

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Department of Psychiatry Erasmus MC
Project Title:	Using induced pluripotent stem cells (iPSCs) to model schizophrenia
Abstract:	Recent developments in cell biology have allowed for the emergence of a powerful new approach for investigating the neurobiology of psychiatric disorders, such as schizophrenia. In particular, using patient-derived induced pluripotent stem cells (iPSCs), we are now able to model the molecular and cellular mechanisms underlying the pathophysiology of schizophrenia, using a combination of cell-type specific differentiation, whole-cell electrophysiology, long-term calcium imaging, <i>in vivo</i> transplantation and molecular profiling. Our approach is predicated upon family-based analyses using iPSCs derived from affected and unaffected siblings, as well as using CRISPR/Cas9 editing to derive the most optimal controls. Together, this project will provide a highly motivated student with the unique opportunity to learn some of the most advanced techniques in modern cell biology, leveraged towards a focused effort to elucidate the neurobiology of schizophrenia.
Requirements of candidate:	Background: <i>Neuroscience, cell culture, molecular biology</i> Master degree: Yes IELTS Grade: 7.0 (<i>minimal 6.0 per component</i>) or TOEFL: 100 (<i>minimal 20 per component</i>)
Supervisor information:	<i>Prof. dr. Steven A. Kushner, Prof. dr. Witte J.G. Hoogendijk</i> s.kushner@erasmusmc.nl , w.hoogendijk@erasmusmc.nl http://www.psych.nl/research/neurobiological_psychiatry.html

Selected Publications:

- De Esch CE, Ghazvini M, Loos F, Schelling-Kazaryan N, Widagdo W, Munshi ST, van der Wal E, Douben H, Gunhanlar N, Kushner SA, Pijnappel WW, de Vrij FM, Geijssen N, Gribnau J, Willemsen R (2014). Epigenetic characterization of the FMR1 promoter in induced pluripotent stem cells from human fibroblasts carrying an unmethylated full mutation. *Stem Cell Reports*, in press.
- Achterberg KG, Buitendijk GH, Kool M, Goorden SM, Post L, Slump DE, Silva AJ, van Woerden GM, Kushner SA, Elgersma Y (2014). Temporal and region-specific requirements of α CaMKII in spatial and contextual learning. *Journal of Neuroscience*, 34(34): 11180-11187.
- Yiu AP, Mercaldo V, Yan C, Richards B, Rashid AJ, Hsiang HL, Pressey J, Mahadevan V, Tran MM, Kushner SA, Woodin MA, Frankland PW, Josselyn SA (2014). Neurons are recruited to a memory trace based on relative neuronal excitability immediately before training. *Neuron*, 83(3): 722-735.
- Ellegood J, Markx S, Lerch JP, Steadman PE, Genç C, Provenzano F, Kushner SA, Henkelman RM, Karayiorgou M, Gogos JA (2014). Neuroanatomical phenotypes in a mouse model of the 22q11.2 microdeletion. *Molecular Psychiatry*, 19(1): 99-107.
- Ellegood J, Markx S, Lerch JP, Steadman PE, Genç C, Provenzano F, Kushner SA, Henkelman RM, Karayiorgou M, Gogos JA (2014). A highly specific pattern of volumetric brain changes due to 22q11.2 deletions in both mice and humans. *Molecular Psychiatry*, 19(1): 6.
- Cross-Disorder Group of the Psychiatric Genomics Consortium (2013). Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs. *Nature Genetics*, 45(9): 984-94.
- Galliano E, Potters JW, Elgersma Y, Wisden W, Kushner SA, De Zeeuw CI, Hoebeek FE (2013). Synaptic transmission and plasticity at inputs to murine cerebellar Purkinje cells are largely dispensable for standard nonmotor tasks. *Journal of Neuroscience*, 33(31): 12599-12618.

- Bergink V, Burgerhout KM, Weigelt K, de Witt HJ, Pop VJ, Kushner SA, Drexhage HA (2013). Immune system dysregulation in first-onset postpartum psychosis. *Biological Psychiatry*, 73(10): 1000-1007.
- Cross-Disorder Group of the Psychiatric Genomics Consortium (2013). Identification of risk loci with shared effects on five major psychiatric disorders: a genome-wide analysis. *Lancet*, 381(9875): 1371-9.
- Bergink V, Bouvy PF, Vervoort JS, Koorengevel KM, Steegers EA, Kushner SA (2012). Prevention of Postpartum Psychosis and Mania in Women at High Risk. *American Journal of Psychiatry*, 169(6): 609-615.
- Lieverse R, Van Someren EJ, Nielen MM, Uitdehaag BM, Smit JH, Hoogendijk WJ (2011). Bright light treatment in elderly patients with nonseasonal major depressive disorder: a randomized placebo-controlled trial. *JAMA Psychiatry*, 68(1):61-70.
- van Woerden GM, Hoebeek FE, Gao Z, Nagaraja RY, Hoogenraad CC, Kushner SA, Hansel C, de Zeeuw CI, Elgersma Y (2009). β CaMKII controls the direction of plasticity at parallel fiber-Purkinje cell synapses. *Nature Neuroscience*, 12(7): 823-825.
- Han JH, Kushner SA, Yiu AP, Hsiang HL, Buch T, Waisman A, Bontempi B, Neve RL, Frankland PW, Josselyn SA (2009). Selective erasure of a fear memory. *Science*, 323(5920): 1492-1496.
- Krab LC, de Goede-Bolder A, Aarsen FK, Pluijm SMF, Bouman MJ, van der Geest JN, Lequin M, Catsman CE, Arts WFM, Kushner SA, Silva AJ, de Zeeuw CI, Moll HA, Elgersma Y (2008). Effect of simvastatin on cognitive functioning in children with Neurofibromatosis type 1: a randomized controlled trial. *JAMA*, 300(3): 287-294.
- Han JH, Kushner SA, Yiu AP, Cole CA, Matynia A, Brown RA, Neve R, Guzowski JF, Silva AJ, Josselyn SA (2007). Neuronal competition and selection during memory formation. *Science*, 316(5823): 457-460.