BIOGRAPHICAL SKETCH

Name:	Position/Title:
DENAXA, MYRTO, BSc, MA, Ph.D.	Group Leader/Research Associate/ Developmental Neurobiology

Postal Address Neuroscience Department,
BSRC Alexander Fleming,
34 Fleming Street, 16672, Vari, Greece
Tel. +30-210-965-6310(6311)
E-mail denaxa@fleming.gr

Education

Institution and Location	Degree	Year Conferred	Field of Study
University of Patras, Patra, Greece	B.S.	1997	Biology
University of Crete, Heraklion, Greece	M.A.	1997-99	Cell & Devel. Biol.
University of Crete, Heraklion, Greece	Ph.D.	1999-2004	Cell & Devel. Biol.
National Institute for Medical Research (Pachnis Lab), London, UK	Postdoc Fellow	2004-08	Mol. Neurobiology

B. Research and Professional Experience

POSITIONS HELD-TRAINING

2018- Group Leader/Research Associate, BSRC Alexander Fleming, Athens, Greece
2014-17 Senior Research Assistant, Pachnis Lab, The Francis Crick Institute, London, UK
2008-14 Investigator Scientist, Dpt. of Molecular Neurobiology, Pachnis Lab, NIMR, London, UK

AWARDS/FUNDING

1999: First prize for presentation in the Hellenic Society for Neuroscience Conference (HSFN)
2001: Prize for presentation in the Hellenic Society for Neuroscience Conference (HSFN)
2002: FENS Stipend for the 2002 FENS
2004-2007: MRC Career Development Fellowship
2018-2020: Stavros Niarchos Foundation Fellow

TEACHING ACTIVITIES

2017 Lecture-Athens International Master's Program in Neurosciences, UOA
2017 Seminar-Postgraduate Program in Biomedical Sciences, Dept. of Medicine, UOP
1998 - 1999 Introductory Microbiology practical courses for 1st year Biology students, UOC

SUPERVISION OF RESEARCH STUDENTS

2004-2011: Co-supervisor with Dr. Vassilis Pachnis for Dr. Angeliki Achimastou Ph.D
"The role of LHX6 in the specification of interneurons in the mammalian cortex"
2011-2013: Co-supervisor with Dr. Vassilis Pachnis for Dr. Melanie Kalaitzidou Ph.D
"The role of SATB1 in medial ganglionic eminence-derived cortical interneuron differentiation"

C. CONTRIBUTIONS TO SCIENCE

The role of adhesion molecules in cortical interneuron migration

Throughout my master and PhD studies in Dr. Karagogeos lab (Faculty of Medicine, UOC, Greece) I have worked on the regulation and function of adhesion molecules of the immunoglobulin superfamily (IgSF), mainly TAG-1 (Contactin-1), and its role in various developmental processes. My research, provided not only evidence for a new role for TAG-1, but also demonstrated for the first time, that a short-range permissive cue distributed along the paths of the migrating cortical interneurons, participates in this migratory system **(Denaxa et al., 2001)**. Subsequently, my research extended in exploring the in vivo role of TAG-1 in CNS development by analyzing the phenotype of mice deficient for TAG-1. This work further established the important role of TAG-1 in CNS development by demonstrating that TAG-1 is required in vivo for the proper migration of neurons in certain CNS structures **(Denaxa et al., 2005)**.

Genetic cascades in cortical interneuron specification

During my post-doc in Dr. Pachnis lab (National Institute for Medical Research, London, UK) my research has been focused on dissecting the genetic cascades that regulate the specification of cortical GABAergic interneurons. In Liodis et al., we have studied the role of the LIM-homeodomain transcription factor Lhx6 in the development of cortical interneurons by characterising the phenotype of Lhx6 mutant mice. Our work demonstrated for the first time that Lhx6 has fundamental roles in the migration of cortical GABAergic interneurons and the specification of two distinct cortical interneuronal subtypes, namely the parvalbumin (PV) and somatostatin (SST) expressing interneurons **(Liodis et al., 2007)**. Subsequently, through a genome-wide approach I have identified a number of genes expressed in cortical interneurons whose function is under Lhx6 control. Among them, the Sry-related HMG box-containing transcription factor Sox6 has been shown to be important for the normal positioning and differentiation of cortical interneurons **(Brito et al., 2009)**.

Nature versus nurture: Activity dependent pathways in cortical interneuron maturation

Another gene identified by my initial screen was the nuclear matrix and genome organizer protein Satb1. My study demonstrated that Satb1 coordinately controls the expression of multiple subtype-specific and interneuron-wide genes, in a manner that defines their mature functional state. Interestingly, this work provided for the first time, evidence that the expression of Satb1 is under the control of neuronal activity, an exciting finding, which revealed a possible mechanistic understanding as to how spontaneous activity in the immature brain drives neuronal maturation. The impact of this publication in the field of neuroscience was further demonstrated by the fact that it made the TOP 10 publication list of Neural Cell News web site (November 14, 2012) **(Denaxa et al., 2012)**. Inspired by this finding and following publications supporting the idea of fine-tuning interneuron genetic programs by environmental input, I have decided, as a senior investigator scientist in the Francis Crick Institute (Pachnis team), to tackle this nature versus nurture question into fundamental mechanisms of interneuron development, such as how is the number of cortical interneurons defined in the adult brain? My most recent work **(Denaxa et al., in press)** provides evidence that the extent of cortical interneuron apoptosis during a critical early postnatal period is plastic, cell type specific and can be reduced in a cell autonomous manner by acute increases in neuronal activity. Most interestingly, for the first time we show that the physiological state of the emerging neural network controls the activity levels of local cortical interneurons to modulate their numbers in a homeostatic manner. These exciting results provide fundamental insight into the mechanisms that match the size of cortical interneuron populations to the physiological requirements of cortical circuits but additionally pave the way for better understanding the impact of neuronal activity on cell transplantation-based therapies.

D. PUBLICATIONS

1. **Denaxa M**, Chan C-H, Schachner M, Parnavelas JG and Karagogeos, D **(2001)** The adhesion molecule TAG-1 mediates the migration of cortical interneurons along the corticofugal fiber system. **Development** 128 (22)

2. **Denaxa M**, Pavlou O, Tsiotra P, Papadopoulos GC, Liapaki K, Theodorakis C, Karagogeos, D. and Papamatheakis, J. **(2003)** The upstream regulatory region of the cell adhesion molecule TAG-1 gene contains elements driving neural specific expression in vivo. **Molecular Brain Research** 118 (1-2)
3. Ekonomou A, Kazanis I, Malas S, Wood H, Alifragis P, **Denaxa M**, Karagogeos D, Constanti A, Lovell-Badge R, Episkopou V. **(2005)** Neuronal migration and ventral subtype identity in the telencephalon depend on SOX1. **PLoS Biology** 3(6)
4. **Denaxa M,** Kyriakopoulou K, Theodorakis K, Trichas G, Vidaki M, Takeda Y, Watanabe K, Karagogeos D**. (2005)** The adhesion molecule TAG-1 is required for proper migration of the superficial migratory stream in the medulla but not of cortical interneurons. **Developmental Biology** 288(1)
5. Brogna S, Bourtzis K, Gomulski LM, **Denaxa M**, Babaratsas A, Gasperi G, Savakis C. **(2006)** Genomic organization and functional characterization of the alcohol dehydrogenase locus of *Ceratitis capitata* (Medfly). **Insect Molecular Biology.** 15(3)
6. Liodis P, **Denaxa M**, Grigoriou M, Akufo-Addo C, Yanagawa Y, Pachnis V. **(2007)**. Lhx6 activity is required for the normal migration and specification of cortical interneuron subtypes. **Journal of Neuroscience** 27(12)
7. **Denaxa M,** Sharpe PT, Pachnis V. **(2009)** The LIM homeodomain transcription factors Lhx6 and Lhx7 are key regulators of mammalian dentition. **Developmental Biology** 333(2)
8. Batista-Brito R, Rossignol E, Hjerling-Leffler J, **Denaxa M,** Wegner M, Lefebvre V, Pachnis V, Fishell G. **(2009)** The cell-intrinsic requirement of Sox6 for cortical interneuron development. **Neuron** 63(4)
9. **Denaxa M**, Kalaitzidou M, Garefalaki A, Achimastou A, Lasrado R, Maes T, Pachnis V. **(2012)** Maturation-promoting activity of SATB1 in MGE-derived cortical interneurons. **Cell Reports** 2(5)
10. Neves G, Shah MM, Liodis P, Achimastou A, **Denaxa M**, Roalfe G, Sesay A, Walker MC, Pachnis V. **(2013)** The LIM homeodomain protein Lhx6 regulates maturation of interneurons and network excitability in the mammalian cortex. **Cerebral Cortex** 23(8)
11. Tivodar S, Kalemaki K, Kounoupa Z, Vidaki M, Theodorakis K, **Denaxa M**, Kessaris N, de Curtis I, Pachnis V, Karagogeos D. **(2015)** Rac-GTPases Regulate Microtubule Stability and Axon Growth of Cortical GABAergic Interneurons. **Cerebral Cortex** 25(9)
12. Liu K, Zhang S, Kim J, Kim DW, **Denaxa M**, Bao H, Kim E, Liu C, Pachnis V, Hattar S, Song J, Brown S, Blackshaw S. **(2017)** Zona incerta Lhx6-positive neurons promote sleep by local inhibition of wake-promoting hypocretin neurons. **Nature** 548(7669)
13. **Denaxa M***, Neves G, Rabinowitz A, Kemlo S, Liodis P, Burrone J, Pachnis V. **(2018)** Activity-dependent control of inhibitory interneuron number in the mammalian cortex. *corresponding author **Cell Reports in press**

E. MEMBER OF SCIENTIFIC SOCIETIES

1. HSFN (Hellenic Society for Neuroscience) since 1999.
2. FENS (Federation of European Neurosciences) since 1999.