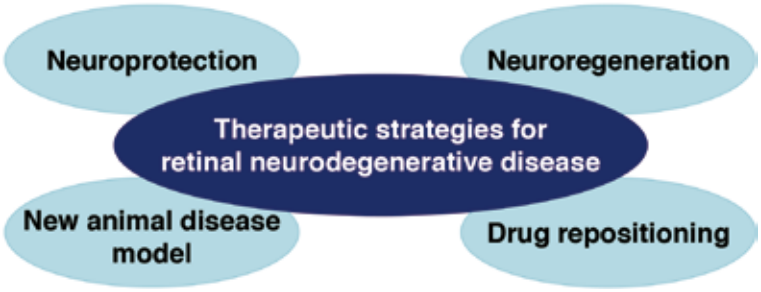
Project Leader **Takayuki Harada** Visual Research Project

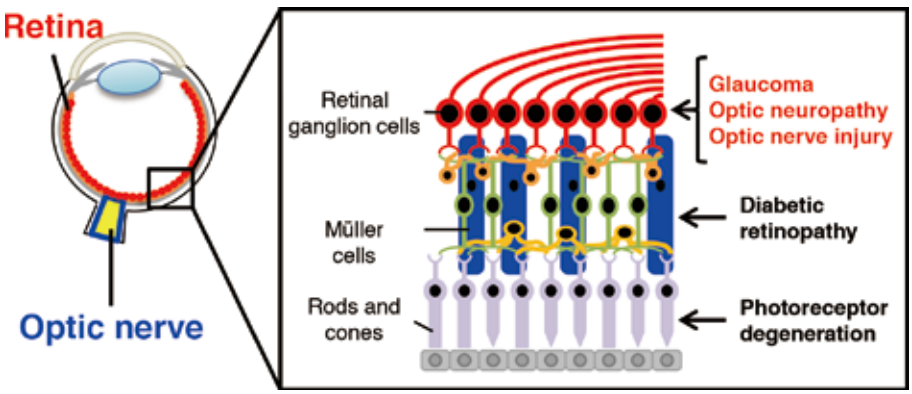
Elucidation of Pathology and Development of Therapeutic Strategies for Retinal Neurodegenerative Diseases

More than 1.6 million people in Japan are visually impaired, representing economic social losses estimated at more than 8 trillion yen. In the particular context of the increased penetration of Western lifestyles and an aging society, the increase in the number of patients with conditions such as glaucoma and diabetic retinopathy, which could be called “adult eye diseases,” has become a major social issue.
To achieve improved quality of life (QOL) for the visually impaired in an increasingly aging population, we seek to elucidate detailed pathogenic mechanisms and develop new therapies through the development of a model of intractable eye disease.

Our objectives

“We are focusing on elucidating the molecular mechanisms of neuroprotection and neuroregeneration, and our final goal is the prevention or treatment of blindness in retinal neurodegenerative disorders such as glaucoma and traumatic injury.”





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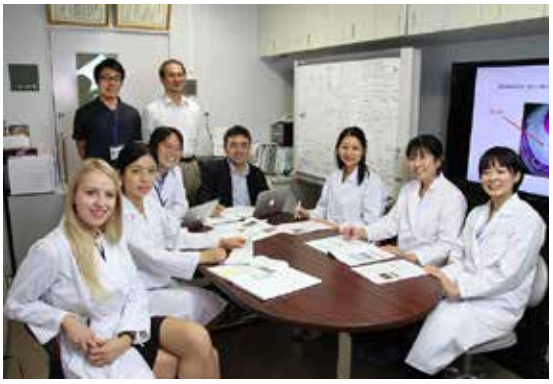
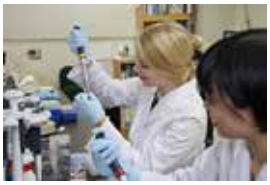
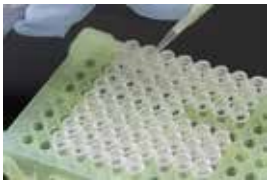
Our major aim

- **To develop a neuroprotective retinal therapy using animal disease models**
- **To elucidate the mechanisms involved in the onset of optic neuritis**
- **To establish a method to promote regeneration of the optic nerve**



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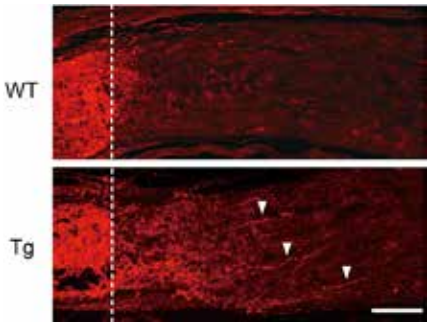
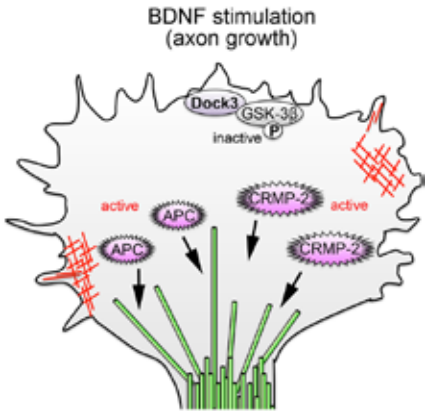
Senior Research Scientist **Kazuhiko Namekata**

Dock family proteins

The dedicator of cytokinesis (Dock) family is composed of atypical guanine exchange factors (GEFs) that induce actin polymerization. To date, 11 Dock family members have been identified. Dock3 is predominantly expressed in the central nervous system. In the growth cone, Dock3 induces actin polymerization by activating WASP family verprolin-homologous protein (WAVE) and modulates microtubule dynamics through inactivation of GSK-3β, leading to axon elongation. In addition, Dock3 plays a role in protecting retinal ganglion cells from neurotoxicity and oxidative stress. Dock3 may be a therapeutic target for optic neuropathy including glaucoma.



Axonal regeneration was enhanced in Dock3 overexpressing mouse (Tg) (Arrow heads indicate regenerating axons)



Visual Research