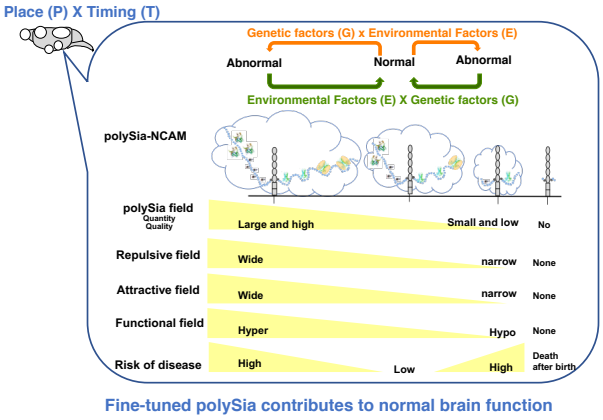
Principal Investigator: Chihiro SATO

Grant Title: Effects of environmental factors on the expression of polysialic acid in brain

Abstract

Schizophrenia, bipolar disorder, autism spectrum disorder and major depression are well-known mental disorders. To understand and treat these diseases, it is important to focus on disease-related molecules that are known to be ubiquitous in the brain and to be particularly altered in mental disorders. The polysialic acid (polySia/PSA) chain, which specifically modifies the neuronal cell adhesion molecule (NCAM) protein, is known to be aberrantly expressed in mental disorders. So far, I studied the relationship between the polySia chain and mental disorders, performing pioneering biochemical analysis of disease-related SNPs of the polySia synthase ST8SIA2 gene and found that all the disease-related SNPs finally lead to the impairments of structures and functions of polySia (Sato and Hane 2018; Sato and Kitajima 2019).

As it is important to consider both genetic factors and environmental factors to clarify the causes of mental disorders, I focused on the effects of environmental factors on polySia expression in brain in this research. I adopted the tail suspension test that exposed mice to acute stress as a negative environmental factor. We also adopted the enriched environment as a positive environmental factor. We analyzed the polySia expression in five brain regions, olfactory bulb, prefrontal cortex, amygdala, hypothalamus, and hippocampus, by the immunochemical and chemical analyses. Finally, we found that a 7-min acute stress led to alterations of the polySia expression brain region-specifically. In olfactory bulb and prefrontal cortex, the polySia expression was decreased. On the other hand, the enriched environment led to the increased expression of polySia in the same regions. The mechanism of the decrease of polySia by acute stress was shown to relate with sialidase from microglia or astrocyte (Abe et al. 2019). Therefore, I can conclude that not only genetic factors but also environmental factors affect the brain region-specific polySia expression.



Fine-tuned polySia contributes to normal brain function

Our reaserch clearly demonstrtates that polySia is expressed in an appropriate time (T) and at appropriate cell types of an appropriate brain region (P), and that the expression of polySia can thus be defined by the T and P parapmeters. We could actually determine the T and P parameters under the normal state. Once normal polySia structures were impaired by genetic (G) and/or environmental factors (E), the T and P parameters changed to the abnormal ones. Thus, it is indicated that we would be able to understand the state of brain by monitoring the T and P parameters for polySia. In addition, if we could succeed in monitoring the T and P parameters invasively, we might find out apprioriate G x E factors to lower the risk of disease using these parameters. In this regard, we are now investigating such GREEN factors other than RED factors for medical application purposes (Sato 2019).

Ref.(1)Abe C, Yi Y, Hane M, Kitajima K, Sato C. (2019) Acute stress-induced change in polysialic acid levels mediated by sialidase in mouse brain. Sci Rep. 9, 9950; (2) Sato C, Kitajima K. (2019) Sialic acids in neurology. Adv Carbohydr Chem Biochem. 76, 1-64; (3) Sato C. (2019) polysialic acids. Trends Glycosci Glycotech. 31, E1-E3.