NINDS boosts research for biomarkers in Parkinson’s disease

Research in biomarkers is thriving; pioneered by the Alzheimer’s disease community, the quest for biomarkers is now also advancing in other neurological diseases, particularly Parkinson’s disease (PD). Launched by the US National Institute of Neurological Disorders and Stroke (NINDS) on January 15, the Parkinson’s Disease Biomarkers Program (PDBP) will now join in the endeavour, adding to the great expectations surrounding this field of research. The Program is a landmark collaborative effort and reflects the strong commitment of NINDS to support progress in this field. Progress would be even faster if biomarkers discovered in PDBP could be validated also in cohorts recruited by other research initiatives.

The PDBP has three major components, which should synergistically contribute to the ultimate goal of identifying biomarkers to be used in phase 2 and 3 trials of neuroprotective therapies. First, nine cutting-edge research projects have been funded aiming at the discovery of biomarkers for diagnosis and prognosis. Second, the Repository at the Coriell Institute for Medical Research will store the biological samples collected in these research projects, and facilitate their distribution among researchers. The third element is a Data Management Resource, created to provide the bioinformatics support for each study site to record and manage all the data.

The nine research projects could change the PD biomarkers landscape. The aim is to identify novel biomarkers in CSF, blood, or urine by use of state-of-the-art screen platforms and advanced techniques, such as proteomics, analyses of genetic dark matter (ie non-coding genes) or exosomes (ie secreted vesicles), and next-generation RNA sequencing; high-resolution diffusion tensor imaging and R2* MRI will be used to track nigrostriatal pathology; clinical features, including olfaction, cognition and sleep, will be characterised in patients from early stages to advanced disease; and new statistical techniques and software will be developed to improve the analyses of data. However, although the research component is certainly ambitious, it is the third element in the Program that makes this initiative unique.

The PDBP Data Management Resource was developed with the aim to eventually serve all NINDS-funded PD researchers, not only PDBP investigators. The use of the platform is expected to be extended this year to the NINDS Udall Centers of Excellence.

NINDS is keen to coordinate efforts with other biomarkers research initiatives in the standardisation of data collection and sharing via their Data Management Resource, and in the validation of novel findings. In that respect, the ongoing Parkinson’s Progression Markers Initiative (PPMI) and the BioFIND study, both spearheaded by the Michael J Fox Foundation, are good partners for PDBP, as the three studies apply the same protocols for banking of biospecimens; nonetheless, challenges remain to be tackled for a fruitful partnership, especially to bring PDBP and PPMI together. PPMI, an international longitudinal study for the identification and clinical validation of biomarkers, was launched in 2010 and has recruited almost 400 patients with early Parkinson’s disease and about 200 controls. But the enrollment phase is close to its end, and data are already managed through a PPMI website. The collaboration between PDBP and BioFIND is underway. BioFIND is an observational study focused on clinical markers in patients at later disease stages; recruitment began in the autumn of 2012 and, unlike PPMI, BioFIND is also sponsored in part by NINDS.

Additional collaboration opportunities are expected to emerge between PDBP and some PPMI ancillary studies that are being incorporated into its study plan; for example, in August, 2012, PPMI was extended to include a prodromal cohort, defined as individuals with hyposmia, REM sleep behaviour disorder, or LRRK2 mutations, who also have a detectable dopamine transporter deficit but no motor symptoms. Recruitment has just started. This summer, another ancillary study will start recruitment of 400 LRRK2 mutation carriers. If PDBP is to be fully successful in the quest for biomarkers, the opportunity to validate findings in these cohorts should not be missed. ■ The Lancet Neurology

For more on the PDBP see http://pdbp.ninds.nih.gov/
For the Repository at Coriell see http://ccc.coriell.org/
For more on the PPMI see Editorial Lancet Neurol 2010, 9: 1139
For more on BioFIND see https://www.michaeljfox.org/page.html/biofind-clinical-study