A Brief History of NNPDF-Supported Research

NNPDF was the first non-profit, family-based organisation to fund research on Niemann-Pick Disease

As we celebrate the 15th Anniversary of NNPDF, the Foundation is recognising its achievements in the field of NPD research and developing a strategy to guide NNPDF-sponsored research over the next 5-10 years. NNPDF's contribution to both laboratory research and clinical investigations is substantial.

Laboratory-based Research

The SPMD1 (NPA/B) gene was discovered in 1992, the NPC1 gene in 1997 and the NPC2 (HM1) gene in 2003. On the advice of the Scientific Advisory Board, NNPDF supported work to identify the gene for NPC1 – a major milestone. The Foundation also provided funding for work to identify the gene for NPC2. Scientists, including those who received funding from NNPDF, have identified the proteins expressed by the genes - Acid Sphingomyelinase, NPC1 protein, and NPC2 protein. Work is now taking place to elucidate the functions of the NPC1 and NPC2 proteins and how they may interact with each other.

Much of what scientists have learned about the basic mechanisms involved in Niemann-Pick disease has derived from investigations of similar genetic structures in non-human models. Animal and yeast models have been an invaluable resource in facilitating scientific advances. NNPDF has provided funding to characterize the disease process in these models and to help develop and maintain research colonies of non-human mammals.

Clinical Investigations

Current clinical investigations of miglustat (type C), rhASM enzyme replacement therapy (type B), and stem cell therapy (type A), have the potential to slow or stop the progression of these diseases providing scientists and families with more time to make advances toward a cure. As a Foundation we monitor progress of these investigations closely, looking for the optimum approach or combination of approaches that will lead us to effective treatments for all Niemann-Pick diseases. NNPDF also facilitates

participation in and disseminations of information from these investigations. The assistance of NNPDF was crucial in identifying patients to enable statistically viable data to be gathered in preparation for clinical trials, in recruiting patients for the trials, and in supporting families through the process.

NNPDF Family Support

Families, supported by the Foundation, have contributed greatly to the identification of the mutations involved (more than 18 in SPMD1, 230 in NPC1 and 15 in NPC2) by providing blood and tissue samples. Carrier testing is now available for families where the genetic mutation is known. Pre-natal diagnosis is available for families and recently Pre-implantation Genetic Diagnosis (PGD) has also become available in some cases. None of this would have been achieved so quickly without the involvement of families who came to the Foundation for information and support.

The Future

Progress is being made in slowing NPD by the research projects supported by NNPDF. We need to accelerate this progress by working in collaboration with scientists and clinicians who are preparing drug screenings, animal experiments, and clinical trials, and with the pharmaceutical companies interested in supporting clinical trials and developing additional drugs. We also need to look toward approaches that involve gene therapy and chaperone therapy to stop NPD, and approaches such as stem cell therapy that may reverse the damage caused by NPD.

We need to encourage scientists working on all aspects of NPD to focus their efforts on treatments and a cure. We may need to attract scientists who are developing therapeutic technology and approaches for other diseases, and bring them together with scientists and clinicians working on Niemann-Pick disease. Additional collaborations with the pharmaceutical industry may also be appropriate.

While scientists continue their work toward therapeutic discovery, we need to focus on the support structures that translate discoveries to treatments and a cure. As scientists discover drugs, products, or procedures that are thought to be beneficial, NNPDF should ensure that the appropriate mechanisms are in place to accelerate the application of these tools via pre-clinical research, clinical trials, development, and

FDA approval and marketing to ensure that beneficial therapies reach those with Niemann-Pick disease as quickly as possible. We have already gained valuable experience in understanding these processes in our close collaboration with Actelion in the development of Zavesca and with Genzyme in the development of rhASM.

NNPDF must continue to support families affected by NPD. To that end, the Foundation must provide scientific information in lay terms via the listserve, website, newsletter, and at the Family Conference, to help families understand the research that is underway to find treatments and a cure. This will allow families to make informed decisions about providing blood and tissue samples, family histories, taking part in clinical investigations and clinical trials, and continuing their support of NNPDF.

A strong foundation for progress is laid by advances in basic science. We are indebted to scientists who have identified the genes, deciphered their mutations, analyzed the composition and functions of the proteins, and elucidated the mechanisms of the damage that is being done. NNPDF is also indebted to the many scientists who have taken basic information about NPD and used it to conduct research to identify treatments and a cure. NNPDF is committed to continuing its support of research on Niemann-Pick Disease.