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Parkinson's Disease GLP/GCP di-22:6-BMP Biomarker Assay: Disease Screening and LRRK2 Inhibition/Efficacy Assessments

Impaired lysosomal processing is a common feature of Parkinson's disease (PD) neurodegeneration in both familial and idiopathic PD. Nextcea's patented di-22:6-BMP biomarker is a lysosomal phospholipid that increases with PD-associated endolysosomal / lysosomal dysfunction[1-5]. It's used to better assess the efficacy of potential disease modifying therapies that target PD-associated mutations (LLRK2, GBA) and lysosomal pathways.

For example, decreased urinary di-22:6-BMP is observed in LRRK2 knockout rodents and animals treated with LRRK2 inhibitors compared to controls, reflecting LRRK2 kinase activity. The timing of the response is compound and dose dependent[1,2].

Nextcea provides non-GLP and GLP LC-MS/MS assays for the quantitation of di-22:6-BMP in animal and human matrices. A true reference standard is used for sensitive, specific and accurate di-22:6-BMP quantitation. The laboratory turnaround time for 500 samples (from receipt to reporting of results) is typically within two (non-GLP) to four weeks (GLP/GCP).

Sample Requirements

Non-clinical Samples (Rats and Monkeys)

Sample Type	Collection	Sample Volumes/Weight	Storage/Shipping of Specimens
Urine	overnight urine collection in cooling cage pan	~1 mL (rodent) ~5 mL (monkey)	▪ Store in -80°C freezer. ▪ Ship frozen on dry ice.
Tissues	snap-frozen	~500 mg	
CSF		~1 mL	

Clinical Samples (Humans)

Sample Type	Collection	Sample Volumes/Weight	Storage/Shipping of Specimens
Urine	preferred mid-stream urine sample	~10 mL	▪ Store in -80°C freezer. ▪ Ship frozen on dry ice.

1 Baptista MAS, Merchant K, Bryce D, Ellis M, et al., 2015. LRRK2 kinase inhibitors of different structural classes induce abnormal accumulation of lamellar bodies in type II pneumocytes in non-human primates but are reversible and without pulmonary functional consequences. Presented at the MJFF Parkinson's Disease Therapeutic Conference; October 21, 2015.

2 Fuji RN, Flagella M, Baca M, Baptista MAS et al., 2015. Effect of selective LRRK2 kinase inhibition on nonhuman primate lung. Science Translational Medicine 7(273): 273ra15.

3 Nixon R., 2016. The lysosome in aging-related neurodegenerative diseases, in: Maxfield, F.R., Willard, J.M., Shyan, L. (Eds.), Lysosomes: Biology, Diseases, and Therapeutics. John Wiley & Sons, Inc., Hoboken, New Jersey, pp. 137-179.

4 Miranda AM, Lasiecka ZM, Xu Y, Neufeld J, et al., 2018. Neuronal lysosomal dysfunction releases exosomes harboring APP C-terminal fragments and unique lipid signatures. Nature Communications 9(1):291.

5 Manzoni C, 2017. The LRRK2–macroautophagy axis and its relevance to Parkinson's disease. Biochemical Society Transactions 45(1): 155-162.