



Cellular Physiology

(Neurophysiology and Neurooncology)

Professor Hideki Matsui

Major Research Interests

Basic Science

Understanding Neuronal and Brain Functions

Protecting the Brain against Depression

Challenges in the Treatment of Brain Cancer

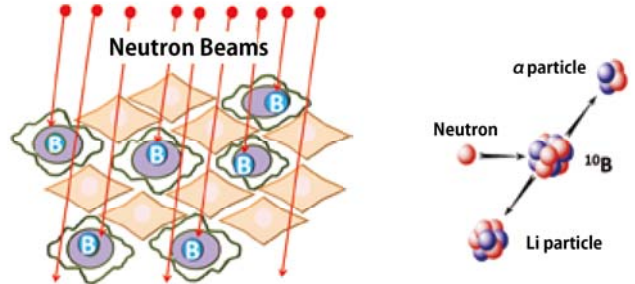
Translational Research

Molecules

Organism (Body)

Development of Boron Delivery Agents for BNCT of Glioblastoma Multiforme

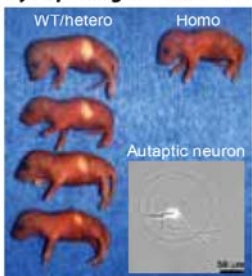
Boron neutron capture therapy (BNCT) is a potentially promising brain cancer therapy. When cancer cells containing boron ten are shot by neutron beams, nuclear fission takes place in the cells and alpha particles and lithium particles are generated. Taking advantage of powers of these particles, the cells can be destroyed. However, current boron drugs have two major problems; low cancer cell specificity and low uptake and retention efficiencies.



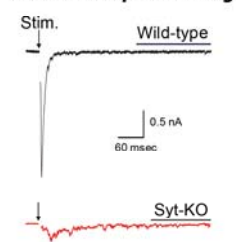
We have been challenging these problems with two experimental techniques. First, we have packed boron drugs in immunoliposomes conjugated with specific antibodies against cancer cell surface antigens. Second, we have put cell-penetrating peptides to boron compounds. Now, in collaboration with Neutron Therapy Research Center, Okayama University, we are trying to test the efficacies of these new boron delivery drugs with tumor-bearing animal models.

Molecular Mechanisms of Neurotransmitter Release

Synaptotagmin KO mice

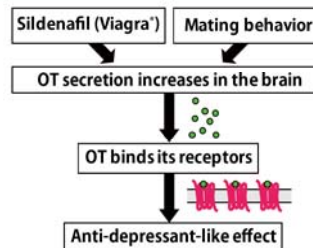
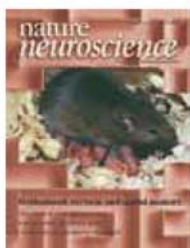


Patch clamp recording



Brain function is founded on the transmission of information from one neuron to another at synapse. Synaptic transmission is mediated by neurotransmitters, which are stored in synaptic vesicles and exocytosed by fusion of the vesicles with the plasma membrane. To explore how neurons release transmitters, we combine molecular biological and electrophysiological techniques, especially focusing on elucidation of structure/function of synaptotagmin 1, a calcium-binding protein that localizes in synaptic vesicles. We have studied synaptic transmission in neurons cultured from synaptotagmin 1 knock-out mice, and found the roles of the binding of calcium ions to synaptotagmin 1 in triggering of fast transmitter release. We are now trying to examine how the Ca^{2+} binding of synaptotagmin 1 is converted into neurotransmitter release.

Novel Roles of Oxytocin in the Central Nervous System

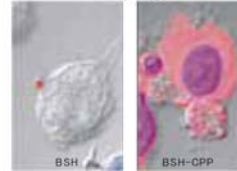


We discovered that oxytocin (OT) increases special memory in lactating female mice. Recently, we found that sildenafil, which is sold as an erectile dysfunction drug Viagra, has an anti-depressant-like effect through OT receptor signaling pathway when injected in male mice. We also found that when mated with female mice, the male shows an anti-depressant-like effect. These results suggest that sildenafil may become a promising antidepressant without the side effect of sexual dysfunction. They might also suggest that an improvement of the personal and social life where one can have a better personal contact with his/her partner may lead to the prevention and treatment of depression without medication.

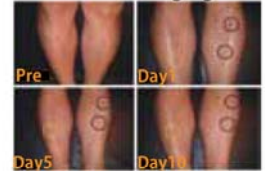
Protein Therapy

Applications of Cell-penetrating Peptides (CPP) to Drug Discovery

Boron-delivery agent for BNCT



Skin whitening agent



Boron compound CPP

Neg. cont. Tyrosinase Inhibitor CPP

Hair restorer



VIVIT CPP

Featured Publications

- Ookubo *et al.*, The transdermal inhibition of melanogenesis by a cell-membrane-permeable peptide delivery system based on poly-arginine. *Biomaterials* **35**:4508, 2014.
- Michiue *et al.*, The acceleration of boron neutron capture therapy using multi-linked mercap toundecahydrododecaborate fused cell-penetrating peptide. *Biomaterials* **35**:3396, 2014.
- Fujimura *et al.*, Cyclin G2 promotes hypoxia-driven local invasion of glioblastoma by orchestrating cytoskeletal dynamics. *Neoplasia* **15**:1272, 2013.
- Matsushita *et al.*, Antidepressant-like effect of sildenafil through oxytocin-dependent cyclic AMP response element-binding protein phosphorylation. *Neuroscience* **200**:13, 2012.
- Masumoto *et al.*, Ca^{2+} -independent syntaxin binding to the C_{β} effector region of synaptotagmin. *Mol Cell Neurosci* **49**:1, 2012.
- Fujimura *et al.*, Expression of a constitutively active calcineurin encoded by an intron-retaining mRNA in follicular keratinocytes. *PLoS One* **6**:e17685, 2011.
- Matsushita *et al.*, Oxytocin mediates the antidepressant effects of mating behavior in male mice. *Neurosci Res* **68**:151, 2010.
- Feng *et al.*, Development of a bifunctional immunoliposome system for combined drug delivery and imaging *in vivo*. *Biomaterials* **31**:4139, 2010.
- Noguchi *et al.*, A new cell-permeable peptide allows successful allogeneic islet transplantation in mice. *Nat Med* **10**:305, 2004.
- Tomizawa *et al.*, Oxytocin improves long-lasting spatial memory during motherhood through MAP kinase cascade. *Nat Neurosci* **6**:384, 2003.

Contact Us

Hideki Matsui, M.D., Ph.D.
Professor
Okayama Univ. Graduate School of Medicine, Dentistry and Pharmaceutical Sciences
2-5-1 Shikata Cho, Kita Ku, Okayama Shi, Okayama Prefecture 700-8558, Japan
E-mail: matsuihi@cc.okayama-u.ac.jp, Tel: +81-86-235-7105