

Joint AANEM Foundation/MDA Grant to Fund SMA Research



Dr. d'Ydewalle

The first development grant jointly funded by the American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM) Foundation and the Muscular Dystrophy Association (MDA) was awarded in August of 2015 to Constantin d'Ydewalle, a postdoctoral fellow at Johns Hopkins School of Medicine in Baltimore. Dr. d'Ydewalle was awarded \$180,000 over 3 years to test a gene therapy designed to increase levels of SMN protein in spinal muscular atrophy (SMA).

The work may lead to the development of a new treatment that could be useful by itself or in combination with other therapies in development.

Dr. d'Ydewalle graduated from the University of Leuven, Belgium with a BS and MS in biomedical sciences, and a PhD in medical sciences in the field of NM disorders. In 2012, he joined the laboratory of Dr. Charlotte Sumner at the Johns Hopkins University School of Medicine, neurology department. Dr. d'Ydewalle recently shared his thoughts on the award:

What spurred your interest in this field, and your interest in SMA research?

There are two reasons why I wanted to study SMA. First, SMA is a devastating inherited NM disease that affects newborns and children. But it also affects their parents, family, and friends. Talking to parents of affected children about how SMA affects their daily lives motivates me day after day to study SMA and to contribute, even if it is only a bit, to the development of SMA therapeutics. Secondly, the SMA field is so collaborative, with pharmaceutical companies working hand in hand with academic institutions and nonprofit organizations. I strongly believe that this collaborative effort will eventually pay off in a real cure for SMA.

My main focus within the SMA field is to understand how

SMN expression is regulated. In the past years, several SMA therapeutic strategies have been developed that target SMN2 splicing to increase SMN protein levels. These include antisense technology (Isis Pharmaceuticals, now Ionis Pharmaceuticals) and orally available small molecules (Roche and Novartis). Most of these drugs are currently in (late phase) clinical trials. However, these drugs have a ceiling effect, as they only target the SMN2 RNA that arises from the available SMN2 copies. Increasing SMN2 expression at the RNA level in combination with SMN2 splicing modulators will likely have additive effects, which could be crucial in severe SMA cases. In addition, understanding how SMN expression is regulated over time will provide important information as to when SMA therapeutics needs to be delivered.

How will this award help you in your research?

This career development grant jointly funded by the AANEM Foundation and the MDA is one of the first grants I have been awarded in my career. The MDA and its competitive research programs are highly regarded in the field of NM disorders. I therefore consider this development grant as a major milestone in my career. This grant is critical for my career development as a junior researcher and it will contribute to paving the way for a position as an independent investigator. With this financial support, I hope that my research can contribute to a better understanding of SMA pathogenesis and to the development of new SMA therapeutics.

Is there anything else about this research or award that you would like to share with AANEM members?

Career development grants such as this one have enabled a lot of researchers to perform cutting-edge research that has led to a better understanding of SMA pathogenesis and to the development of SMA therapeutics. While there is currently no treatment and no cure, the National Institutes of Health (NIH) selected SMA as the disease closest to treatment of more than 600 neurological disorders. The SMA community, profit and nonprofit organizations such as the MDA and the AANEM Foundation, and researchers worldwide have all contributed to SMA research, and with their continued support and efforts, we will find a cure for SMA in a very near future.

I believe that a better understanding of the mechanism of regulation of gene expression in the nervous system by long non-coding RNAs will have implications not only for SMA but also for other neurological disorders. Insights into these mechanisms could provide crucial information about why nerve cells are the most vulnerable cell type in the nervous system and could identify novel therapeutic targets for neurological disorders.

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