

Singapore scientists develop zebrafish model for studying Parkinson's Disease

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Scientists at the Genome Institute of Singapore (GIS), a biomedical research institute of the Agency for Science, Technology and Research (A*STAR), have recently developed a zebrafish model for Parkinson's disease that can be used for understanding the mechanism underlying its development. The knowledge gained will be helpful for future screening of new drugs to treat Parkinson's disease (PD).

This study describes the first zebrafish model for LRRK2 mutation-related PD. It is able to overcome some limitations of other animal models of LRRK2 and demonstrates that zebrafish, a tropical freshwater fish that can often be found in aquariums, can be used to study the development of human diseases. Led by GIS Group Leader Dr Liu Jianjun, the finding was published in [PLoS Genetics](#) on April 22, 2010.

To explore the biological functions of LRRK2, the scientists studied this gene in zebrafish by blocking its normal function. This resulted in Parkinsonism-like [phenotypes](#) in zebrafish, including locomotive defects and loss of neurons, similar to those of PD patients. It was found from the study that the defects of the fish can be rescued by expressing the normal protein of LRRK2. Significantly, the administration of Levodopa (L-dopa), a compound that is widely used to treat PD, can also rescue the locomotive defects caused by the modification of the zebrafish LRRK2 protein.

[Parkinson's disease](#) (PD) is a [degenerative disease](#) of the brain that often impairs motor skills, speech and other functions. The discovery of

several gene mutations in affected patients clearly demonstrated the involvement of [genetic factors](#) in the development of PD. LRRK2 was discovered from previous studies by the same team of researchers to be one of the most important genetic causes of PD in the Asian population.

"This work shows how the use of a simple model system in fish can help decipher the root causes of a serious human disorder like Parkinson's disease, " said Professor Edison Liu, Executive Director of the GIS.

Dr Lim Kah Leong, Associate Professor of the National Neuroscience Institute and Duke-NUS Graduate Medical School, added "This novel and elegant study has illuminated the role of an otherwise poorly understood but important domain of LRRK2 that is associated with an increased risk for Parkinson's disease amongst Asian populations. The use of zebrafish as a disease model is a clever approach. I am definitely pleased to note that our arsenal of experimental organisms for drug screening has expanded with this study."

The zebrafish model derived from this study serves as a vertebrate model suitable for large-scale drug screening and provides a good disease model for PD. Using a novel technology known as the Zinc-finger nucleases (ZFNs), further research is being carried out to generate additional mutations of zebrafish LRRK2 gene. Such mutated zebrafishes can be used for advancing investigation for the biological mechanism of PD and screening of new drugs for PD treatment.

More information: The research findings can be found in the April 22, 2010 print issue of PLoS GENETICS under the title "Deletion of the WD40 Domain of LRRK2 in Zebrafish Causes Parkinsonism-Like Loss of Neurons and Locomotive Defect".

Provided by Agency for Science, Technology and Research (A*STAR)

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