BIOGRAPHICAL SKETCH

NAME: Tomomitsu Miyoshi

POSITION TITLE: Assistant Professor, Department of Physiology, Osaka University, Japan

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Osaka University, Suita, Japan	B.S.	04/1987	03/1993	Medicine
Osaka University, Suita, Japan	Ph.D.	04/1993	09/1999	Physiology

A. Personal Statement

My research focuses on the functional evaluation and functional reconstruction of the injured nervous system, with the visual system as the main target. Using electrophysiological techniques, I have studied cell death and axonal regeneration of retinal ganglion cells, and restoration of visual function by visual prosthesis for photoreceptor cell disease.

B. Positions, Scientific Appointments and Honors

Positions

2017 – Present Vice Director, Center for Medical Research and Education, Graduate School of Medicine, Osaka University, Suita, Japan

1998 – Present Assistant Professor, Department of Physiology, Graduate School of Medicine, Osaka University, Suita, Japan

Scientific Appointments

2023 – Present Editorial Board, Animal Eye Research (The official journal of the Japanese Society of Comparative and Veterinary Ophthalmology)

Honors

2014 President's Award for Encouragement of Osaka University

C. Contributions to Science

1. Basic research on retinal prosthesis

Retinal prosthesis is a medical device for patients blinded by degenerative diseases of the photoreceptor cells, such as retinitis pigmentosa. The device is implanted into the eye and achieves artificial visual sensation by electrically stimulating the remaining neurons in the patient's retina. We proposed the new retinal stimulation method, Suprachoroidal Transretinal Stimulation (STS), which is safer than the already existing methods. In collaboration with ophthalmologists, engineering scientists, and an eyecare company, I am working towards the practical application of the STS-type prosthesis (Fujikado et al., 2012). For example, the retinal activity by STS was evaluated using intrinsic signal imaging of the retina and single-neuron recording in the lateral geniculate nucleus of medium-sized animals (Okawa et al., 2007; Miyoshi et al., 2021). The newly designed devices were tested and evaluated with animal experiments (Kanda et al., 2014; Lohmann et al., 2016; Morimoto et al., 2021). In addition, new stimulation methods are being developed (Nakano et al., 2017a, b).

Okawa, Y., Fujikado, T., Miyoshi, T., Sawai, H., Kusaka, S., Mihashi, T., Hirohara, Y., Tano, Y. (2007) Optical imaging to evaluate retinal activation by electrical currents using suprachoroidal-transretinal stimulation. Invest Ophthalmol Vis Sci 48: 4777-4784.

Fujikado, T., Kamei, M., Sakaguchi, H., Kanda, H., Morimoto, T., Ikuno, Y., Nishida, K., Kishima, H., Maruo, T., Sawai, H., Miyoshi, T., Osaka, K., Ozawa, M. (2012) Clinical trial of chronic implantation of suprachoroidal-transretinal stimulation system for retinal prosthesis. Sensors and Materials 24(4): 181-187.

Kanda, H., Mihashi, T., Miyoshi, T., Hirohara, Y., Morimoto, T., Terasawa, Y., Fujikado, T. (2014) Evaluation of electrochemically treated bulk electrodes for a retinal prosthesis by examination of retinal intrinsic signals in cats. Jpn J Ophthalmol 58(4): 309-319.

Lohmann, T. K., Kanda, H., Morimoto, T., Endo, T., Miyoshi, T., Nishida, K., Kamei, M., Walter, P., Fujikado, T. (2016) Surgical feasibility and biocompatibility of wide-field dual-array suprachoroidal-transretinal stimulation prosthesis in middle-sized animals. Graefe's Arch Clin Exp Ophthalmol 254(4): 661-673.

Nakano, Y., Terasawa, Y., Kanda, H., Osawa, K., Miyoshi, T., Sawai, H., Fujikado, T. (2017a) Effectiveness of triangular and saw-tooth pulses in a retinal prosthesis with suprachoroidal-transretinal stimulation (STS). Jpn J Vis Sci 38: 53-59.

Nakano, Y., Terasawa, Y., Kanda, H., Tashiro, H., Osawa, K., Miyoshi, T., Sawai, H., Fujikado, T. (2017b) Sinusoidal electrical pulse more efficiently evokes retinal excitation than rectangular electrical pulse in retinal prostheses. Sensors and Materials 29(12): 1667.

Miyoshi, T., Morimoto, T., Sawai, H., Fujikado T. (2021) Spatial resolution of suprachoroidal–transretinal stimulation estimated by recording single-unit activity from the cat lateral geniculate nucleus. Front Neurosci 15: 717429.

Morimoto, T., Fujikado, T., Kanda, H., Miyoshi, T., Endo, T., Nishida, K., Kishima, H., Saito, T., Ito, K., Ozawa, M., Nishida, K. (2021) Testing of newly developed wide-field dual-array suprachoroidal–transretinal stimulation prosthesis in dogs. Transl Vis Sci Technol 10: 13.

Nishida, K., Morimoto, T., Terasawa, Y., Sakaguchi, H., Kamei, M., Miyoshi, T., Fujikado, T., Nishida, K. (2023) The influence of stimulating electrode conditions on electrically evoked potentials and resistance in suprachoroidal transretinal stimulation. Jpn J Ophthalmol 67: 182-188.

2. Functional evaluation and restoration of damaged retinal neurons

As retinal neurons are part of the central nervous system, the cells do not proliferate, and damaged axons of retinal ganglion cells (RGCs) do not regenerate. RGCs are almost completely lost by optic nerve transection. However, by transplanting peripheral nerve into the transected optic nerve stump, some cells can escape cell death and regenerate their axons in the graft. We characterized the physiological properties of axotomized and axon-regenerated ganglion cells of cat with a functionally differentiated visual system (Miyoshi et al., 1999; Takao et al., 2002; Kurimoto et al., 2003). We have also shown that electrical stimulation promotes survival and axonal regeneration of damaged retinal ganglion cells and inhibits photoreceptor degeneration in animal models (Morimoto et al., 2002, 2005, 2007, 2010, Tagami et al., 2009). Several substances were also shown to promote survival and axonal regeneration of RGCs (Kurimoto et al., 2006; Kashimoto et al., 2008; Oono et al., 2009).

Miyoshi, T., Watanabe, M., Sawai, H., Rasminsky, M., Sugioka, M., Ohde, H. and Fukuda, Y. (1999) Receptive field properties of adult cat's retinal ganglion cells with regenerated axons. Exp Brain Res 124:383-390.

Morimoto, T., Miyoshi, T., Fujikado, T., Tano, Y. and Fukuda, Y. (2002) Electrical stimulation enhances the survival of axotomized retinal ganglion cells in vivo. Neuroreport 13(2): 227-230.

Takao, M., Miyoshi, T., Watanabe, M. and Fukuda, Y. (2002) Changes in visual response properties of cat retinal ganglion cells within two weeks after axotomy. Exp Neurol, 177:171-182.

Kurimoto, T., Miyoshi, T., Suzuki, A., Yakura, T., Watanabe, M., Mimura, O. and Fukuda, Y. (2003) Apoptotic death of beta cells after optic nerve transection in adult cats. J Neurosci, 23:4023-4028.

Morimoto, T., Miyoshi, T., Matsuda, S., Fujikado, T., Tano, Y., Fukuda, Y. (2005) Transcorneal electrical stimulation rescues axotomized retinal ganglion cells by activating endogenous retinal IGF-1 system. Inv Ophthalmol Vis Sci 46:2147-2155.

Kurimoto, T., Ishii, M., Tagami, Y., Nishimura, M., Miyoshi, T., Tsukamoto, Y., Mimura, O. (2006) Xylazine promotes axonal regeneration in crushed optic nerve of adult rats. Neuroreport 17:1525-1529.

Morimoto, T., Fujikado, T., Choi, JS., Kanda, H., Miyoshi, T., Fukuda, Y., Tano, Y. (2007) Transcorneal electrical stimulation promotes the survival of photoreceptors and preserves retinal function in royal college of surgeons rats. Invest Ophthalmol Vis Sci 48:4725-4732.

Kashimoto, R., Kurimoto, T., Miyoshi, T., Okamoto, N., Tagami, Y., Oono, S., Ito, Y., Mimura, O. (2008) Cilostazol promotes survival of axotomized retinal ganglion cells in adult rats. Neuroscience Lett 436(2):116-119.
Oono S, Kurimoto T, Nakazawa T, Miyoshi T, Okamoto N, Kashimoto R, Tagami Y, Ito Y, Mimura, O. (2009) Pyroglutamic acid promotes survival of retinal ganglion cells after optic nerve injury. Curr Eye Res 34(7):598-605.
Tagami, Y., Kurimoto, T., Miyoshi, T., Morimoto, T., Sawai, H., Mimura, O. (2009) Axonal regeneration induced by repetitive electrical stimulation of crushed optic nerve in adult rats. Jpn J Ophthalmol 53(3) 257-266.
Morimoto, T., Miyoshi, T., Sawai, H., Fujikado, T. (2010) Optimal parameters of transcorneal electrical stimulation (TES) to be neuroprotective of axotomized RGCs in adult rats. Exp Eye Res 90:285-291.

3. Evaluation of visual properties of normal and genetically modified animals

The nature of visual system neurons in normal and various genetically modified animals has been investigated using electrophysiological techniques. In cats, it was found that the relay cells in the lateral geniculate nucleus receive projection from more retinal ganglion cells than previously thought (Suematsu et al., 2013). Electrophysiological responses of the visual center were also assessed in genetically modified mice (Masu et al., 1995; Sato et al. 2008).

Masu, M., Iwakabe, H., Tagawa, Y., Miyoshi, T., Yamashita, M., Fukuda, Y., Sasaki, H., Hiroi, K., Nakamura, Y., Shigemoto, R., Takada, M., Nakamura, K., Nakao, K., Katsuki, M., Nakanishi, S. (1995) Specific deficit of the ON response in visual transmission by targeted disruption of the mGluR6 gene. Cell 80: 757-765.
Sato, S., Omori, Y., Katoh, K., Kondo, M., Kanagawa, M., Miyata, K., Funabiki, K., Koyasu, T., Kajimura, N., Miyoshi, T., Sawai, H., Kobayashi, K., Tani, A., Toda, T., Usukura, J., Tano, Y., Fujikado, T., Furukawa, T. (2008) Pikachurin, a dystroglycan ligand, is essential for photoreceptor ribbon synapse formation. Nat Neurosci 11(8): 923-931.
Suematsu N., Naito T., Miyoshi T., Sawai H., Sato H. (2013) Spatiotemporal receptive field structures in retinogeniculate connections of cat. Front Syst Neurosci 7:103.

Bibliography (main 50 papers):

Original Papers

1. Masu, M., Iwakabe, H., Tagawa, Y., **Miyoshi, T.**, Yamashita, M., Fukuda, Y., Sasaki, H., Hiroi, K., Nakamura, Y., Shigemoto, R., Takada, M., Nakamura, K., Nakao, K., Katsuki, M., Nakanishi, S. (1995) Specific deficit of the ON response in visual transmission by targeted disruption of the mGluR6 gene. Cell 80: 757-765.
2. Fukuda, Y., Watanabe, M., Sawai, H. and **Miyoshi, T**. (1998) Functional recovery of vision in regenerated optic nerve fibers. Vision Res 38:1545-1553.
3. **Miyoshi, T**., Watanabe, M., Sawai, H., Rasminsky, M., Sugioka, M., Ohde, H. and Fukuda, Y. (1999) Receptive field properties of adult cat's retinal ganglion cells with regenerated axons. Exp Brain Res 124:383-390.
4. Takao, M., Wang, Y., **Miyoshi, T.**, Fujita, I. and Fukuda Y. (2000) A new intraretinal recording system with multiple-barreled electrodes for pharmacological studies on cat retinal ganglion cells. J Neurosci Methods 97:87-92.
5. Takao, M., Morigiwa, K., Sasaki, H., **Miyoshi, T**., Shima, T., Nakanishi, S., Nagai, K. and Fukuda, Y. (2000) Impaired behavioral suppression by light in metabotropic glutamate receptor subtype 6-deficient mice. Neuroscience 97:779-787.
6. Morimoto, T., **Miyoshi, T.**, Fujikado, T., Tano, Y. and Fukuda, Y. (2002) Electrical stimulation enhances the survival of axotomized retinal ganglion cells in vivo. Neuroreport, 13(2): 227-230.
7. Takao, M., **Miyoshi, T.**, Watanabe, M. and Fukuda, Y. (2002) Changes in visual response properties of cat retinal ganglion cells within two weeks after axotomy. Exp Neurol 177:171-182.
8. Kurimoto, T., **Miyoshi, T.**, Suzuki, A., Yakura, T., Watanabe, M., Mimura, O. and Fukuda, Y. (2003) Apoptotic death of beta cells after optic nerve transection in adult cats. J Neurosci 23:4023-4028.

9. Morimoto T., **Miyoshi T.**, Matsuda S., Fujikado T., Tano Y., Fukuda Y. (2005) Transcorneal electrical stimulation rescues axotomized retinal ganglion cells by activating endogenous retinal IGF-1 system. Invest Ophthalmol Vis Sci 46:2147-2155.
10. Kurimoto, T., Ishii, M., Tagami, Y., Nishimura, M., **Miyoshi, T.**, Tsukamoto, Y., Mimura, O. (2006) Xylazine promotes axonal regeneration in crushed optic nerve of adult rats. Neuroreport 17:1525-1529.
11. Morimoto, T., Fujikado, T., Choi, JS., Kanda, H., **Miyoshi, T.**, Fukuda, Y., Tano, Y. (2007) Transcorneal electrical stimulation promotes the survival of photoreceptors and preserves retinal function in royal college of surgeons rats. Invest Ophthalmol Vis Sci 48:4725-4732.
12. Okawa, Y., Fujikado, T., **Miyoshi, T**., Sawai, H., Kusaka, S., Mihashi, T., Hirohara, Y., Tano, Y. (2007) Optical imaging to evaluate retinal activation by electrical currents using suprachoroidal-transretinal stimulation. Invest Ophthalmol Vis Sci 48: 4777-4784.
13. Kashimoto, R., Kurimoto, T., **Miyoshi, T.**, Okamoto, N., Tagami, Y., Oono, S., Ito, Y., Mimura, O. (2008) Cilostazol promotes survival of axotomized retinal ganglion cells in adult rats. Neuroscience Lett 436(2):116-119.
14. Sato, S., Omori, Y., Katoh, K., Kondo, M., Kanagawa, M., Miyata, K., Funabiki, K., Koyasu, T., Kajimura, N., **Miyoshi, T.**, Sawai, H., Kobayashi, K., Tani, A., Toda, T., Usukura, J., Tano, Y., Fujikado, T., Furukawa, T. (2008) Pikachurin, a dystroglycan ligand, is essential for photoreceptor ribbon synapse formation. Nat Neurosci 11(8): 923-931.
15. Tagami, Y., Kurimoto, T., **Miyoshi, T.**, Morimoto, T., Sawai, H., Mimura, O. (2009) Axonal regeneration induced by repetitive electrical stimulation of crushed optic nerve in adult rats. Jpn J Ophthalmol 53(3) 257-266.
16. Oono, S., Kurimoto, T., Nakazawa, T., **Miyoshi, T.**, Okamoto, N., Kashimoto, R., Tagami, Y., Ito, Y., Mimura, O. (2009) Pyroglutamic acid promotes survival of retinal ganglion cells after optic nerve injury. Curr Eye Res 34(7):598-605.
17. Morimoto, T., **Miyoshi, T.**, Sawai, H., Fujikado, T. (2010) Optimal parameters of transcorneal electrical stimulation (TES) to be neuroprotective of axotomized RGCs in adult rats. Exp Eye Res 90:285-291.
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19. Fujikado, T., Kamei, M., Sakaguchi, H., Kanda, H., Morimoto, T., Ikuno, Y., Nishida, K., Kishima, H., Maruo, T., Sawai, H., **Miyoshi, T.**, Osaka, K., Ozawa, M. (2012) Clinical trial of chronic implantation of suprachoroidal-transretinal stimulation system for retinal prosthesis. Sensors and Materials 24(4): 181-187.
20. Tamura, S., **Miyoshi, T.**, Sawai, H., Mizuno-Matsumoto, Y. (2012) Random bin for analyzing neuron spike trains. Comput Intell Neurosci 2012:153496.
21. Nishitani, Y., Hosokawa, C., Mizuno-Matsumoto, Y., **Miyoshi, T.**, Sawai, H., Tamura, S. (2012) Detection of m-sequences from spike sequence in neuronal networks. Comput Intell Neurosci 2012:862579.
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23. Suematsu N., Naito T., **Miyoshi T.**, Sawai H., Sato H. (2013) Spatiotemporal receptive field structures in retinogeniculate connections of cat. Front Syst Neurosci 7:103.
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26. Kanda, H., Mihashi, T., **Miyoshi, T.**, Hirohara, Y., Morimoto, T., Terasawa, Y., Fujikado, T. (2014) Evaluation of electrochemically treated bulk electrodes for a retinal prosthesis by examination of retinal intrinsic signals in cats. Jpn J Ophthalmol 58(4): 309-319.
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30. Hirota, M., Kanda, H., Endo, T., Lohmann, T. K., **Miyoshi, T.**, Morimoto, T., Fujikado, T. (2016) Relationship between reading performance and saccadic disconjugacy in patients with convergence insufficiency type intermittent exotropia. Jpn J Ophthalmol 60(4):326-32.
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43. Nishitani, Y., Hosokawa, C., Mizuno-Matsumoto, Y., **Miyoshi, T.**, Tamura, S. (2019) Learning process for identifying different types of communication via repetitive stimulation: Feasibility study in a cultured neuronal network. AIMS Neuroscience 6(4): 240-249.
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Book Chapters

1. **Miyoshi, T.**, Kurimoto, T. and Fukuda, Y. (2006) Attempts to restore visual function after optic nerve damage in adult mammals. in Brain Repair, Springer. pp 133-147.