PepGen joins forces with researchers to tackle brain comorbidity in DMD

January 30, 2020

We are excited to announce that PepGen will be part of an international project focusing on the role of the brain in Duchenne and Becker muscular dystrophy. Further details on this project can be found in the press release below:

The BIND project is the first project of this scale to improve characterisation of brain involvement in Duchenne and Becker Muscular Dystrophy (DMD and BMD respectively), a previously overlooked field. This EU-funded project connecting 19 partners aims to address a crucial aspect of DMD and BMD that was already recognised in 1861, when Duchenne de Boulogne first described the neuromuscular condition. In the last few decades however, most of the efforts have focused on improving outcomes related to muscle weakness, whilst brain involvement has received less attention.

The BIND project's ambition is to elucidate the role of dystrophin in the brain. This protein is deficient in DMD and only partly functional in BMD. The project aims to develop new outcome measures that could inform the field for future clinical trials and will promote more rigorous assessment and intervention of brain comorbidities. The ultimate goal of this project is to improve understanding and measurement of dystrophin in the brain, thus working towards better treatments, care and outcomes for all those living with DMD and BMD.

Most clinical experts are aware of the occurrence of brain comorbidities in a proportion of individuals affected by DMD and BMD. These X-linked recessive disorders are the result of absent or partly functioning dystrophin protein in muscle. Improved standards of care and novel therapies have greatly improved the quality and quantity of life for DMD and BMD patients over the past decade.

History of brain comorbidities in DMD and BMD

Dystrophin is also produced in the brain by a complex process that allows the production of multiple brain variants (isoforms). Depending on the type and location of the mutation in the DMD gene, the effects on production of the dystrophin protein vary. The production of the brain isoforms also depends on the location of the mutation, with a clear impact on intellectual disability and neurobehavioural complications, such as autistic spectrum disorder or attention deficit disorder in people with DMD/BMD. Currently, none of the approaches in clinical development to improve muscle function are expected to address the brain comorbidities. These comorbidities can limit quality of life for a proportion of individuals affected by DMD or BMD.

The BIND project (Brain Involvement iN Dystrophinopathies) hopes to achieve a deeper understanding of involvement of the brain in DMD and BMD, and how this impacts the lives of patients and their families. With a large multidisciplinary consortium covering areas of clinical research, molecular biology and protein biochemistry, it aims to identify the biological role of brain dystrophin.

"We were so occupied studying muscles, we almost forgot to focus on dystrophin in the brain," said Francesco Muntoni from the UCL Great Ormond Street Institute of Child Health (ICH) and Great Ormond Street Hospital for Children NHS Foundation Trust in London. He is the BIND project coordinator and responsible for the scientific management of the project. "With this project, we hope to better understand involvement of the brain, and enhance the quality of life of those affected by Duchenne and Becker".

Project goals:

- Localising the isoforms that the DMD locus produces in the brain and their function;
- Improve understanding of postnatal brain restoration of the different dystrophin isoforms using preclinical models;
- Defining the spectrum of brain comorbidities in DMD and BMD individuals, and how to best assess them;
- Creating optimal and uniform outcome measures to assess brain comorbidities in DMD and BMD.

As well as being of great importance for the Duchenne and Becker community, this project might also benefit the broader neuromuscular and neurodevelopmental field. Brain comorbidity neurobiology is poorly understood, and standards of care not widely disseminated and implemented. This four-year project describing the contribution of a specific protein (dystrophin) to brain function could be of crucial value for the broader neurobiology field, including autistic spectrum disorders.

An overview of all BIND project consortium partners

A close collaboration with the World Duchenne Organization ensures optimal involvement and outreach to patients and their families. Elizabeth Vroom, chair of the WDO, is glad to be part of the BIND project. "While there has been a lot of focus on the physical changes in DMD and BMD, treatment of neuropsychological problems is still lacking much-needed attention. It's very promising that this project addresses dystrophin in the brain," she said.

The kick-off meeting held in London on the 22nd and 23rd of January 2020 saw 50 participants from eight 8 countries in Europe , and Japan. At the meeting, the implementation plan for the scientific progress for the first year of the project was discussed and agreed. A summary of the proposal and the full list of the participant institutions and their investigators can be found at the website of the European Commission (link).

Consortium partners

1. University College London, United Kingdom
2. Consorzio Futuro in Ricerca, Italy
3. Leiden University Medical Center, Netherlands
4. Region Hovestaden, Denmark
5. University of Newcastle upon Tyne, United Kingdom
6. National Center of Neurology and Psychiatry, Japan
7. Neuro-PSI, Centre National de la Recherche Scientifique, France
8. Universite de Versailles Sant Quentin-en-Yvelines, France
9. Stichting Kempenhaeghe, Netherlands
10. Universita Cattolica del Sacro Cuore, Italy
11. Universidad Complutense de Madrid, Spain
12. Imagine Institut des Maladies Genetiques Necker Enfants Malades Fondation, France
13. Transpharmation Ireland Limited, Ireland
14. Great Ormond Street Hospital for Children NHS Foundation Trust GOSH, United Kingdom
15. World Duchenne Organization, Netherlands
16. Synthena, Switzerland
17. PepGen Limited, United Kingdom
18. Duchenne Data Foundation, Netherlands
19. Trinity College Dublin, Ireland

Press inquiries

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This project has received funding by the European Union's Horizon 2020 research and innovation programme under grant agreement No 847826