



Project Leader **Kazunori Sango** Diabetic Neuropathy Project

Pathogenesis-based Therapeutic Approaches to Diabetic Neuropathy

Peripheral neuropathy is one of the most common complications of Diabetes Mellitus, and its irritating symptoms such as pain and numbness can be the cause of insomnia and depression, and when allowed to progress to more advanced disease stages can result in serious consequences such as lower limb amputation and lethal arrhythmia. In addition, recent studies have indicated that diabetes is a major risk factor for cognitive disorders such as Alzheimer's disease.

Takaku S, Yako H, Niimi N, Akamine T, Kawanami D, Utsunomiya K, and Sango K. (2018) "Establishment of a myelinating co-culture system with a motor neuron-like cell line NSC-34 and an adult rat Schwann cell line IFRS1." *Histochem. Cell Biol.* 149: 537-543.

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Sango K, Mizukami H, Horie H, and Yagihashi S. (2017) "Impaired axonal regeneration in diabetes. Perspective on the underlying mechanism from in vivo and in vitro experimental studies." *Front. Endocrinol.* 8: 12.

Niimi N, Yako H, Tsukamoto M, Takaku S, Yamauchi J, Kawakami E, Yanagisawa H, Watabe K, Utsunomiya K, and Sango K. (2016) "Involvement of oxidative stress and impaired lysosomal degradation in amiodarone-induced schwannopathy." *Eur. J. Neurosci.* 44: 1723-1733.



"We are trying to improve QOL for diabetics and help them to live longer lives by elucidating the pathogenesis of neurological disorders and establishing effective treatments."



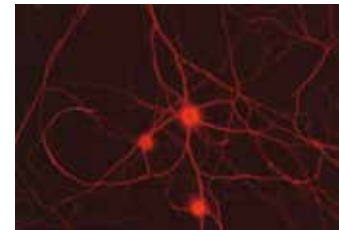
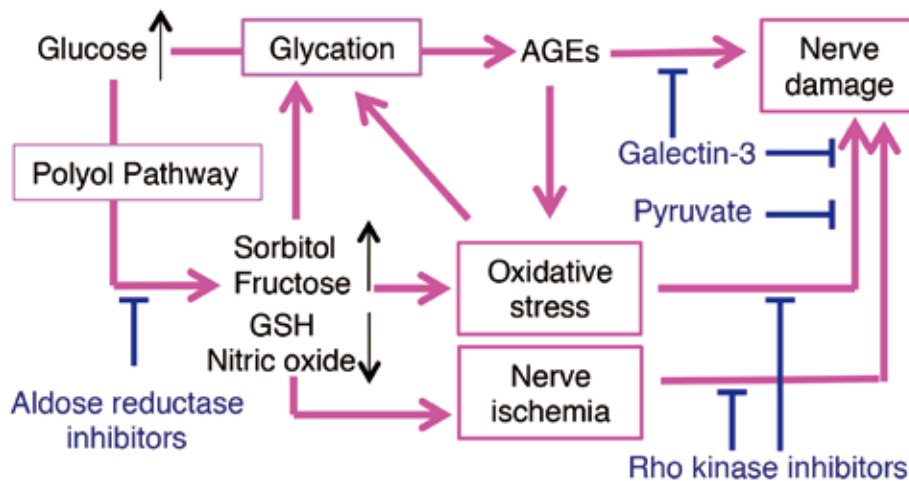
The goals of our project are as follows: 1) Establishing effective pathogenesis-based treatments for diabetic peripheral neuropathy. 2) Elucidating mechanistic link between metabolic dysfunction and neurodegenerative diseases.



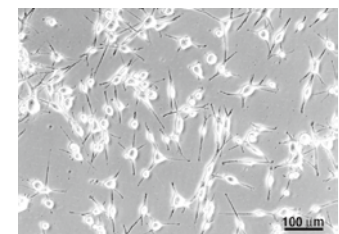
Diabetic Neuropathy

Project 1: Therapeutic Approaches to Diabetic *Peripheral Neuropathy* [Sango, Yako, Niimi, Takaku, Akamine]

Metabolic disorders and vascular abnormalities caused by hyperglycemia appear to be closely related to the development and progression of diabetic peripheral neuropathy. Using diabetic model animals and culture systems of adult rodent **dorsal root ganglion (DRG) neurons** and **immortalized Schwann cells**, we seek to establish effective pathogenesis-based treatments for peripheral neuropathy.



Adult rat DRG neurons



Immortalized mouse Schwann cells IMS32

Project 2: Mechanistic link between *Metabolic dysfunction* and *Neurodegenerative Diseases* [Suzuki, Oba]

Neurodegenerative diseases are considered to share a common molecular pathogenesis involving protein misfolding and aggregation. Recently, increasing evidence suggests a relationship between metabolic syndrome and Alzheimer's disease. By using *Drosophila* model, we aim to understand the molecular mechanism by which metabolic condition influences misfolding protein-induced neurodegeneration.

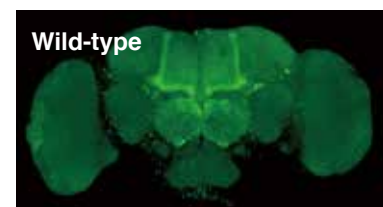


High-nutrient diet

Nutrient-restricted diet

Drosophila models of neurodegenerative diseases

- Alzheimer's
- Parkinson's
- Polyglutamine
- ALS etc...



Protein aggregation (brain)

Diabetic Neuropathy