Teleost fish models of Parkinson's disease

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We have created various Parkinson's disease models using medaka and zebrafish. These small teleost fish of course belong to vertebrates and share similar anatomy of the nervous system with us human. In medaka, various toxins including MPTP, 6-OHDA, proteasome-inhibitors, and lysosome-inhibitor induced reduction of spontaneous swimming and dopamine/noradrenaline neurodegeneration and some of them also disclosed inclusion bodies. Particularly, the dopamine cluster in the middle diencephalon was always vulnerable to these toxins.

We also reported various genetic models using medaka and zebrafish. ATP13A2 mutant medaka showed Cathepsin D reduction, finger-print like inclusions and dopamine/noradrenaline neurodegeneration. GBA KO medaka showed alpha-synuclein positive inclusions but the neurodegeneration was independent of alpha-synuclein accumulation. PINK1 KO phenotype was different among medaka and zebrafish, the former did not show neurodegeneration and the latter showed marked dopamine/noradrenaline neurodegeneration. In medaka PINK1 KO, additional depletion of Parkin caused Parkinson's disease phenotype. Again the dopamine cluster in the middle diencephalon was always vulnerable in these genetic models. Recent study showed that ablation of the dopamine neurons in this middle diencephalon cluster reduces spontaneous locomotion indicating this cluster might correspond to human nigral dopamine neurons.

In this symposium, we also introduce Africa medaka as a naturally occurring Parkinson fish. Then we will discuss about the pathological mechanisms of Parkinson's disease based on these fish models.