MultiPark

Define where the Environment stands today, in 5 years and in 10 years in relation to the development of the research, and the society, on the basis of: how the forefront of research has evolved and what is needed to stay in the absolute forefront of research. - how the development of society influences the requirements of the research field to develop, including work related to sustainable development goals

Building on a long tradition of excellence in neuroscience, MultiPark is an internationally leading research environment at Lund university (LU) for multi-disciplinary studies on the common neurodegenerative diseases: Parkinson's disease, Alzheimer's disease and related brain disorders. These diseases pose a major and growing public health concern globally as the number of people afflicted soars. Already today health-related costs for neurodegenerative diseases are higher than those for cancer and cardiovascular disease combined. The most urgent, yet still unmet medical need are treatments for these diseases that slow down or stop disease progression. In Multipark we work to elucidate disease mechanisms at molecular, cellular and circuitry levels that already now provide new insights and will continue to do so, guiding the development of new therapies, such as restoration of lost brain functions based on cell- and gene-based replacement strategies. This is complemented by work to develop more accurate and refined biomarkers for early diagnosis that will allow treatments with potential disease modifying therapies, using novel precision drugs or gene editing approaches, even before disabling symptoms develop.

MultiPark's vision is to create innovative approaches for the understanding, diagnosis, treatment and eventually cures for neurodegenerative diseases. By doing so, we fulfill the dual mission of our strategic research area: to pursue scientific excellence and to benefit society at large by improving the quality of life for people living and ageing with these disorders and their families.

MultiPark was originally focused on Parkinson's disease with the idea to tackle all aspects of the disease, spanning from molecules to patient care. However, it became increasingly clear that many features of neurodegeneration - the similarity of disease-causing proteins, the overlapping pathologies and clinical symptoms, and the involvement of inflammation - are shared by other major neurodegenerative diseases, in particular Alzheimer's disease and Huntington's disease. The MultiPark network has therefore evolved significantly in order to create a dynamic research environment assembled to incorporate studies on the major age-related—neurodegenerative diseases, with research ranging from unraveling the underlying disease mechanisms, improving diagnostics, and developing efficient treatments and care.

Our main scientific goals for 2020-2025 are:

To understand the origins and progression of neurodegenerative disease - Establish and explore new disease models based on reprogrammed patient cells and new animal models that better re-capitulate disease related pathology in order to obtain state-of-the art experimental tools for mechanism-oriented studies and drug screening.

- Increase our molecular and cellular understanding of the aggregation of proteins characterizing these diseases using cutting edge methods, including intensified collaborations with MAX IV and ESS.

- Integrate pathophysiological studies, OMICS, artificial intelligence and machine learning to derive new knowledge from state of the art-experimental models and unique human cohorts to allow for better understanding of disease mechanisms and to identify factors resulting in resilience to these disease changes.

To develop early and differential diagnostics and prognostics

- Develop accurate and cost-effective diagnostics using minimally invasive methods that can be used to improve the diagnostic work-up in primary care and lower-middle income countries, as well as when screening for individuals suitable for specific interventions.

- Develop novel methods for detecting therapeutic effects of novel interventions on neurodegeneration and plasticity during both the early presymptomatic and the later manifest stages of the diseases.

- Improve methodologies for quantitative monitoring of neurological, cognitive and psychiatric deficits and symptoms, which can be used to improve the evaluation of interventions in symptomatic patients in both clinical routine practice and clinical trials.

To create new therapeutic approaches for prevention, disease modification and management of unmet medical needs

- Continuously support, develop and run state-of-the-art facilities for studies of disease mechanisms, plasticity and repair; exploration of novel disease modifying therapeutic interventions; and the creation of new cellular and animal models that better reflect human disease.

- Improve our ability to conduct clinical trials by supporting important infrastructure and develop more refined methods to evaluate relevant target engagement of novel disease-modifying drugs in the human brain.

- Establish novel therapeutic approaches for developing more effective symptomatic, new disease modifying and/or plasticity-enhancing treatments.

- To establish a strong translational platform for rapidly moving scientific discoveries, including Advanced Therapy Medicinal Products (ATMPs), into pioneering clinical trials.

A major strength of MultiPark *today* is that it spans from internationally leading pre-clinical research to translational and multidisciplinary clinical research across the spectrum of the main neurodegenerative diseases. With our combined experimental, translational, clinical and health science expertise we are well positioned for a strong future of progress in the coming decade. However, the technology advances in neuroscience research globally are moving at an unprecedented speed. To stay in the forefront of these rapid developments and capture their potential to transform tomorrow's therapies and diagnostics creates new challenges and demands for constant renewal of strategies and advanced infrastructures in our environment. Our *new* strategic plan for 2020-2025 is designed to ensure that our already strong environment is equipped to meet these

demands, maintain international leadership in our field, and accelerate the translation of new discoveries to patient care.

Define measurements ("measures" a better term) taken to maintain and strengthen the research environment at the forefront of research, including new demarcations/boundaries or collaborations

Our goal is to act strategically and in a target-oriented manner to continuously implement new technologies and concepts. Not only will this increase the impact of our research today, it will also ensure that our strong neuroscience environment remains at the international forefront in the future. To develop innovative approaches to therapy and patient-centered care, we will systematically promote a bidirectional exchange between experimental and clinical/health care research at all possible levels.

Environment

The widening of MultiPark in our prior Strategic plan 2014-2019 to include all major age-related neurodegenerative diseases, including Alzheimer's, Parkinson's and Huntington's diseases, has significantly increased the scope of our network. A focus for the coming 5-year period will be to promote increased transfer of methods and knowledge across traditional disease boundaries and organisatiorial structures to further strengthen our environment and provide new perspectives.

Research interactions within LU. A long-term goal of MultiPark is to provide a more comprehensive and centralized environment for research on neurodegenerative diseases with increased physical links in our organization, which spans four departments of the faculty of medicine and several other faculties including natural science, engineering, social sciences and humanities.

Research interactions within Region Skåne. Several Multipark members are active physicians in Region Skåne and Skåne University Hospital. Within our research projects patients are recruited, assessed and treated at the Departments of Neurology, Memory disorders and Neurosurgery. State of the art brain imaging is performed in facilities organized by the hospital. We plan to expand this close collaboration to accelerate implementation of novel diagnostics and treatments into clinical practice and to facilitate bilateral translational research projects.

Research interactions with industry. A major goal of Multipark is to develop and implement therapeutic products around the world. This requires extensive collaboration with the major industrial parties involved in brain diseases. Consequently, MultiPark plans to actively strengthen strategic collaborations with industrial partners to achieve these goals.

Outreach activities. MultiPark's success also depends on effective interactions and communication with patient organizations and the community at large. We will strengthen these interactions by recruiting a communicator/liason manager.

Research training and career development. MultiPark runs a lecture series called Frontiers in Neuroscience, where internationally leading researchers are invited to give seminars at LU. We will continue to use this program to foster international contacts, promote new collaborations, and strengthen our links to leading centers in our field. PhD students and postdocs receive travel grants from MultiPark to present their work at conferences and subsequently at our local noontime seminars. By these efforts we ensure that our network remains a

vibrant, creative and dynamic research environment that fosters a new generation of excellent scientists and leaders.

Infrastructure

MultiPark has established a number of experimental and clinical platforms that are essential for our research. These platforms are widely used and of particular value to young group leaders who are in the process of developing their own research programs. To stay in the forefront of research we need to implement new transformative methods and advanced diagnostic tools. For our environment it is essential to not only maintain but to update and extend our infrastructures, which will be a main focus in the coming 5 years:

- *Technical platforms:* Today MultiPark supports a number of important state-of-the-art technical platforms and infrastructures for e.g. experimental animal models, virus production, advanced imaging and molecular analysis, which are essential to maintain and develop.
- *Clinical infrastructures:* MultiPark supports biobanks (DNA, plasma, serum, and CSF; brain tissue from large cohorts of patients at different disease stages with matched controls), platforms with experienced research staff trained in Good Clinical Practice (GCP), who perform clinical assessments, positron emission tomography (PET) imaging, including development of novel radiotracers for detection of Parkinson- and Alzheimer-related pathologies, and processing of ultrahigh field magnetic resonance imaging (MRI).
- *Translational platform:* Our vision is that MultiPark will act as a critical bridge and close the gap between excellent preclinical research and the validation and implementation of new therapies within our SFO. This will be achieved by actively promoting necessary competences and facilities needed to undertake clinical trials. MultiPark will work in collaboration with other relevant SFOs and the newly established Wallenberg Center for Molecular Medicine (WCMM) and coordinate efforts with health care (SUS/RS/MV) .
- *Maintain academic excellence.* MultiPark creates and supports programs designed to encourage the development and recruitment of a new generation of research leaders. We will establish a scientific advisory board (SAB) of internationally leading researchers. The support and recruitment of young internationally prominent researchers has been important to maintain our international standing and is facilitated by an attractive environment with shared technical platforms.

How the environment will strengthen education

The Lund Graduate School of Neuroscience was created, maintained and organized by MultiPark and is pivotal in providing interactions between students and young researchers in our environment. While primarily geared to PhD students, it also incorporates our postdocs. Travel awards are used for our PhD students and postdocs to present their work at noontime seminars, where they discuss their ongoing research with their local peers. This is widely seen as successful glue to strengthen interactions in our environment. Our goal is to further increase such research discussions, also at the PI level via e.g. roundtable discussions and PI seminars. This will strengthen academic discourse and exchange in our environment. A future aim for MultiPark is to contribute more to undergraduate and masters education in neuroscience. Given the large expertise

in our environment, we could further positively contribute to education at all levels at LU. MultiPark also supports national, Scandinavian and European educational efforts on neurodegenerative diseases for clinicians and the public.

How the environment will cooperate with other SFOs, other faculties, other universities and social actors

MultiPark partners with other SFOs at different levels. While most links have been with SFOs in our medical faculty, bridges towards SFOs at other LU faculties, including Natural Sciences, LTH and Humanities and Social science, are growing. MultiPark also has close ties with newly formed research centres jointly supported by LU and RegionSkåne, in particular, the Stroke Centre, the Huntington Centre, the Neuronanomedicine Centre and the Wallenberg Center for Molecular Medicine. For large infrastructure investments we will increasingly collaborate with other strategic research areas, including WCMM, Lund Bioimaging Centre and MAX IV. Further, MultiPark has close collaborations with patient organizations such as Svenska Parkinsonförbundet, Alzheimer Sverige, and the Huntington Disease Centre. We contribute and have co-organized Parkinson's days where patients and patient´s families visit our facilities to interact with our researchers. MultiPark hosts the national Parkinson research network SWEPARs headquartered at LU and the Swedish national Parkinson Patient Registry, ParkReg (presently 7400 registered patients).

How the environment works with equality diversity and inclusion perspective

MultiPark is fully committed to creating equality of opportunity and promoting diversity and inclusivity at all levels of our network. Already, the network includes men and women at all career levels. We will continue the work for gender equality and diversity by paying specific attention to ensuring that our female scientists become more visible in leadership and management, actively work for a growing international representation and monitor that e.g. our seminar speakers reflect diversity in science.

What are the needs for research infrastructure

Modern and up-to-date infrastructures are essential for a thriving and dynamic research environment. Our SFO works to strengthen infrastructures in a strategic manner to promote cutting-edge research output for our researchers. MultiPark-supported infrastructures are also open to research groups external to MultiPark, who can access high-end equipment and lab facilities and contribute to a dynamic exchange of scientific ideas. Collaboration with health services are essential, and will be improved further, in order to pursue world-leading and cost-effective translational and clinical research.

What support the Environment needs from the University- and Faculty management in order to achieve its goals, for example in terms of recruitments.

MultiPark benefits from organizational structures and administrative support that allow for optimal progress for our researchers to succeed in their research, education, innovation and outreach work, with which LU and our faculty can provide major help. MultiPark is helped by visibility within LU and to the outside research world and society as a whole. In this regard, high-level, up-to-date and user-friendly websites that promote our environment internationally and externally are very helpful.