GS03-3 **Therapeutic effects of fatty acid-binding protein ligands in Parkinson's disease mice**

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[Background] Aggregation of α-synuclein (αS) is facilitated in the presence of polyunsaturated fatty acids such as arachidonic acid (AA). AA is intracellularly transported by fatty acid-binding protein 3 (FABP3). We previously reported that FABP3 overexpression aggravates αS oligomerization in the presence of AA. In this concept, we focused on the involvement of FABP3 in αS pathology and synthesized novel FABP3 inhibitory ligands.

[Methods] Mice were injected with 1-methyl-1,2,3,6-tetrahydropiridine (MPTP) and followed by chronic administration of MF1 (high affinity for FABP3), MF3 (low affinity for FABP3), or L-DOPA.

[Results] Chronic administration of oral MF1 improved motor impairments as well as L-DOPA seen in MPTP-treated mice. MPTP treatment induced αS accumulation in dopaminergic cell bodies and neuronal loss in the substantia nigra. While MF1 administration suppressed these neuropathologies, MF3 or L-DOPA treatment failed to do. Finally, MF1 administration restored MPTP-induced αS oligomerization and hyperphosphorylation (S129) in the substantia nigra.

[Conclusion] MF1 suppressed dopaminergic cell death unlike L-DOPA, and this effect involved restoration of αS pathology. It is suggested that novel FABP3 inhibitory ligands could be disease-modifying drugs for Parkinson's disease.