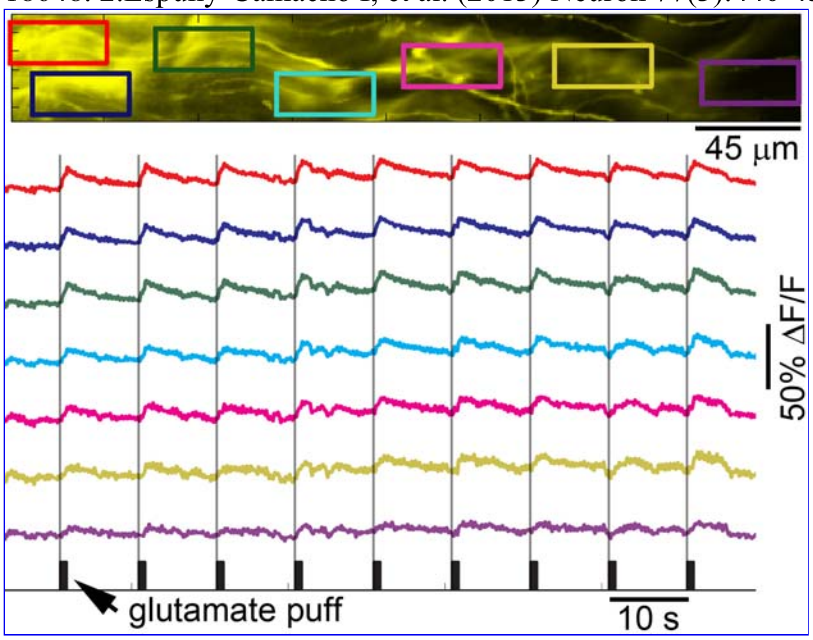
Print this Page

NEUROSCIENCE 2014

Presentation Abstract

Program#/Poster#:	590.29/A61
Presentation Title:	Functional imaging of human iPSCs-derived neurons integrated in mouse cortex using 2-photon microscopy *in vivo*
Location:	WCC Hall A-C
Presentation time:	Tuesday, Nov 18, 2014, 1:00 PM - 2:00 PM
Presenter at Poster:	Tue, Nov. 18, 2014, 1:00 PM - 2:00 PM
Topic:	++A.04.b. Induced pluripotent stem cells and models of disease
Authors:	**C. A. TRUJILLO**[1], H. UHLIROVA[2], K. KILIC[3], P. A. SAISAN[3], Q. CHENG[3], K. L. WELDY[3], A. M. DALE[4], *A. R. MUOTRI[1], A. DEVOR[4,5]; [1]Pediatrics/Cellular Mol. Med., [2]Radiology, [3]Neurosciences, [4]Neurosciences and Radiology, UCSD, La Jolla, CA; [5]Martinos Ctr. for Biomed. Imaging, MGH/Harvard Med. Sch., Charlestown, MA
Abstract:	Recent advances in stem cell technology have enabled generation of neuronal cell lines from induced pluripotent stem cells (iPSCs) derived from human peripheral tissues. This opens unprecedented opportunities for investigation of human brain disease linked to known genetic variations. However, the lack of the natural brain microenvironment in a dish can influence the phenotype and maturation. One potential strategy to overcome these limitations is transplantation of iPSC-derived neuronal precursor cells (NPCs) into the mouse brain. Previous studies have proved the feasibility of this “chimeric” approach and demonstrated that the transplanted neurons form synaptic connections using electrophysiological recordings in brain slices (1, 2). Ideally, however, activity of human neurons should be measured in the intact mouse brain. In the present study, we addressed this challenge by using in vivo 2-photon calcium imaging. Human iPSC-derived NPCs were injected into the brains of newborn mice. In adult mice, the cell bodies of human neurons were typically found in clusters along the injection track. Calcium indicator OGB1 was loaded using the standard procedures at the location of a cluster and was uptaken by both mouse and human neurons. Human dendrites, however, extended outside the volume of loaded mouse tissue allowing selective measurements of their activity. Stimulation

was delivered using a puff of glutamate through a glass micropipette inserted into the tissue within ~100 microns from the imaging field of view (FOV). Glutamate produced clear increases in OGB1 fluorescence in the human dendrites. Figure 1 illustrates the response to 9 consecutive stimulus trials; the regions of interest are color-coded on the FOV image. Thus, human iPSC-derived neurons in vivo have functional glutamate receptors and calcium channels. The chimeric approach may become a translational tool for studying disease mechanisms and evaluating candidate drugs on adult human neurons. 1.Muotri AR, et al. (2005) PNAS 102(51):18644-18648. 2.Espuny-Camacho I, et al. (2013) Neuron 77(3):440-456.



Disclosures: **C.A. Trujillo:** None. **H. Uhlirova:** None. **K. Kilic:** None. **P.A. Saisan:** None. **Q. Cheng:** None. **K.L. Weldy:** None. **A.M. Dale:** None. **A.R. Muotri:** None. **A. Devor:** None.

Keyword (s): STEM CELL

CALCIUM IMAGING

TRANSPLANTATION

Support: NIH grant EB00790

NIH grant S10RR029050

CIRM grant TR2-01814

NIH grant 1-DP2-OD006495-01

International Headache Society Postdoctoral Fellowship