

Stavros MALAS, Ph.D.

# Professor, Foundation Chair for the establishment of the Veterinary School

# **EDUCATION**

1988 - 1991	B.Sc. in Genetics, University College London
1991 - 1994	Ph.D. in Mouse Molecular Genetics, University College London
1995 - 1998	<b>Post-Doctoral Research Associate</b> with Prof. Vasso Episkopou, Trained in mouse genetic engineering, embryonic development and tissue engineering, Clinical Sciences Centre, Medical Research Council, London UK.
1999 - 2001	<i>Senior Research Associate</i> with Prof. Vasso Episkopou, Head of the Mammalian Neurogenesis Group. Assigned the task of lab coordinator and join-supervision of PhD student. Worked on the discovery of new Sox genes and their role in early embryonic brain development. Developed the first genetic model of generalized mouse epilepsy. Clinical Sciences Centre, Medical Research Council, London UK.

# **RESEARCH EXPERIENCE**

Jun. 1991- Sep.Graduate Research Assistant with Prof. Susan Povey. Human1991Biochemical Genetics Unit, Medical Research Council, Dep. Of<br/>Genetics, University College London, London, UK. Mapping of the<br/>BCL1 gene in CEPH families-trained in human microsatellite analysis.

	Post - Doctoral Research Associate with Prof. Vasso Episkopou,
1995- 2001	Clinical Sciences Centre, Hammersmith Hospital NIMR, Mill Hill,
	London, UK. Role of Sox1 in neural cell fate determination.

- **Principal Investigator**, The Cyprus Institute of Neurology and
  **2001** Genetics, Embryonic CNS development, Genetic Engineering of mouse models of human conditions.
- 2003 –2011Affiliated Scientist, University of Cyprus, Department of Biology,<br/>Nicosia, Cyprus.

# TEACHING EXPERIENCE AND AWARDS

1993 - 1994	Graduate Teaching Assistant, Third year project supervision. Department of Genetics, UCL, London, Laboratory Research course.
1995 - 2001	Joint PhD supervision with Prof. Vasso Episkopou, Clinical Sciences Centre, Medical Research Council, London UK.
2002 - 2013	Principal PhD Supervisor, Dep. of Biology, University of Cyprus, Nicosia, Cyprus.
2004 – 2009	Principal PhD Supervisor, University College London, UK. Non-resident PhD program in collaboration with Prof. Bill Richardson.
2013 – present	Principal PhD Supervisor, Cyprus School of Molecular Medicine, The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus.
July 2006	Lectures on "Embryonic Stem Cells as a means to repair tissue" and on "Designer Mouse". European Medical Genetics faculty, Bologna, Italy.
1991-1994	Personal Wellcome Trust Prize Award. Awarded to top three UCL graduates in Life Sciences.
1991-1994	The Galton Laboratory Personal Student Award. University College London, Department of Genetics.

# ACADEMIC SUPERVISION

1.	POSTODOCTORAL FELLOWS	3
1.	POSTODOCTORAL FELLOWS	3

- 2. PhD THESES
- 3. MASTER'S THESES 4

#### **POST-DOCTORAL FELLOWS**

*George Lapathtis, PhD*. (2003- 2007) The development of genetic mouse models CNS development. The Cyprus Institute of Neurology and Genetics.

5

*Michael Orford, PhD.* (2002-2008) Study of the role of SOX genes in CNS development. The Cyprus Institute of Neurology and Genetics.

*Christina Sidera, PhD.* (2004-2007) Study the role of SOX21 during embryogenesis. The Cyprus Institute of Neurology and Genetics.

#### PhD THESES SUPERVISED

*Nikolas Genethliou, PhD.* (2003-2008) A study on the role of SOX1 in the regulation of Glial Specification in the Development of Spinal Cord in mice. University of Cyprus, Department of Biology.

*Helen Panayi, MSc.* (2004-2009) Studying the role of SOX1 during Spinal Cord Development. *University College London*. Academic Supervisor: Prof. Bill Richardson.

*Elena Panayiotou, PhD* (2008-2013) Late Wave of Neurogenesis Generates Novel Dorsal and Ventral Neurons in the Spinal Cord and Central Canal. University of Cyprus, Department of Biology.

*Neoklis Makrides, MSc.* (20014-2018) A study on the role of SOX14 and SOX21 during midbrain development. Cyprus School of Medical Genetics. The Cyprus Institute of Neurology and Genetics.

#### Under supervision (Final Year):

**Andreas Syrimis, MSc.** (2014-2018) Molecular analysis of Cypriot families with Aniridia. Cyprus School of Medical Genetics, The Cyprus Institute of Neurology and Genetics. Joint supervision with Dr George Tanteles.

#### MASTER'S THESES SUPERVISED

*Antonia Stavraki, MSc* (2013-2014). The role of Soxl and Foxn4 in the developing midbrain. Post-Graduate Program in Neurosciences, Cyprus School of Medical Genetics, The Cyprus Institute of Neurology and Genetics. Nicosia, Cyprus.

*Ouranio Anastasiou, MSc* (2013-2014). Studying the role of SOX21 and SOX14 in the developing mesencephalon. Post-Graduate Program in Neurosciences, Cyprus School of Medical Genetics, The Cyprus Institute of Neurology and Genetics.

**Reshma Shah, MSc** (2015-2016). Studying the role of SOX1 in the development if the ventral midbrain during late neurogenesis. Post-Graduate Program in Neurosciences, Cyprus School of Medical Genetics, The Cyprus Institute of Neurology and Genetics.

*Soteria Polyviou, MSc* (2015-2016). Studying the role of Notch signalling in the development of Superior Colicullus SOX21 and SOX14 in the developing mesencephalon. Post-Graduate Program in Neurosciences, Cyprus School of Medical Genetics, The Cyprus Institute of Neurology and Genetics.

#### PHD THESES EXAMINED (EXTERNAL EXAMINER)

- Andriani Ioannou. Molecular cloning and functional characterization of Xenopus laevis nucleotide binding protein 1 (xnubp1) during early embryonic development. University Of Cyprus, Faculty of Pure and Applied Sciences, Department Of Biological Sciences.
- 2. *Antonis Ververis.* The role of Kif2A during in cytoskeletal formation. University Of Cyprus, Faculty of Pure and Applied Sciences, Department Of Biological Sciences.
- 3. *Christiana Polydvrou*. ETS2-dependant trophoblast signaling is required for the gastrulation progression after primitive streak initiation. University Of Cyprus, Faculty of Pure and Applied Sciences, Department Of Biological Sciences.
- 4. Louiza Papazachariou. Frequent COL4 mutations in familial microhematuria accompanied by later-onset Alport nephropathy due to focal segmental glomerulosclerosis. University Of Cyprus, Faculty of Pure and Applied Sciences, Department Of Biological Sciences.

## **MEMBERSHIPS**

2004	The UK society of Developmental Biologists
2006	International Society for Developmental Neuroscience
2002	Society of Human Genetics, Cyprus

## **PROFESSIONAL ADVISORY TASKS**

#### 2008-2009 1. Special Advisor to Commissioner for Health

Advised the European Commissioner for Health on specific issues related to her portfolio. Assigned the task to define the rules and procedures for the establishment of **European Reference Centers and European Reference Networks** for the treatment of Multiple Sclerosis across Europe. A report has been prepared for an action plan needed to be undertaken by DG-SANCO. Under this capacity, I have represented the Commissioner to the European Multiple Sclerosis Platform <a href="http://www.ms-ineurope.org/">http://www.ms-ineurope.org/</a>.

# 2007-2010 2. Innovative Medicines Initiative (IMI) States Representatives Group (SRG), Chairman

The Innovative Medicines Initiative (IMI) (<u>http://imi.europa.eu/member-</u> statesgroup en.html) is the largest public-private partnership in the world, established between the European Commission (public) and the European Federation of Pharmaceutical Industries and Associations (EFPIA). Its role is to fund pre-competitive research in drug development in order to generate knowledge about specific areas in the drug-development process and make the latter a more cost-effective procedure. I have been a member of the IMI States Representatives Group (IMI-SRG) since 2005 and in November 2007 I was unanimously nominated as the interim Chair of this Group. In 2008 the IMI was formally launched and I was duly elected as the first Chairman of the Group. My responsibilities were to coordinate the activities of the IMI-SRG and represent the Group at meetings of the Governing Board. As the Chair, I was responsible for assisting the Governing Board to implement the IMI-JU policies at the level of the Member States. I had also been involved in the final stage of the selection of the Executive Director. Through my engagement in this very high-level group, I have gained an understanding of the key challenges and bottlenecks faced by the process of innovative drug-development both for treating human and animal diseases.

# **2006-2011 3.** Member of the European Strategy Forum for Research Infrastructures (ESFRI)

ESFRI (<u>http://cordis.europa.eu/esfri/</u>) is a high-level Forum set up by the European

Council of Ministers in 2004 to identify research infrastructures that Europe needs to create over the next few years that will have a European-wide remit. This forum has published a Roadmap of Infrastructures needed across many fields of Science (<u>http://cordis.europa.eu/esfri/roadmap.htm</u>). In addition to being a member of ESFRI, I was also a member of one of the Working Groups that was assigned the task to identify and propose key infrastructures needed to be created across Europe in the field of Biomedical Research. In this capacity, I have been involved in the evaluation of proposals to be included in the Roadmap. This Forum and the Working Group have given me the opportunity to participate actively in top-level policy making and take part in the planning of research policy for the medium and long-term needs of Europe.

#### 2002-2011

#### 4. Cyprus Representative to Program Committee for Health FP5 to FP7.

A high level group assigned the task to oversee the implementation of the European Commission's Competitive programs for research. My role in this Committee was to express the national view on the areas of Health deemed of highest priority for funding and advice the Research Promotion Foundation on Biomedical Research policy related to Framework Program for Health. Have been the longest-serving member to this Committee from all EU delegates.

# **2011-2012 5.** Developed a strategy document for Innovative Health care provision for the European Union entitled: "Building an Open Innovation ecosystem in Europe for healthcare"

In addition to my participation in policy development for research, in early 2011 I secured a competitive grant from the European Commission to develop a strategy for Health care provision for Europe based on the concept of open innovation. This project acted as a federating platform for disciplines not directly related to health care provision and provided the opportunity for scientists across a wide spectrum of scientific fields to propose ways for building an innovation ecosystem for health care provision based on unconventional approaches. The final strategy report was presented in an international meeting on October 10<sup>th</sup> 2012 and was formally adopted by the European Council as a guidance document for future policy development. The final strategy document can be found at

https://www.imi.europa.eu/sites/default/files/archive/uploads/documents/Cyprus/ReportInnovaHealthCyprusOctober2012.pdfProjectdescription:https://cordis.europa.eu/project/rcn/101107en.htmlen.htmlen.html

#### **STATE FUNCTIONS**

#### 2011-2012 1. Minister of Health of the Republic of Cyprus

Appointed as Minister for Health of the Republic of Cyprus. During that period I had the main task to re-conceive and implement a structural reform program for introducing a National Health System, while at the same time managed a 600m Euros annual budget for state-provided Health Services. Represented Cyprus at all international fora organized at Ministerial level. From July to October 2012 I acted as President of the European Council for Health. During this period I managed the implementation of the legislative and non-legislative portfolio under the Cyprus Presidency of the EU in cooperation with DG-SANGO and all members States.

#### July 2012-October 2012 2. President of the European Competiveness Council

From July 20012 to December 2012 the Republic of Cyprus held the Presidency of the European Council. Due to my long-standing involvement in European Policy relating to research, I was appointed by the Council of Ministers as President of the Competitiveness Council in addition to been President of the European Council for Health. During my Presidency, I had faced the extremely difficult task to resolve two highly entrenched positions across Europe that threatened the adoption of H2020. These issues were successfully resolved at a meeting on October 10<sup>th</sup> 2012, characterized by the European Commissioner for Research as landmark agreement for the future of the most widereaching research program in the history of the EU.

#### **REVIEWER AND EDITOR IN PEER REVIEW JOURNALS**

- 2013 Guest Review Editor at Frontiers in Physiology Craniofacial Biology Section
- **2016** Review Editor at Frontiers in Cell and Develop. Biology- Stem Cell Research
- 1998 Reviewer Mammalian Genome
- 2013 Reviewer-Frontiers in Cellular Neuroscience

#### **INVITED SPEAKER AND PARTICIPATION IN SCIENTIFIC MEETINGS**

Over the last twenty five years, I participated in many scientific meetings and conferences and have been invited as guest speaker from various organizations such as the GlaxoSmith-Kline (Neuroscience Centre, UK), University College, Imperial College, University of Barcelona, The Karolinska Institute in Sweden, The Fleming Institute (Athens), The European Commission, The University of Cyprus and the University of Nicosia.

#### **RESEARCH INFRASTRUCTURES ESTABLISHMENTS**

In 2001 begun the development of an animal facility at the Cyprus Institute of Neurology and Genetics (CING) to support a wide range of research activities across the country. The

facility was completed in 2003. It is now supporting tens of research projects of researchers from public and private Institutions and has helped researchers at the CING and Cyprus as a whole to diversify their research objectives, upgrade the scope of research and attract research funding from across the world. The facility has the capacity to generate genetically modified mice using all modern techniques but above all has achieved a standard of animal health care well above many such facilities across the world. The facility houses animals with complete lack of the immune system and supports also research projects with focus on cancer.

# **CURRENT-COLLABORATIONS**

#### **PUBLIC SECTOR**

#### **1. UNIVERSITY OF CAMBRIDGE**

This is an ongoing collaboration with Professor Magdalena Zernicka-Goetz (<u>http://www.cam.ac.uk/research/features/of-mice-and-women</u>), who is working on the very early stages of embryo development. She has discovered that one of the factors our lab works on (SOX21), plays a key role in the first decision an embryo makes a few days after fertilization (even at 4-cell stage), that is to decide which cells will make the embryonic and which the extraembryonic tissue. Our lab has discovered that this decision involves two factors (SOX21 and SOX14), for which our lab has unique genetic models in mice and can study the process. We are currently at the early stages of this collaboration and have already sent some of our mouse lines to the Cambridge lab.

#### 2. AGRICULTURAL RESEARCH INSTITUTE OF CYPRUS

This is an inter-disciplinary collaboration between three research Institutes,

(Agricultural Research Institute http://www.moa.gov.cy/moa/ari/ari.nsf/index en/index en?OpenDocument, the Cyprus Institute (www.Cyl.ac.cy, and the CING – www.cing.ac.cy) aiming at federating the knowledge required from various fields (animal genomics and genetics, bioinformatics and agricultural genetics) to be applied in the national agricultural industry and in particular stock breeding. The ultimate aim is to create a national program, through the creation of a new Institute, which will support the production of genetically improved (milk-producing) small ruminants. This program has been conceived four years ago and a proposal has been submitted for funding to the European Commission under the Teaming Program. The proposal was ranked 5<sup>th</sup> out of 208 and we are currently in the second phase claiming 30m Euros. This is a paradigm of how previously distinct fields of study converge to address a scientific problem with huge economic implications.

#### 1. OPTHALMOS RESEARCH and EDUCATIONAL INSTITUTE

This is an ongoing collaboration with Dr Tassos Georgiou (<u>http://www.ophthalmiccentre.com/</u>) who has filed an international patent for the effect of Omega-3 for the treatment of degenerative, age-related eye-diseases. So far, two publications have ensued and the collaboration is ongoing with new avenues of investigation been pursued. The possibility of self-repair (stem cell activation) by the retina, as a result of Omega-3 administration is a strong possibility and if proved to be the case it will open up a totally new area or investigation in the area of stem cell research.

# **RESEARCH FUNDING as Principal Coordinator (Total-€ 2,611,462)**

- 2001-2004 Career Development Award. Infrastructure Grant to set up Developmental and Functional Genetics Lab and the Animal Experimentation Facility at the Cyprus Institute of Neurology and Genetics. Sponsor: Research Promotion Foundation, Cyprus. Lab budget: (€ 1,150,000).
- **2. 2002-2005** The cord blood as a source of stem cells for clinical and research use. Sponsor: Research Promotion Foundation, Cyprus. Lab budget: (85,000)
- 2003-2007 Genetic Mechanisms that Determine Neuronal Progenitor Identity in the Ventral Spinal Cord. European Union-FP5 €1,629,845. Coordinator. Lab budget: (€348,000)
- **4. 2003-2006** Evaluation of Soxl, Sox2 and ABCG2 as markers of neural progenitor cells, Co-ordinator: Dr. Stavros Malas (CING, CYPRUS). Funding Organization: Research Promotion Foundation, Cyprus, Lab budget: (€127,500)
- 5. 2005-2008 The discovery of genetic factors that determine the identity if V2 interneurons in the ventral spinal cord using DNA microarrays. Sponsor: Research Promotion Foundation, Cyprus. Lab budget: (€ 121,082)
- 2005-2008 The use of BAC technology to elucidate the role of the transcription factor Sox14 in spinal cord development. Sponsor: Research Promotion Foundation, Cyprus. Lab Budget: (€ 161,755)
- **7. 2005-2008** A functional study of SOX14 in the development of the ventral spinal cord. Sponsor: Research Promotion Foundation, Cyprus. Lab Budget: (€ **67,237**)

8. 2005-2008 A functional study of SOXB1 transcription factors in early development of the ventral spinal cord. Sponsor: Research Promotion Foundation, Cyprus. Lab Budget: (€ 109,480)

**9.** 2005-2008 The evaluation of Sox1, Sox2 and ABCG2 as markers of neural stem cells. Sponsor: Research Promotion Foundation, Cyprus. Lab Budget: (€ 89,250).

- **10. 2006-2009** A study of the function of SOX1 in the embryonic telencephalon. Research Promotion Foundation, Cyprus. Lab budget (**€68,000**).
- **11. 2011-2013,** Open Innovation for Health: A 2020 Strategy. European Commission FP7: Lab Budget: (€64,260).
- 12. 2017-2018 AGRICYGEN: A HORIZON 2020 project funded under the Teaming program for setting up a Research Institute with a remit to improve the genetic composition of sheep and goats in Cyprus. Currently under phase II claiming a 30m Euros grant. Lab Budget: (€7,900).
- 2018-2021 Deciphering the role of SOX2, SOX14 and SOX21 in pre-implantation embryo development. Research Promotion Foundation, Cyprus. Lab budget: (€211,998).

# PEER-REVIEWED PUBLICATIONS

- 1. Syrimis A, Nicolaou N, Alexandrou A, Papaevripidou I, Nicolaou M, Loukianou E, Christophidou-Anastasiadou V, <u>Malas S</u>, Sismani C and Tanteles GA. Aniridia due to a novel microdeletion affecting PAX6 regulatory enhances: case report and review of the literature. *Journal of Genetics* (accepted for publication).
- Syrimis A, Nicolaou N, Alexandrou A, Papaevripidou I, Nicolaou M, Loukianou E, Sismani C, <u>Malas S</u>, Christophidou-Anastasiadou V and Tanteles GA. Molecular analysis of Cypriot families with aniridia reveals a novel *PAX6* mutation. *Molecular Medicine Reports* (accepted for publication).
- 3. Neoklis Makrides, Elena Panagiotou, Pavlos Fanis, Christos Karaiskos, George Lapathitis and **Stavros Malas.** Sequential role of SOXB2 factors in GABAergic neuron specification of the dorsal midbrain. Frontiers in Mol. Neuroscience, (in press).
- Panayiotou E, Papacharalambous R, Antoniou A, Christophides G, Papageorgiou L, Fella E, Malas S, Kyriakides T. Genetic background modifies amyloidosis in a mouse model of ATTR neuropathy. Biochem Biophys Rep. 2016 Aug 11;8:48-54.
- 5. Kalogerou M, Kolovos P, Prokopiou E, Papagregoriou G, Deltas C, **Malas S**, Georgiou T. Omega-3 fatty acids protect retinal neurons in the DBA/2J hereditary glaucoma mouse model. Exp Eye Res. 2018 Feb;167:128-139.
- Prokopiou E, Kolovos P, Kalogerou M, Neokleous A, Papagregoriou G, Deltas C, Malas S, Georgiou T. Therapeutic potential of omega-3 fatty acids

supplementation in a mouse model of dry macular degeneration. BMJ Open Ophthalmol. 2017 Jun 19;1(1):e000056.

- 7. Panayiotou E, Fella E, Papacharalambous R, **Malas S**, Saraiva MJ, Kyriakides T. C1q ablation exacerbates amyloid deposition: A study in a transgenic mouse model of ATTRV30M amyloid neuropathy. PLoS One. (2017); 12(4).
- Francius C, Hidalgo-Figueroa M, Debrulle S, Pelosi B, Rucchin V, Ronellenfitch K, Panayiotou E, Makrides N, Misra K, Harris A, Hassani H, Schakman O, Parras C, Xiang M, Malas S, Chow RL, Clotman F. Vsx1 Transiently Defines an Early Intermediate V2 Interneuron Precursor Compartment in the Mouse Developing Spinal Cord. Front Mol Neurosci. 2016;9:145.
- Identification of a novel population of V2 interneurons in the developing mouse spinal cord. Cédric Francius, María Hidalgo-Figueroa, Kara M Ronellenfitch, E Panayiotou Worth, Krishna Misra, Carlos M. Parras, Ming Xiang, Stavros Malas, Richard Chow, Frédéric Clotman. (2015). Int J Dev Neurosci. ;47
- 10. Panayiotou E, **Malas S**. Adult spinal cord ependymal layer: a promising pool of quiescent stem cells to treat spinal cord injury. Front Physiol. (2013); 28;4:340.
- 11. Karnavas T, Mandalos N, **Malas S**, Remboutsika E. SoxB, cell cycle and neurogenesis. Front Physiol. (2013);4:298. 10.3389/fphys.2013.00298.
- 12. Panayiotou E, Panayi E, Lapathitis G, Francius C, Clotman F, Kessaris N, Richardson WD, **Malas** S. Pax6 is expressed in subsets of V0 and V2 interneurons in the ventral spinal cord in mice. Gene Expr Patterns. 2013 Dec;13(8):328-34.
- 13. Dardiotis E, Panayiotou E, Feldman ML, Hadjisavvas A, **Malas S**, Vonta I, Hadjigeorgiou G, Kyriakou K, Kyriakides T. Intraperitoneal melatonin is not neuroprotective in the G93ASOD1 transgenic mouse model of familial ALS and may exacerbate neurodegeneration. Neurosci Lett. 2013 Aug 26;548:170-5.
- 14. Elkouris M, Balaskas N, Poulou M, Politis PK, Panayiotou E, Malas S, Thomaidou D, Remboutsika E. Sox1 maintains the undifferentiated state of cortical neural progenitor cells via the suppression of Prox1-mediated cell cycle exit and neurogenesis. Stem Cells. 2011 Jan;29(1):89-98.
- 15. Panayi H, Panayiotou E, Orford M, Genethliou N, Mean R, Lapathitis G, Li S, Xiang M, Kessaris N, Richardson WD, Malas S. Sox1 is required for the specification of a novel p2-derived interneuron subtype in the mouse ventral spinal cord. J Neurosci. 2010 Sep 15;30(37):12274-80.
- Tschernatsch M, Singh P, Gross O, Gerriets T, Kneifel N, Probst C, Malas S, Kaps M, Blaes F. Anti-SOX1 antibodies in patients with paraneoplastic and nonparaneoplastic neuropathy. J Neuroimmunol. 2010 Sep 14;226(1-2):177-80.

- Genethliou N, Panayiotou E, Panayi H, Orford M, Mean R, Lapathitis G, Gill H, Raoof S, De Gasperi R, Elder G, Kessaris K, Richardson D and Malas S. Sox1 links the function of neural patterning and Notch signalling in the ventral spinal cord during the neuron-glial fate switch. Biochem Biophys Res Communic. 2009, 390 (4):1114-20.
- 18. Genethliou N, Panayiotou E, Panayi H, Orford M, Mean R, Lapathitis G, **Malas S**. Spatially distinct functions of PAX6 and NKX2.2 during gliogenesis in the ventral spinal cord. Biochem Biophys Res Commun. 2009 Apr 24; 382(1):69-73.
- 19. Orford M, Mean R, Lapathitis G, Genethliou N, Panayiotou E, Panayi H, **Malas S**. Generation of an ABCG2(GFPn-puro) transgenic line--a tool to study ABCG2 expression in mice. Biochem Biophys Res Commun. 2009; 26;384 (2):199-203.
- 20. Ekonomou A\*, Kazanis I\*, **Malas S**\*, Wood H, Alifragis P, Denaxa M, Karagogeos D, Constanti A, Lovell-Badge R, Episkopou (2005), Free in PMC, "Neuronal Migration and Ventral Subtype Identity in the Telencephalon Depend on SOX1", PLoS Biol. 2005 May 17;3(6):e186. (\*Joint first author).
- 21. **S. Malas,** M. Postlethwaite, A. Ekonomou, B. Whalley, S. Nishiguchi, H. Wood, B. Meldrum, A. Constanti and V. Episkopou (2003). SOX1-deficient mice suffer from epilepsy associated with abnormal ventral forebrain development and olfactory cortex hyperexcitability. Neuroscience, 119(2): 421-32.
- 22. **Malas S**, Duthie S, Deloukas P, Episkopou V. (1999). The isolation and highresolution chromosomal mapping of human SOX14 and SOX21; two members of the SOX gene family related to SOX1, SOX2, and SOX3. *Mammalian Genome 10:* 9:934-7.
- 23. **Malas, S**; Duthie, SM; Mohri, F;Lovell-Badge, R;Episkopou, V. (1997) .Cloning and mapping of the human SOX1: a highly conserved gene expressed in the developing brain. *Mammalian Genome 8: 11; 866-868.*
- 24. **Malas, S**; Sartor, M; Duthie, S;Hadjantonakis, K; Lovellbadge, R; Episkopou, V (1996). Genetic and physical mapping of the murine Sox1 gene. *Mammalian Genome 7: 8; 620-621.*
- 25. Malas S., Pilz A., Lalley P., Pate L., Stephenson D., Abbott C., (1996). The isolation and mapping of PCR markers specific to mouse chromosome 2. *Mammalian Genome 7: 2; 145-148.*
- 26. **Malas, S**. and Olga Forero. (1995). PCR markers associated with the mouse nicotinic-acetylcholine-receptor-subunit genes β4, β7 and β4 on mouse chromosomes 2, 7 and 9. *Mouse Genome 93: 2, 433-435*.

- 27. **Malas S.**, Jo Peters and Cathy Abbott (1994). The genes for endothelin 3, vitamin D 24-hydroxylase and melanocortin 3 receptor map to distal chromosome 2, in the region of conserved synteny with human chromosome 20. *Mammalian Genome*, 5 (9) 577-579.
- 28. Cathy Abbott., **Stavros Malas**, Alison Pilz, Lorna Pate, Robin Ali, & Jo Peters (1994). Linkage mapping around the ragged, Ra, and wasted, wst, loci on distal mouse chromosome. *Genomics 20, 94-98.*
- 29. Gangadharan U., **Malas S**., Coulton G.R., Brown S.D.M (1995). Chromosomal localisation of the 43 kDa acetylcholine receptor associated protein in the mouse and human. *Mouse Genome 93, 1, 155-157.*
- 30. Povey S. et al (1994). Two loci for Tuberous Sclerosis: one on 9q34 and one on 16p13. *Ann. Hum. Genet.* 58, 107-127.
- 31. Franklin, D et al (1991). A genetic map of 9q34 by multiple two point analysis. *Cytogen. Cell Genet. 58, 3-4, p1938.*
- 32. Burley, MW et al. (1991). Linkage studies in Tuberous Sclerosis. *Cytogen. Cell Genet.* 59; 3-4 p1935-1936.

#### **BRIEF RESEARCH OUTLINE**

The development of the mammalian body comes about through a series of progressive cell fate restrictions leading to the production of specialized tissue-specific cells from tissue-specific stem cells. Understanding how these unique stem cells give rise to specialized cells is crucial to understanding both normal and abnormal development and for developing cell repair therapies for human conditions.

Our lab has studied this process in the embryonic Central Nervous System (CNS) in mice. Specifically we approach this question by studying the role of a group of proteins, coded for by members of the **SOX gene family**, to understand their role in cell fate acquisition in the developing CNS using a variety of genetic approaches. These proteins are all expressed in CNS stem cells and in some differentiated cells but their role has been difficult to address primarily due to their structural similarly and, partly, functional redundancy.

For years now we have been able to assign a unique function for SOX1, the first member of this family, in the developing forebrain and spinal cord. In the forebrain we showed that SOX1 is required for the development of ventral forebrain and in particular the olfactory tubercle. These studies uncovered an expected role of this structure in the initiation of generalised seizures. Importantly SOX1-deficient mice remain the only available genetic model of generalised seizures with a very focal developmental lesion. This worked led to the publication of two papers in Plos Biology and Neuroscience.

In the spinal cord we have discovered that SOX1 is specifically required for the development of a new type of ventral neurons that were previously unknown and showed

that these cells change fate and in mice lacking SOX1. This worked was published in the prestigious journal, The Journal of Neuroscience. Finally, we discovered that SOX1 is also essential for the development of central-canal contacting neurons, a group of cells with an unknown function yet.

More recently we focused on the developing dorsal midbrain. We discovered that SOX21 and SOX14 have a unique and sequential role in the specification and maturation process of GABAergic lineages. This worked has been accepted for publication in a highly reputable journal, *Frontiers in Molecular Neuroscience*.

In addition to working on cell fate specification, our lab has developed a unique array of genetically modified mouse lines offering a powerful handle to studying stem cell behaviour in the CNS. During the last three years we developed pioneering techniques of in utero manipulation of embryos both using electroporation and viral infection.

Our current research will continue on the development of the embryonic brain. During the last year we turned our attention to a very challenging biological question-to understand the role of SOX14 and SOX21 at the stage of the very first cell fate decision of the developing embryo, the segregation of embryonic vs extraembryonic cell lineages. To this end we have set up an exciting collaboration with a group at Cambridge University which discovered that SOX21 is a key player in this very first cell fate decision. The mice we have developed in our lab is a unique resource to answer this question.

## Collaborative research projects

Because of our expertise in animal experimentation and genetic manipulation, we have established a collaboration with a local eye specialist interested to test the effects of  $\Omega$ 3 administration on animal models of macular degeneration. Our results (published recently in two papers) provide evidence of a possible retinal repair mechanism through the activation of a yet unknown pool of quiescent stem cells. We will pursue this collaboration due to the wider implication on issues relating to stem cell research in adults.

Lately, I have taken the initiative to organize a trans-disciplinary collaboration between scientists with knowledge in animal genetics and genomics, bioinformatics, computing sciences and crop-production in order to tackle a scientific challenge of enormous economic value to Cyprus. The dairy industry in Cyprus is the second largest revenue-generator from exports in the country. The immense growth of the industry requires increasing amounts of goats and sheep milk in order to meet the huge increase in the production of the local cheese, haloumi. To this end, we have submitted a scientific proposal to the European Commission to secure funding from the Horizon 2020 Program. The specific call has been designed to support the creation of very large research infrastructures with immediate economic impact to the country. This proposal went through the first phase and was ranked 5<sup>th</sup> out of 208 submitted across Europe. Currently at the second stage of evaluation. The aim is to create a new Institute which will bring together scientists from the above-mentioned fields in order to generate the necessary knowledge and expertise for a country-wide program to produce genetically improved small ruminants (through genotype-phenotype correlations) with high milk-producing capacity.