analysis of the *Pitx3* knock out and by the start of a new research line on forkhead proteins (*FoxO*). The work lead to two major findings:

1. The data from the *Pitx3* knock-out analysis (aphakia mouse) formed a new chapter in the understanding of the role of *Pitx3* in the development of midbrain dopamine neurons (publication 62). We showed that *Pitx3* is essential for the formation of the SNc and the ventral part of the VTA. Moreover it was clear from the analysis that the defect was apparent at the early stage of terminal differentiation. Most importantly, the defect was not present in all midbrain dopamine neurons but mainly in the ventral medial SNc and ventral VTA.
2. The cloning and functional characterization of *FoxO6*, a novel member of the *FoxO* family (*FoxO1*, *FoxO3* and *FoxO4*). We showed that *FoxO6* had unique properties in terms of nucleo-cytoplasmic shuttling, as a result of PKB signaling, compared to its family members (publication 68). Later we showed the mechanism of the altered shuttling behavior and showed that phosphorylation by PKB does inactivate *FoxO6* by inhibiting DNA interaction without the extra level of inhibition of nuclear removal (publication 55). We have gained quickly a good position by this work. A review from our team received much enthusiasm as highlighted by 82 citations so-far and the 25th place of most downloaded papers in the publication year (publication 61).

The fact that a subset of the complete group of dopamine neurons was affected in the *Pitx3* knock-out (*Pitx3* itself is expressed in all midbrain dopamine cells) initiated the novel idea that the molecular coding of the SNc and VTA is not the same. A real step forward was made by the identification of subset specific markers and coding differences in the ventricular zone. This concept of subset specification was a crucial step in the way the field regarded the molecular pathways leading to the development of dopamine neurons of the SNc and VTA (publication 46). In addition, it became clear that the neurons populating the SNc and VTA are not generated exclusively in the midbrain but also in the diencephalon. Therefore, the name of this neuronal group was changed to mesodiencephalic dopaminergic (mdDA) neurons and has been used as such from that point on.

This was a crucial moment in my career, i established my own group and my work clearly surpassed the initial identification and function-description of transcription factors involved in the development of mdDA neurons. My interest went into two additionally research directions:

1. The live visualization of dopamine neurotransmission through multi-pinhole SPECT. Prof dr. Freek Beekman designed a spectacular micro-SPECT system to follow tracers in the mouse brain with a resolution of 0.3 mm. Together we started to image live dopamine transmitter events in a living mouse. This work has lead to two high impact publications (publication: 54 and 33).

2. Understand how subset specification is established, which subsets exist and what the relationship is between subset and specific connectivity. A crucial finding in the understanding of subsets specific molecular coding was established through the identification of a subset specific transcriptional target of Pitx3. This gene, (retinal) aldehyde dehydrogenase 2 (Ahd2, Raldh1) is expressed, in the adult brain, in the ventral cells of the SNc and VTA, the neurons that are lost in the Pitx3 mutant (publication 35). A second novel finding was that retinoic acid (RA) has a role in terminal differentiation of this specific set of neurons in addition to its role in the ventricular zone. Ahd2 is present in ventricular zone cells, its transcription is terminated when cells leave the ventricular zone and under the control of Pitx3, Ahd2 is transcribed again in a (lateral) subset of mdDA neurons and is essential for the synthesis of RA out of retinal. We were able to show the dependence of mdDA differentiation for RA signalling by rescuing the Pitx3 knock-out phenotype through the exogenous application of RA.

Although I am still working on- and interested in the FoxO6 knock out (we have generated ko animals) my main interest lies with the molecular programming of mdDA neuronal subsets. My lab is currently investigating 1) why Ahd2 activation is only happening in the described subset; 2) we are mapping transcriptional targets of Engrailed, Lmx1a/b, and Nurr1 to get a better idea about the molecular programming that is initiated within mdDA neurons; 3) the functional interaction between Pitx3/Nurr1 (publication 30) and En1 and 4) we are finalizing the identification of adult subset specific markers. At this moment my research group consist of 4 PhD students, 3 postdocs, 2 technicians, one eu-program manager and every year about 3 master students.

The work described above has been very fruit-full and has lead to a leading position of my research group mainly in the field of development and engineering of mdDA neurons, marked by many invitations to write reviews/books on the topic, the high amount/level of peer-reviewed publications and the invitations to speak at the international level about my work.

In the summer of 2011, i decided to move the work-group to the Swammerdam Institute for Life Sciences at the University of Amsterdam and started the "Molecular Neuroscience" section. I have new opportunities to build further on the scientific output and have more funding/equipment available to perform cutting edge work in the direction of molecular programming of neuronal systems.

## 5.4 Trainees

### 5.4.1 PhD students:

1. 1997-2001: Cerial Asbreuk: "Cloning and characterization of neurohypophysial transcription factors involved in development and function of the hypothalamo/hypophysial axis."
2. 1998-2002: Marjan Kromkamp: "Expression patterns of genes involved in brain development and human brain disorders".
3. 2000-2004: Simone Smits: Analysis of Pitx3 mutants.
4. 2000-2004: Lars van der Heide: PKB Signaling in the developing and adult nervous system
5. 2001-2005: Patrick Wijchers: Cloning of Forkhead genes related to midbrain development and function.
6. 2003-2007: Koen Hornman: Development and function of the mesDA system, involvement of Pitx3.
7. 2004-2008: Frank Jacobs: Identification of target genes of the homeodomain gene Pitx3.
8. 2007-2011: Teresa Alves Dos Santos: Identification of Pitx3 regulated genes in midbrain dopamine neurons
9. 2007-2012: Elisa Hoekstra: Molecular coding of mdDA neurons during development
10. 2009-2010: Kerstin Iffland: Role of RA through DLK1 signalling in the development of mdDA neurons.
11. 2009-2013: Jesse Veenliet, The role of RA signalling in subset specification of mdDA neurons.
12. 2011-2015: Ricardo Paap, Cortical development, the role of FoxO6 in stem cell maintenace.
13. 2011-2015: Simone Mesman, Ventricular zone coding of the mesodiencephalic area
14. 2011-2015: Willemieke Kouwenhoven, Crosstalk between En1, Pitx3 and Nurr1 in development of mdDA neurons
15. 2013-2017: Iris Wever, Epigentic influence of Lim homeodomain proteins in neuronal specification of mdDA neurons.
16. 2013-2017: Erik van Heesbeen, Epihentic mechanisms in neuronal specification and differentiation.

#### **5.4.2 (co-)Promoter:**

1. Co-promotor of Ciel Asbreuk (PhD in 2002).
2. Co-promotor of Marjan Kromkamp (PhD in 2002).
3. Co-promotor of Lars van de Heide (PhD in 2004).
4. Co-promotor of Simone Smits (PhD in 2005)
5. Co-promotor of Patrick Wijchers (PhD in 2005).
6. Co-promotor of Frank Jacobs (PhD in 2009).
7. Promotor of Teresa Alvers dossantos (PhD in 2011).
8. Promotor of Elisa Hoekstra (PhD in 2012).
9. Promotor of Jesse Veenliet (PhD in 2014)
10. Promotor of Willemieke Kouwenhoven (PhD in 2016)
11. Promotor of Ricardo Paap (PhD in 2016)
12. Promotor of Simone Mesman (PhD in 2016)
13. Promotor of Iris Wever (PhD in 2017)
14. Promotor of Erik van Heesbeen (PhD in 2017)

#### **5.4.3 Master Students:**

1. 1998-1999: Kyra Campbell: Cloning of Xenopus Pitx3.
2. 1999-2000: Leontien Spierings: Analysis of Pitx3 protein in Human SNc in healthy controls and Parkinsonian brain.; Erik Baaijens: Analysis of new markers in the mesDA system; Max Custers: Provision of cRNA probes for ISH analysis of mesDA markers.
3. 2001-2002: Frank Jacobs: Cloning of homeodomain and forkhead genes from the mesDA systems.; Wiebe Hielkema: Recombinant protein production/purification and generation of antibodies.; Suzanne van der Nobelen: Subtraction library screening of wt and AK mesDA tissue.; Koen Hornman: Generation of a TH-Pitx3 knock-in construct.
4. 2004: Rolf Meijer: analyzing the molecular code on developing midbrain dopaminergic neurons; Joris van Arnsbergen: Analyzing signaling cascades in midbrain dopaminergic neurons; Marijke de Backer: mGluR distribution in the developing and adult mouse brain.
5. 2005/2006: Joanna Korecka, Hanneke Verstegen
6. 2007: Susan van Erp, Mark Mizze, Thomas Gora.
7. 2008: Louk van der Kallen, Willem de Munnik, Jesse Veenliet.
8. 2009: Diewertje Bink, Gerard Scheppink.
9. 2010; Simone Mesman, Ricardo Paap, Roel Neijts
10. 2011; Roel Neijts, Iris Wever; Cindy Wagemans
11. 2012-2013; Jurrien Fransen, Robert Post, Nina Haring, Sasja Franke, Anika Bongaarts, Sonja Jeanette Kruse, Jaivi Aalbers

#### 5.4.4 Other trainees

1. 1997-1999: Dr. Pilar Cazorla: "Characterisation of the novel homeodomain gene Pitx3".
2. 1997-1998: Prof. Dr. Michael Selmanoff : "Cloning of novel homeodomain genes involved in the development and function of the hypothalamus".
3. 2004-2007: Dr. Simone Smits: Development of the mesDA system.
4. 2005-2007: Dr. Cornelle Noorlander: The role of prenatal antidepressant use for the setting of the serotonin system.
5. 2008-2011: Dr. Koushik Chakrabarty: Gene profiling of early developmental events in mesodiencephalic dopaminergic neurons.
6. 2009-2010: Dr. Evelyn Groot, Early dopaminergic subset specification on the mesodiencephalic-ventricular zone.
7. 2009-2012: Dr. Wadia Almirza, Unraveling the key players in RA signaling during mdDA neurodevelopment.
8. 2011-2013: Dr. E. Hoekstra, Role of Lmx1a and Lmx1b in mdDA neuronal specification.
9. 2011-2013; Dr. L. van der Heide, TGF-beta signalling in mdDA neurons.

#### 5.5 Selection of invited lectures

1. March 5, 1999: Molecular cascades in development of the mesDA system; Invited by Andreas Hartmann, INSERM, Paris, France
2. March 19, 1999: Cloning and analysis of homeobox genes in CNS development; Invited by Dr. M. Linskens, University of Groningen, The Netherlands
3. May 19, 1999: Homeodomain transcription factors and MesDA development; Invited by Joost Verhagen, Netherlands Brain Institute, Amsterdam, The Netherlands
4. December 10, 1999: Molecular cascades in mesDA development and function; Invited by Dr. Jochem Graw, Max Plank Institute, Munich, Germany
5. April 6-9, 2000: Molecular cascades in mesDA development and function; Invited by: Professor K.V. Sudakov, Russian Academy of Medical Sciences, P.K. Anokhin Institute of Normal Physiology, Moscow, Russia.
6. November 24, 2000: New directions in the development and function of the mesencephalic dopaminergic system; Invited by: Dr. Bert Joosten, Department of Neurology, University Medical Center, Utrecht, The Netherlands
7. June 9-14, 2002: Development of the substantia nigra pars compacta is depending on the homeodomain gene Pitx3; Invited by: The 2002 Dopamine Conference in Portland, Oregon, USA
8. January 31, 2003: Development of the substantia nigra pars compacta is depending on the homeodomain gene Pitx3; Invited by: Dutch Neuro Federation Research Class 2003
9. July 17, 2003: Development of the substantia nigra pars compacta is depending on the homeodomain gene Pitx3; Invited by: Dr. Horst Simon, Department of Anatomy and Cell Biology III, University of Heidelberg, Heidelberg, Germany.
10. November 8-12, 2003: Early developmental failure of substantia nigra dopamine neurons in mice lacking the homeodomain gene Pitx3; Invited by: The 2003 American Society of Neuroscience Meeting, New Orleans, USA
11. December 18, 2003: Early developmental failure of substantia nigra dopamine neurons in mice lacking the homeodomain gene Pitx3; Invited by: Dr. Silke Rinkwitz, University of Oldenburg, Oldenburg, Germany
12. May 27, 2004: The homeobox gene Pitx3 and its role in the development of dopamine neurons of the substantia nigra; Invited by: Prof. Dr. Luis Puellas, Department of Human Anatomy and Psychobiology, Faculty of Medicine, University of Murcia, Murcia, Spain.
13. June 6, 2005: The role of Pitx3 in survival of midbrain dopaminergic neurons; Invited by: The 16th International congress on Parkinson disease and related disorders, The world congress on Parkinson disease, Berlin, Germany
14. March, 8, 2006: Developmental origin and fate of meso-diencephalic dopamine neurons; Invited by Ronald van Kesteren, VU, Amsterdam The Netherlands

15. July 3, 2006: Origin and subset specification of mesodiencephalic dopaminergic neurons; Invited by: International Symposium entitled Development of Neurotransmitter Systems. The Collaborative Research Center - Sonderforschungsbereich 488 of the German Research Foundation - Molecular and Cellular Bases of Neural Development and the Interdisciplinary Center for Neuroscience (IZN) at Heidelberg University
16. May 30-June 2, 2007: Early development and neuronal specification of mesodiencephalic dopaminergic neurons; Invited by Thomas Perlmann for the symposium: 50 years of Dopamine, Stockholm, Sweden.
17. August 30-Sept 1, 2007: The role of Ahd2 in neuronal specification and maintenance of SNc neurons; Invited by Anders Bjorklund and Thomas Perlmann for the Nobel symposium: Development and Engineering of Dopamine Neurons: From Genes to Therapy, Stockholm, Sweden.
18. November 30-Dec 1, 2007: A Pitx3 regulatory network in development and maintenance of mesodiencephalic dopamine neurons. Invited by I. Dori and G. C. Papadopoulos for the symposium: brain: from cells to behavior, Tessaloniki, Greece.
19. January 22-27, 2008: Visiting professor, V International Course on Morphological Interpretation in Neuroembryology, Murcia Spain. Invited by Luis Puelles.
20. April 17, 2008: Vulnerability of dopaminergic neurons: a Pitx3 regulatory network, Heinrich-Heine-University, Duesseldorf, Germany.
21. June 4-6, 2008: Molecular programming of mesodiencephalic dopaminergic neurons, 2008 Dutch Endo-Neuro-Psycho meeting, Doorwerth, The Netherlands.
22. November 26, 2008: A Pitx3 induced gene regulatory network in the formation and maintenance of substantia nigra dopamine neurons, 2008 RMI symposium, Utrecht, The Netherlands.
23. Januari 7, 2009: A Pitx3 induced gene regulatory network in the formation and maintenance of substantia nigra dopamine neurons, Invited by Siew-lan Ang, MRC, London, UK
24. Februari 6, 2009: How to build the central nervous system, Emma Andersson, Karolinska Intitute, Stockholm, Sweden (Opponent of Thesis defence of Emma Andersson).
25. December 3, 2009: A Pitx3 regulated network in the differentiation program of mdDA neurons, FP7 “mdDAneurodev” consortium meeting, Utrecht, The Netherlands.
26. December 11, 2009: Subset specification in the mdDA neuronal population, Judith Homberg, University of Nijmegen, Nijmegen, The Netherlands.
27. May 6, 2010: A Pitx3 regulated network in the differentiation program of mdDA neurons, Thomas Perlmann, karolinska Intitute, Stockholm, Sweden.
28. June 17, 2010: Development of the vertebrate mesodiencephalic dopaminergic system, Stefano Gustincich, DOPAMINET consortium meeting, London, UK.
29. September 4, 2010: Retinoic acid dependent and independent Pitx3 driven mdDA neuronal differentiation, Ernest arenas, 8th international Stem cell School in regenerative medicin 2010, karolinska Intitute, Stockholm, Sweden.
30. April 15, 2011: A Pitx3 regulated network in the development of mdDA neurons, Alain Prochianz, Paris, France.
31. April 28-29, 2011: A Pitx3 regulated network in the development of mdDA neurons, Shared “Dopaminet” and “mdDAneurodev” FP7-meeting, Freiburg, Germany
32. June 17, 2011: A Pitx3 regulated network in the development of mdDA neurons, International Translational Neuroscience Conference, Kaunas, Lituania.
33. June 28, 2011: Retinoic acid dependent and independent Pitx3 driven mdDA neuronal differentiation, FEBS symposium, Torino, Italy.
34. November 11, 2011: A Pitx3 regulated network in the development of mdDA neurons., Sjef Copray, Molecular Medicin Seminars Series 2011, Groningen, The Netherlands.
35. Januari 27, 2012: A Pitx3 regulated network in the development of mdDA neurons., Tania Vitalis, Paris, France.
36. February 14, 2012: A Pitx3 mediated program of dopaminergic subset-specification., Eric Bellefroid, Bruxelles, Belgium.



37. March 15/16, 2012: A Pitx3 mediated program of dopaminergic subset-specification., Alain Prochianz, Paris, France. International meeting on developmental neuroscience hosted by Alain Prochianz's Institution (Smidt, co-organiser).
38. April 16, 2012: Molecular specification of mdDA neuronal subsets., Antonio Simeone, CNRS, Italy
39. May 3, 2012: Molecular specification of mdDA neuronal subsets., Anders Bjorklund, Annual Neuroscience meeting Lund University, Lund, Sweden
40. May 24, 2013: Molecular specification of mdDA neuronal subsets, invited speaker to session "TRANSCRIPTION FACTORS AS MEDIATORS OF DOPAMINE NEURODEGENERATION IN PARKINSON'S DISEASE" in the meeting "DOPAMINE 2013, Alghero, Italy"
41. November 8-13, 2013: Molecular specification of mdDA neuronal subsets, invited speaker, SFN 2013, San Diego, USA

## **5.6 Selection of current and past collaborations with (foreign) academic groups**

1. Function of the Engrailed 1 and 2 genes: Dr. Horst H. Simon, University of Heidelberg, Heidelberg, Germany. (Manuscript is published)
2. Analysis of cRet genetically modified mice, Edgar Kramer, Max Planck Institute of Neurobiology, Martinsried, Germany. (Manuscript is published)
3. Serotonin action in the developing CNS, Hans van Hooft, AMC, Amsterdam The Netherlands. (2 Manuscripts Published)
4. Developmental effects of prenatal SSRI exposure, Gerard Visser, Neonatologie, WKZ, Utrecht. The Netherlands (Manuscript published) Until 2011
5. Genetics of Parkinson's Disease, Peter Heutink, VU, Amsterdam, The Netherlands Until 2011
6. FP7 partners in mdDAneurodev project: O. Marin; T. Perlmann, W. Wurst, A. Simeone, W. Driever, A Prochianz and J. Pasterkamp. EU project until 2012
7. Role of Foxd2 in development of mdDA neurons, Tsutomu Kume, Ph.D. Assistant Professor Department of Medicine Vanderbilt University Medical Center 332 PRB, Nashville, TN 37232-6300, USA (Manuscript in preparation)
8. Analysis of the DLK-1 knock out, Y. Wang and H.S. Sul, Department of Nutritional Science and Toxicology, University of California, Berkeley, Berkeley, CA 94720, USA. (Manuscript published)
9. Analysis of connectivity in the Pitx3 ko, Sharon Kolk, PhD, RUN, Nijmegen.
10. Maternal inflammation and mdDA neuronal development, role of epigenetics, Gerard O'Keeffe, Department of Anatomy & Neuroscience, Room 1.11, Biosciences Institute, University College Cork, Cork, Ireland.
11. Identification of MiRNAs in mdDA neurons, Gian Carlo Bellinchi, Institute of Genetics and Biophysics, Naples, Italy

## **5.7 Selection of management activities**

### **5.7.1 Research management**

2001-present:

- Team leader of the Development and function of the mesencephalic dopaminergic system research team (start 2001).
- Member of the organizing committee: Dutch Neurofederation Research Class on Brain Development (2003).
- Chairman: Rudolf Magnus Institute of Neuroscience Summerschool 2003.
- Co-Coordinator of the Section Neurodevelopment of the Rudolf Magnus Institute of Neuroscience.
- Member of organizing committee: Rudolf Magnus Institute of Neuroscience Summerschool 2004.
- Member of the NWO-ALW open program committee (2006)
- Coordinator of a FP7 EU-grant project (2008-2011), medium sized EU-research project.

- Head of the research platform “Neurodevelopment” (start 2008).
- Coordinator of the Neurodevelopment section of the Rudolf Magnus Institute (start 2008).
- Member of the NWO-ALW-VENI committee (2007 and 2008).
- Chairman of the NWO-ALW-VENI committee (2009 and 2010).
- Member of the NWO-Life Sciences domein panel (2009 and 2010).
- Member of the expert committee for the 2010 Marie Curie Individual fellowships evaluation LIFE Panel. EU, Brussels (2010, 2011).
- Member of the University Utrecht VICI coachingscommittee 2011.
- Chairman of the ALW-VIDI committee (2011-current).
- Chairman of the Examination board Bachelor program “Psychobiology” at UvA (2012-current).
- Program developer/director Neurobiology master program cluster UvA (2012-current)

### **5.7.2 IT management**

- Adviser of IT steering group in the medical department, University of Utrecht. (1998-2002)
- Representative of the section molecular neuroscience for IT-support. (1998-2002)
- Interim IT-coordinator Division "Hersenen" of the University Medical Center, Utrecht -until 2005
- Developer/System administer of a Linux server for molecular genetics software -until 2005.
- IT adviser for the department neuroscience and pharmacology, University Medical Center, Utrecht.
- Development and implementation of a new IT infrastructure for the department neuroscience and pharmacology of the University Medical Center, Utrecht -until 2004.
- Manager IT in the department neuroscience and pharmacology, University Medical Center, Utrecht (2004-2011)

### **5.7.3 Managment trainings/activities**

- Managment training 2 days full time. Academic leadership (2007).
- Personal coaching (every two months one session, 2007-now)
- Interim manager/external adviser of the MT, department of Domestic animals, UU, The Netherlands (2009)
- Communication training 2011 (1 day, buro Beysterveld)

### **5.7.4 Personal management**

- Board member of the Budo School on Martial Arts, De Mattekloppers, University of Groningen (1992)
- Chairman of the Budo school on Martial Arts, De Mattekloppers, University of Groningen (1994)
- Chairman of the MR, Driekoningen school, De Meern, The Netherlands (2008-2012)
- Advisor of the PVDV sponsors comittee (2011-present)

## 6 Educational experience

- 1989: Assistant to the course: Science and Society.
- 1991-1994: Development and application of the practical course: Biochemistry for Biologist (1 month).
- 1996-2000: Curriculum health-care (UU): Practical Kinetics of Pharmacology
- 1999, 2000: Development and lecturing: "Disease of the central nervous system".
- 2001: Development and lecturing, PhD course Neuroscience; Development and lecturing, KNAW advanced course on Neurogenomics; Development and lecturing: "Disease of the central nervous system"; Development and lecturing: Advanced Course in Neuroscience (PhD course); Lecturing brain development and function of the mesDA system: in PhD course "Neuroscience", University of Amsterdam, Netherlands Brain Institute.
- 2002/2003: Development and lecturing: Advanced Course in Neuroscience.; Development and lecturing: Neuroscience Course. ; Development and lecturing: "Disease of the central nervous system".; Organizer Research Class 2003.; Chairman: Rudolf Magnus Institute of Neuroscience Summerschool 2003.; Development and lecturing: Masters Neuroscience , elected prestigious master.
- 2004: Coordinator : Advanced Course in Neuroscience.; Development and lecturing: Neuroscience Course. ; "Meet the expert" sessions and involved in study material selection for: "Development and developmental disturbances of the Central Nervous System (CNS)".; Member of the organizing committee: Rudolf Magnus Institute of Neuroscience Summerschool 2004.; Development and lecturing: Masters Neuroscience (prestigious master).
- 2001-2011 Advanced neuroscience course for bachelor students; practical and lectures, new practical and additional lectures were developed in 2009.
- 2005-2010 Neuroscience Course: Development and lecturing; Development and developmental disturbances of the Central Nervous System (CNS): Meet the expert" sessions and involved in course development;
- 2005-2010 Prestigious Master Neuroscience: Development, lecturing, practicals and assignment tutor.
- 2006-2010 Visiting professor developmental neuroscience master course, VU, Amsterdam
- 2008 Visiting professor, V International Course on Morphological Interpretation in Neuroembryology, Murcia Spain.
- 2009 Lecturer at the ONWA PhD course, Utrecht, The Netherlands.
- 2010 Lecturer and practicals (IUE) in the PhD course "Developmental Neurobiology"
- 2011 Lecturer/trainer in the RMI summerschool: "Grant writing".
- 2009-2010: Lecturer at high schools ("Atheneum", year 6); Dutch Brain week
- 2010-2011: Panel member during information day for the NWO VI grant-program.
- 2013- current: Principle developer of master program (2 years) "Molecular Neurosciences (MNS)" UvA
- 2013-current: Lecturer/developer Genetic programming in neurodevelopment (4 weeks) in MNS master course, UvA
- 2012-current: Lecturer/developer Introduction neurodevelopment (1 week) in Neurobiology track medical biology bachelor, UvA.
- 2012-current: Lecturer/developer Neurodevelopment and developmental neuropsychology (3 days) psychobiology bachelor year 2 course, UvA
- 2012-current: Lecturer/developer Molecular techniques (1 day), psychobiology third year course, UvA
- 2011-current: Lecturer/developer Grant writing (1/2 day): Summerschool rudolf magnus institute for neuroscience, UU.
- 2008-current; Lecturer/developer ONWAR course "Molecular Neurobiology", VU-NIN.
- 2013-current: Principle developer of a certified Art9 course according the Dutch law on animal experimentation.

## 7 Selected honors

1. USA National Parkinson Foundation, Richard E. Heikkila Research Scholar Award (award for the best research proposal of 1998).
2. Personal post-doc grant (NWO-MW) (the current Veni award)
3. Rudolf Magnus Institute for Neuroscience Research Award (2000). For innovating research on the development of the mesencephalic dopaminergic system.
4. The Netherlands Brain Foundation (HSN) Award for outstanding research performance (2001).
5. High-potential award, University of Utrecht (2004).
6. Vidi award (eligible for funding), NWO-MW, The Netherlands (2004).
7. Rudolf Magnus Institute for Neuroscience Research Award to Frank Jacobs and Simone Smits (2007). Best publication in 2007: Jacobs FM, Smits SM, Noorlander CW, von Oerthel L, van der Linden AJ, Burbach JP and Smidt MP. Retinoic acid counteracts developmental defects in the substantia nigra caused by Pitx3 deficiency. *Development*. 2007 Jul;134(14): 2673-84. IF 8
8. Vici award, NWO-ALW, The Netherlands (2009).

## 8 List of publications, books and patent applications

### 8.1 Peer refereed international journals (impact factors (IF) are listed)

- Almost all papers are in the top 25 % of journals (based on mean impact factor, 5 year).

1. Inês Chaves, Gijsbertus T.J. van der Horst, Raymond Schellevis, Romana M. Nijman, Marian Groot Koerkamp, Frank C.P. Holstege, Marten P. Smidt and Marco F.M. Hoekman (2014) FoxO3 in control of the hepatic circadian oscillator via direct regulation of Clock. *Current Biology* in Press. IP 11
2. Simone Mesman, Lars von Oerthel and Marten P. Smidt (2014) Mesodiencephalic dopaminergic neuronal differentiation does not involve GLI2A-mediated SHH-signaling and is under the direct influence of canonical WNT signaling. *PLoSOne* in press. IP 4.5
3. Marlies Oostland, M. Renate Buijink, Guus M. Teunisse, Lars von Oerthel, Marten P. Smidt, Johannes A. van Hooft.(2014) Distinct Temporal Expression of 5-HT1A and 5-HT2A Receptors on Cerebellar Granule Cells in Mice. *Cerebellum* (epub may 1) IP 3.
4. Reinhard Roessler, Sebastien A Smallwood, Jesse V Veenliet, Petros Pechlivanoglou, Suping Peng1, Koushik Chakrabarty, Marian JA Groot-Koerkamp, R. Jeroen Pasterkamp, Evelyn Wesseling, Gavin Kessel, Erik Boddeke Marten P Smidt and Sjef Copray. (2014) Detailed analysis of the genetic and epigenetic signature of iPS cell-derived mesodiencephalic dopaminergic neurons. *Stem Cell Reports* 2(4):520-33. doi: 10.1016/j.stemcr.2014.03.001 (Cell press).
5. Smidt MP, van Hooft JA. Subset specification of central serotonergic neurons. (2013) *Front Cell Neurosci*. 7:200. Review. IP 5
6. Smits SM, von Oerthel L, Hoekstra EJ, Burbach JPH, Smidt MP (2013) Molecular Marker Differences Relate to Developmental Position and Subsets of Mesodiencephalic Dopaminergic Neurons. *PLoS ONE* 8(10): e76037. doi:10.1371/journal.pone.0076037 IP 4.5
7. Hoekstra EJ, von Oerthel L, van der Heide LP, Kouwenhoven WM, Veenliet JV, Wever I, Jin YR, Yoon JK, van der Linden AJ, Holstege FC, Groot Koerkamp MJ, Smidt MP. (2013) Lmx1a Encodes a Rostral Set of Mesodiencephalic Dopaminergic Neurons Marked by the Wnt/B-Catenin Signaling Activator R-spondin 2. *PLoS One*. 2013 Sep 16;8(9):e74049. doi: 10.1371/journal.pone.0074049. IP 4.5
8. Jesse V Veenliet\*, Maria TM Alves dos Santos\*, Willemieke M Kouwenhoven, Lars von Oerthel, Jamie L Lim, Annemarie JA van der Linden, Marian JA Groot Koerkamp, Frank CP Holstege and Marten P Smidt (2013) En1 and Pitx3 interplay in dopaminergic subset-specification. *Development* 140, 3373-3384 (2013) doi:10.1242/dev.094565. \*shared first authorship IP7
9. Mareen Engel, Marten P Smidt\*, Johannes A Van Hooft\* (2013) The serotonin 5-HT3 receptor: a novel neurodevelopmental target. *Frontiers in Neuroscience* in press. Shared last author, IP 5

10. Lars P. van der Heide and Marten P. Smidt (2013) The BCL2-code to dopaminergic development and Parkinson's disease. *Trends Mol Med.* 19(4):211-6. IP 11.
11. van Heesbeen HJ, Mesman S, Veenliet JV, Smidt MP. (2013) Epigenetic mechanisms in the development and maintenance of dopaminergic neurons. *Development.* 2013 Mar;140(6):1159-69. doi: 10.1242/dev.089359. IP 7.
12. Nott A, Nitarska J, Veenliet JV, Schacke S, Derijck AA, Sirko P, Muchardt C, Pasterkamp RJ, Smidt MP, Riccio A. (2013) S-nitrosylation of HDAC2 regulates the expression of the chromatin-remodeling factor Brm during radial neuron migration. *Proc Natl Acad Sci U S A.* 110(8):3113-8. IP 10.
13. Hoekstra EJ, Mesman S, de Munnik WA, Smidt MP. (2013) Lmx1b Is Part of a Transcriptional Complex with PSPC1 and PSF. *PLoS One.* 2013;8(1):e53122. doi: 10.1371/journal.pone.0053122. Epub 2013 Jan 4. IP 5
14. Hoekstra EJ, von Oerthel L, van der Linden AJ, Smidt MP. (2012) Phox2b influences the development of a caudal dopaminergic subset. *PLoS One.* 2012;7(12):e52118. doi: 10.1371/journal.pone.0052118. Epub 2012 Dec 14. IP 5
15. Elisa J Hoekstra, Lars von Oerthel, Annemarie J A van der Linden, Raymond D Schellevis, Gerard Scheppink, Frank C.P. Holstege, Marian J Groot-Koerkamp, Lars P van der Heide2, Marten P Smidt (2012) Lmx1a is an activator of Rgs4 and Gbr10 and is responsible for the correct specification of rostral and medial mdDA neurons. *Eur J Neurosci.* 2012 Oct 29. doi: 10.1111/ejn.12022. IP 3.6
16. Frank Meye, Ruud van Zessen, Marten Smidt, Roger Adan, and Geert Ramakers (2012) Morphine withdrawal enhances constitutive mu-opioid receptor activity in the ventral tegmental area. *J Neurosci.* 32(46):16120-8. doi: 10.1523/JNEUROSCI.1572-12.2012. IP 8
17. Smidt MP, von Oerthel L, Hoekstra EJ, Schellevis RD, Hoekman MFM (2012) Spatial and Temporal Lineage Analysis of a Pitx3-Driven Cre-Recombinase Knock-In Mouse Model. *PLoS ONE* 7(8): e42641. doi:10.1371/journal.pone.0042641
18. Koushik Chakrabarty, Lars von oerthel, Anita Hellemons, M. frederic Clotman, Marian J.A. Groot Koerkamp, Frank C.P. Holstege, R. Jeroen Pasterkamp, and Marten P. Smidt (2012) Genome wide expression profiling of the mesodiencephalic region identifies novel factors involved in early and late dopaminergic development. *Biology Open* 1:693-704.
19. Laura A. Smit-Rigter, Cornelle W. Noorlander, Lars von Oerthelb, Pascal Chameau, Marten P. Smidt\*, Johannes A. van Hooft\* (2012) Prenatal fluoxetine exposure induces life-long serotonin 5-HT3 receptor-dependent cortical abnormalities and anxiety-like behaviour *Neuropharmacology* Volume 62, Issue 2: 865–870 \* Shared last author IP 4
20. Frank M.J. Jacobs\*, Jesse V. Veenliet\*, Wadia H. Almirza, Elisa Hoekstra, Lars von Oerthel, Annemarie J.A. van der Linden, Roel Neijts, Marian Groot Koerkamp, Dik van Leenen, Frank C.P. Holstege, J. Peter H. Burbach and Marten P. Smidt, Retinoic acid-dependent and -independent gene-regulatory pathways of Pitx3 in mesodiencephalic dopaminergic neurons, *Development* 2011, 138(23):5213-22. \* shared first author. IP 8
21. Alves dos Santos MTM and Smidt MP. En1 and Wnt signaling in midbrain dopaminergic neuronal development. *Neural Development* 2011, 6:23 doi:10.1186/1749-8104-6-23 IP 3.4
22. Arango C., Gustincich S., Marin O., Parnavelas J. and Smidt M.\*, Chapter I: Brain development, plasticity and ageing in health and disease (Section Editor: Monica Di Luca) (Page 770) in; Di Luca M, Baker M, Corradetti R, Kettenmann H, Mendlewicz J, Olesen J, Ragan I, Westphal M. Consensus Document on European Brain Research, *Eur. J. Neurosci.* 2011 Mar;33(5):768-818 \* Theme leader.
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24. Smidt MP. Specific vulnerability of substantia nigra compacta neurons. *J Neural Transm Suppl.* 2009;(73):39-47. (review upon invitation) IF 2.4
25. Semaphorin 3F is a bifunctional guidance cue for dopaminergic axons and controls their fasciculation, channeling, rostral growth, and intracortical targeting. Kolk SM, Gunput RA, Tran TS, van den Heuvel DM, Prasad AA, Hellemons AJ, Adolfs Y, Ginty DD, Kolodkin AL, Burbach JP, Smidt MP, Pasterkamp RJ. Semaphorin 3F is a bifunctional guidance cue for dopaminergic axons and controls their fasciculation, channeling, rostral growth, and intracortical targeting. *J Neurosci.* 2009 Oct 7;29(40):12542-57. IP 8

26. Smidt MP\* and Burbach JPH. Terminal differentiation of mesodiencephalic dopaminergic neurons: the role of Nurr1 and Pitx3. *Adv. Exp. Med. Biol.* 2009;651:47-57.\*corresponding author. (IP 0.67)
27. Development and engineering of dopamine neurons. Preface. Pasterkamp RJ, Smidt MP, Burbach JP. *Adv Exp Med Biol.* 2009, 651.
28. Smidt MP\* and Burbach JPH A passport to neurotransmitter identity. *Genome Biology* 2009, 10:229. \*corresponding author. IP 9. (review upon invitation)
29. Jacobs FMJ, van der Linden AJA, Wang Y, von Oerthel L, Sul HS, Burbach JPH and Smidt MP. Identification of Dlk1, Ptpru and Khlh1 as novel Nurr1 target genes in meso-diencephalic dopamine neurons. *Development* 2009 Jul;136(14):2363-73 (selected to feature on the In this Issue page of Issue 136.14). IF 8
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34. Kas MJ, van der Linden AJ, Oppelaar H, von Oerthel L, Ramakers GM, Smidt MP. Phenotypic segregation of aphakia and Pitx3-null mutants reveals that Pitx3 deficiency increases consolidation of specific movement components. *Behav Brain Res.* 2008 Jan 25;186(2):208-14. Epub 2007 Aug 31. PMID: 17919745 IF 2.4
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37. Smidt MP\*, Burbach JP. How to make a mesodiencephalic dopaminergic neuron. *Nat Rev Neurosci.* 2007 Jan;8(1):21-32. Review. PMID: 17180160 \* corresponding author IF 27
38. Burbach JP, Smidt MP. Molecular programming of stem cells into mesodiencephalic dopaminergic neurons. *Trends Neurosci.* 2006 Nov;29(11):601-3. Epub 2006 Oct 9. Review. PMID: 17030431 IF 14
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## 8.2 Patent applications:

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## 8.3 Books (chapters)

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3. Development and Engineering of Dopamine Neurons, Series: *Advances in Experimental Medicine and Biology*, Vol. 651 Pasterkamp, Jeroen R.; Smidt, Marten P.; Burbach, J. Peter H. (Eds.), 2009, 143 p. 26 illus., 5 in color., Hardcover, ISBN: 978-1-4419-0321-1
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## 8.4 Manuscripts (soon to be) submitted

## 8.5 Other scientific contributions

1. Smidt MP. Depression and Dopamine. *Front. Neurosci*. 2009; 3(2): 279. (research highlight).

# 9 Citation information

- Total cites: ISI: 3796; Google scholar 4971
- h-index: ISI: 30; Google scholar: 33

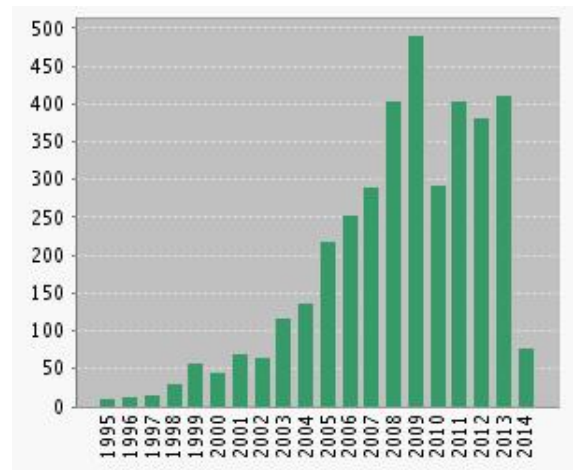
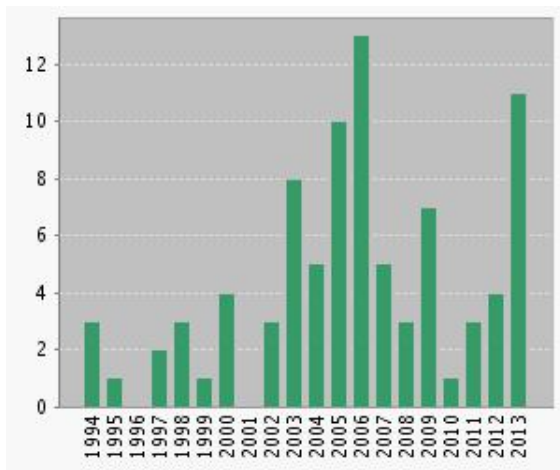


Figure 1: Graphical representation of citation information. (left) Amount of papers published each year. (right) amount of citations each year. (source: ISI, May 2014)