Title: Gene regulation networks in nervous system development and cancer progression

Abstract

The mammalian brain is the most complex organ of all living organisms. The molecular machinery that regulates the generation of this enormous cellular complexity remains largely unknown. Our goal is to tackle this question by understanding the interplay between extracellular signaling cues and intrinsic gene regulation circuitries that control proliferation vs differentiation decisions in neural stem cells (NSCs) in health and disease. Elucidation of these mechanisms will not only provide insights into the basic principles of brain formation, but will also allow novel therapies for the treatment of brain-related diseases and tumors. To this end, we have recently uncovered the function of such a molecular mechanism in neural stem cells and tumor cells of the nervous system. These observations could provide therapeutic possibilities for treatment of neurological disorders and inhibition of tumor progression in central nervous system.

Brief Biosketch

Dr Politis received his BSc degree in Biology from the University of Patras, Greece in 1996. Then he moved to Oxford, where he was awarded his Ph.D. in Biochemistry, Molecular Biology and Genetics from the Department of Biochemistry, Oxford University, UK in 2000. During this period, he worked on epigenetic aspects of eukaryotic transcriptional regulation. During his PhD thesis he was supported with studentships from prestigious organizations such as Biotechnology and Biological Sciences Research Council, Florey-EPA studentship from Queen's College of Oxford University and Welcome Trust Fund. He has also been awarded the NASA planetary biology internship that gave him the opportunity to work in the Chemical Evolution Lab in the field of prebiotic Chemistry at the Salk Institute for Biological Studies, CA, USA. He then obtained a post-doctoral position in the lab of Cellular and Molecular Neurobiology of the Hellenic Pasteur Institute, Athens, Greece. His research in Athens focused on the regulation of neuronal differentiation and specification, studying the role of genes that coordinate cell cycle exit and differentiation of neural stem cells during embryonic development. He joined Biomedical Research Foundation of the Academy of Athens in January 2007 as Principal Investigator (Assistant Professor Level) at the Center for Basic Research. He has also been recently elected as Associate Professor of Biochemistry at the Department of Chemistry, University of Athens, Greece. His research interests are focused on how epigenetic mechanisms can regulate cell differentiation and proliferation during development in health and disease. In his research career he has managed to contribute more than 40 peer-reviewed publications in high profile Journals and Books.

Selected Publications

1. Gkikas D, Tsampoula M, **Politis PK** (2017) Nuclear receptors in neural stem/progenitor cell homeostasis. **Cell Mol Life Sci**. 74: 4097-4120.

2. Kouroupi G, Taoufik E, Vlachos IS, Tsioras K, Antoniou N, Papastefanaki F, Chroni-Tzartou D, Wrasidlo W, Bohl D, Stellas D, **Politis PK**, Vekrellis K, Papadimitriou D, Stefanis L, Bregestovski P, Hatzigeorgiou AG, Masliah E, Matsas R (2017). Defective synaptic connectivity and axonal neuropathology in a human iPSC-based model of familial Parkinson's disease. **Proc Natl Acad Sci U S A.** 114(18):E3679-E3688.

3. Stergiopoulos A and **Politis PK** (2016). Nuclear receptor NR5A2 controls neural stem cell fate decisions during development. ***Nature Communications****. 7:12230.*

4. Arvaniti E, Vakrakou A, Kaltezioti V, Stergiopoulos A, Prakoura N, **Politis PK**, Charonis A. (2016). Nuclear receptor NR5A2 is involved in the calreticulin gene regulation during renal fibrosis. **Biochim Biophys Acta.** 1862: 1774-1785.

5. Arvaniti E, Moulos P, Vakrakou A, Chatziantoniou C, Chadjichristos C, Kavvadas P, Charonis A, **Politis PK**. (2016). Whole-transcriptome analysis of UUO mouse model of renal fibrosis reveals new molecular players in kidney diseases. **Scientific Reports**. 6:26235.

6. Kaltezioti V, Antoniou D, Stergiopoulos A, Rozani I, Rohrer H and **Politis PK** (2014). Prox1 regulates Olig2 expression to modulate binary fate decisions in spinal cord neurons. **The Journal of Neuroscience**. 34: 15816-15831.

7. Antoniou D, Stergiopoulos A and **Politis PK** (2014). Recent advances in the involvement of long non-coding RNAs in neural stem cell biology and brain pathophysiology. **Frontiers in Physiology.** 5:155.

8. Foskolou IP, Stellas D, Rozani I, Lavigne MD and **Politis PK** (2013). Prox1 suppresses the proliferation of neuroblastoma cells via a dual action in p27-Kip1 and Cdc25A. **Oncogene**, 32(8): 947-960.

9. Koutmani Y, **Politis PK**, Elkouris M, Agrogiannis G, Kemerli M, Patsouris E, Remboutsika E, Karalis KP (2013). Corticotropin-releasing hormone exerts direct effects on neuronal progenitor cells: implications for neuroprotection. **Molecular Psychiatry**. 18(3):300-307.

10. Kaltezioti V, Kouroupi G, Oikonomaki M, Mantouvalou E, Stergiopoulos A, Charonis A, Rohrer H, Matsas R and **Politis PK** (2010). Prox1 regulates the *Notch1*-mediated inhibition of neurogenesis. **PLoS Biology**. 8(12):e1000565.
This article was selected for evaluation by the Faculty 1000 (http://f1000.com/8646957)

11. Politis PK, Thomaidou D, Matsas R (2008). Co-ordination of cell cycle exit and differentiation of neuronal progenitors. **Cell Cycle**. 7: 691-697.

12. **Politis PK**, Akrivou S, Hurel C, Papadodima O, Matsas R (2008). BM88/Cend1 is involved in histone deacetylase inhibition-mediated growth arrest and differentiation of neuroblastoma cells. **FEBS Letters**. 582: 741-748.

13. Politis PK, Makri G, Thomaidou D, Geissen M, Rohrer H, Matsas R (2007). BM88/Cend1 regulates cell cycle exit and differentiation of neuronal precursors. **Proc Natl Acad Sci U S A**, 104, 17861–17866.

14. Georgopoulou N*, Hurel C*, **Politis PK***, Gaitanou M, Matsas R, Thomaidou D (2006). BM88 is a dual function molecule inducing cell cycle exit and neuronal differentiation of neuroblastoma cells via cyclin D1 down-regulation and retinoblastoma protein hypophosphorylation. **The Journal of Biological Chemistry** 281, 33606-33620.
*equal first authors.

15. Martinez-Campa C, **Politis P**, Moreau JL, Kent N, Goodall J, Mellor J and Goding CR (2004). Precise nucleosome positioning and the TATA box dictate requirements for histone H4 tail and the bromodomain Bdf1. **Molecular Cell** 15, 69-81.

16. Kent NA, Karabetsou N, **Politis PK** and Mellor J (2001). In vivo chromatin remodelling by yeast ISWI homologs Isw1p and Isw2p. **Genes & Development** 15, 619-626.