Department of Neuroscience
Division of Neuropathology

Satoshi Kurihara, *Professor and Director*
Junko Fujigasaki, *Assistant Professor*
Takahiro Fukuda, *Assistant Professor*

General Summary

Our research projects have concerned neurodegenerative disorders caused by intracellular accumulation of abnormal proteins. We are also studying mouse models of neurodegenerative disorders and autopsy cases by means of standard morphologic analysis and molecular biological analysis.

Research Activities

Tumor markers in pineal parenchymal cell tumor

Pineal parenchymal tumor (PPT) cells usually show immunoreactivity for synaptophysin, neuron-specific enolase, neurofilament protein, class III β-tubulin, tau protein, protein gene product 3.5, chromogranin, serotonin, retinal S-antigen, and rhodopsin. These markers, however, are not specific for PPTs. Melatonin is produced and secreted mainly by the pineal parenchymal cells.

Hydroxyindol-O-methyltransferase (HIOMT) catalyzes the final reaction in melatonin biosynthesis. We hypothesized that HIOMT could serve as a marker of PPTs. We investigated HIOMT localization in humans and HIOMT expression in PPTs, primitive neuroectodermal tumors, and medulloblastomas. In human tissue, HIOMT was expressed in retinal cells, pineal parenchymal cells, neurons of the Edinger-Westphal nucleus, microglia, macrophages, thyroid follicular epithelium, principal and oxyphil cells of the parathyroid gland, adrenal cortical cells, hepatic parenchymal cells, renal tubule epithelial cells, and enteroendocrine cells of stomach and duodenum. HIOMT was expressed in all PPTs studied. The ratio of HIOMT-immunoreactive cells successively decreased in the following tumors: pineocytoma, pineocytomatous areas of PPTs with intermediate differentiation (PPTIDs), pineoblastomatous areas of PPTIDs, and pineoblastomas. In 1 of 3 primitive neuroectodermal tumors and 4 of 8 medulloblastomas, a few HIOMT-immunoreactive cells were observed. Immunohistochemical analysis of HIOMT is useful for diagnosing PPTs, and HIOMT may be a prognostic factor in patients with PPTs.

Expression array analysis of a spinocerebellar ataxia type 7 cell model

Spinocerebellar ataxia type 7 (SCA7) is a polyglutamine disease caused by polyglutamine expansion within a causative protein, ataxin-7. SCA7 is characterized by specific degeneration of cerebellar, brainstem, and retinal neurons. Recent evidence suggests that ataxin-7 regulates transcription and that aberrant regulation of transcription is involved in the pathogenesis of SCA7, yet additional studies are be needed to clarify

the pathogenesis of SCA7. We developed a PC12 inducible cell line expressing mutated ataxin-7 (ataxin-7-Q100). In this cell line, expression of the mutated ataxin-7 is regulated by the presence of tetracycline in the culture medium. Expression array analysis of the cell line was performed to compare gene expression levels between the cells with and without induction of the mutated ataxin-7. Approximately 40,000 genes were analyzed: of these genes. 600 showed increased expression with induction of the mutated ataxin-7, and 300 genes showed decreased expression. Suppression of several retinal specific genes was identified, indicating that the fluctuating expression of these genes might be involved in the retinal pathology of SCA7.

Publications

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Akiyama N, Ohno Y, Fukuda T, Manome Y, Saito S. Enhancing activity of N-glycosylation for constitutive proteins secretions in non-polarized cells. *Biochem Biophys Res Comm* 2009; **381:** 612–8.

Arai T, Takahashi-Fujigasaki J, Joki T, Nagashima H, Ichiba N, Kawakami M, Abe T. Volumetric analysis of a rhabdoid meningioma during preoperative follow-up: a case report. *Acta Neurol Belg* 2008; **108:** 112–5.

Reviews and Books

Takahashi H, Hano H, Shiraishi T, Fukuda K, Fukuda T, et al. (Translation) Robbins and Cotran Atlas of Pathology. In: Klatt EC, ed. Tokyo: Elsevier Japan; 2009. p. 447–6.