AUTOIMMUNE ENCEPHALITIS ALLIANCE

NEWSLETTER

JULY 2020

In this issue...

From Our Executive Director

Greetings AE Family and Friends,

As many of you know, the Alliance has long been committed to a partnership with both patients and physicians in the quest to improve the quality of care for all AE patients. In 2014 the Alliance hosted its first international symposium of interdisciplinary researchers and clinical scientists representing several renowned medical institutions and research programs worldwide. Twenty-four researchers and clinicians from the disciplines of pediatric and adult psychiatry, neurology, rheumatology, and immunology gathered at this event. This symposium was the Alliance's first significant effort in developing a platform for extensive collaboration among physicians and scientists seeking to understand and improve diagnostic tools, treatments, and improved outcomes for AE patients. Building upon that significant first effort in 2014, the Alliance has since established two primary cornerstones of its physician support framework: the Medical Advisory Board (MAB) and the Clinicians Network.

Since its inception, the MAB, an advisory board of 19 dedicated physicians and researchers from various medical subspecialties and institutions, has focused its efforts on three primary areas of support of AE: physician education, centers of excellence, and research. These leading experts and those with whom they collaborate are making significant contributions in research, diagnosis, treatment, and outcomes for AE patients worldwide. They are investing their time and effort in working with their peers and colleagues with the primary objective to share their knowledge, develop diagnostic and treatment guidelines or protocols, and advance best practices in the field of AE.

Early on, the Alliance recognized the vital need to enable patients to connect to physicians capable and willing to treat AE. The Clinicians Network launched in 2014 for this primary purpose. Today the network includes 170 registered clinicians who actively treat AE patients worldwide. Not only do these physicians provide excellent clinical care, but many are also heavily involved in AE research. Physicians can register on the Alliance website, and patients can search this network for a clinician in their area.

Building upon our commitment to improving the lives of the AE community and recognizing the critical need for AE research, this quarter, the Alliance rolled out the **AEA Research Network**. This inaugural effort was launched in May and coincided with a targeted push for dedicated research funds during the national campaign, Giving Tuesday Now. Many of you supported this effort, and for this, we thank you. The Alliance is committed to supporting research efforts by providing seed funding for promising research projects in the field of AE, research collaborations and publications, and resource support through project assistants and fellows. To this end, we are dedicating the month of May for an annual focus on research and research fundraising. The Alliance's MAB will be making recommendations to the Alliance on worthy investments of these research funds for the best interest of AE patients.

In honor of our commitment to supporting research and the devoted physicians and scientists working so diligently to improve our AE patient community's lives, we have dedicated this quarterly newsletter to spotlighting important research initiatives and advancements in the field. I know you join me in supporting and celebrating the ongoing efforts of the many researchers working on your behalf.

Caterri Woodrum

Caterri Woodrum
Executive Director and CEO

MAB SPOTLIGHT

Dr. Susa Benseler

Alberta Children's Hospital, Calgary, Alberta, Canada

For Susa, medicine is a combination of different areas of passion—she loves science and hands-on work and enjoys helping kids and families achieve their full potential. Back in high school, Susa loved math, biology, and chemistry. She was a science tutor for kids in the younger classes and handball coach for girls ages 9–12. The partnership with families and the fact that medicine makes science relevant and impactful is why Susa still loves being a doctor after all these years.

Her interest in autoimmune encephalitis dates back to the '90s when she was part of the pediatric ICU staff. They admitted kids that were terribly ill, but could not find anything on blood tests and imaging studies. That was very frustrating. Kids had uncontrollable seizures, severe cognitive decline, and often mental health symptoms. She was thrilled when the first antibody-mediated disease was reported, as these presentations and the lack of traditional markers finally made sense. This was a valuable lesson—despite the high-tech environment in the hospitals—not all diseases are equally well understood. Keeping an open mind and trusting family is of the essence. Autoimmune encephalitis continues to be Susa's passion, and she is grateful for the outstanding work of the Alliance.

According to Susa, the care for children and adults with AE is a team effort. Transformation of care for children with inflammatory diseases can only be successful when you can build interdisciplinary teams at each center. You need to advance your knowledge and translate this into care continuously. More than a decade ago, Susa and her group established the first childhood CNS vasculitis and inflammatory brain diseases clinic and research program in Toronto. They also built BrainWorks, an international childhood inflammatory brain disease investigator network with a database capturing more than 600 children from around the world. The BrainWorks care protocols need to be continuously updated and ultimately tailored to the individual patient based on a deep understanding of their particular disease. Susa dreams of interdisciplinary, rapid, effective, and safe care models for AE, and to use her own words '*We are getting there.*'

As the leader of BrainWorks, Susa is responsible for updating the network to integrate the growing spectrum of inflammatory brain diseases—in particular, the autoimmune encephalitis diseases—and enable the community to learn from every child, adult, and family. BrainWorks is a network of clinical researchers from around the world. She would like to loop in more basic science researchers to enable and generate in-depth knowledge of AE—work that will help us understand the disease better and select precision medicine approaches for AE.

Susa sees there is much to be done in the field of AE. She hopes we continue to advance our knowledge, and develop an ability to rapidly test for the growing spectrum of inflammatory brain diseases. She also sees the importance of developing new insight into why a disease develops and how to quickly stop it and allow the child's brain to heal. In particular, establishing early rehabilitation strategies for cognitive rehabilitation is a critical area that needs to be developed in her opinion. She further emphasizes the need to build and foster new partnerships—from the benches to bedside to backyards—to achieve optimal outcomes for children and adults with autoimmune encephalitis.

When Susa is not working, she enjoys doing home restoration projects and renovating houses!

Thank you, Dr. Susa Benseler, for improving the lives of those affected by AE.

BrainWorks is a network of doctors, researchers, families, medical specialists, and supportive organizations. BrainWorks has built a web-based database capturing more than 600 children from around the world with inflammatory brain disease. The aim of BrainWorks is to learn from every individual patient affected by devastating inflammation of the brain and spinal cord. The network aims to increase recognition, promote rapid diagnostic evaluation, optimize treatment, and prevent brain damage.

BRAINWORKS

Learn more about the BrainWorks study at:
sickkids.ca/Research/Brainworks/the-brainworks-study/index.html

ASK OUR PANEL

Q:

My husband had autoimmune encephalitis back in 2018. He is doing much better now but is not his full self yet. We have been on an emotional roller-coaster and are worried about this disease coming back. What can you tell us about possible relapses? Do they happen often?

A:

Thankfully most of the time, AE is only one attack and does not relapse. For anti-NMDAR encephalitis, which is the most common and best described AE, the relapse rate is about 15%, so most people will only have one attack and not relapse. There does not seem to be much difference between children and adults.

For other AE syndromes, the relapse rate is harder to define. GAD antibody-associated encephalitis can relapse or have a progressive course, but generally, most AE syndromes are 'monophasic', meaning 'single attack'. Myelin Oligodendrocyte Glycoprotein (MOG) antibody-associated acute disseminated encephalitis relapses in about 10–30% of patients, usually in the months shortly after the first attack.

Often there is no apparent reason for relapse. However, a decline may sometimes be due to the immune system being stimulated or triggered by an infection. In a patient with a relapsing course, it is worth considering whether there could be an 'ongoing' immune trigger such as a chronic infection (i.e., herpes sim-

Have a question for our panel?

Contact us online at:
aealliance.org/contact

plex virus encephalitis) or tumor. Tumors appear to be uncommon in children with AE but are more common in adults for some autoantibody AE syndromes.

Generally, the symptoms are signs of a relapse and are similar to the first attack but usually less severe. For example, recurrence of seizures, hallucinations, movement disorder, or change in memory and can represent a relapse after previous improvements. Usually, the symptoms are continuous rather than transient and continue over several days or weeks (rather than hours).

The treatment of a relapse is similar to the first attack. The principle is 'damping down' the immune system, so corticosteroids, intravenous immunoglobulin or plasma exchange are typically used. When there is a recurrence of disease, this suggests the problem is ongoing, rather than transient. Sometimes it is necessary to consider a more 'long-term' immune treatment such as mycophenolate or rituximab (immune suppressants) for one or more years.

There are no other recognized ways to prevent relapse. Ensuring there is no Vitamin D deficiency is probably the only way to reduce the chance of relapse. It is impossible to prevent infections, particularly in young children. It is sometimes sensible to delay routine vaccinations until the 'active phase' of the autoimmune process has stopped, but vaccination is still vital after a delay. Timing the vaccinations after AE or other autoimmune disorders is tough to advise, but generally, clinicians wait 6-12 months after the disease appears to have stopped. Sadly, there is little data available to firmly inform the timing of routine vaccination in children with AE.

Prof. Russell Dale
The Children's Hospital at Westmead, Australia

Professor Russell Dale is the Clinical Director of the Kids Neuroscience Centre and a pediatric neurologist. He is also the group leader for Clinical Neuroimmunology and Movement disorders. He is an expert in movement disorders and neuroimmune disorders in children, and his main priority is to improve the diagnosis and treatment of children with neurological disease. He is a clinical academic at The Children's Hospital at Westmead and The University of Sydney and has published over 170 peer-reviewed academic papers.

MY AE JOURNEY

Lisa Ventura

Encephalitis Daughter: How a diagnosis of CASPR2-antibody encephalitis for my Dad changed his life and mine.

October 19, 2017, is a date that will be firmly etched in my mind forever. It was the day that my Dad suffered a grand mal seizure seemingly out of the blue, and his life was forever changed as a result.

Being an only child, my Dad is my absolute world. Whatever I did he was always there, and he attended all the events that I was a speaker at or where I read my poetry and writing work to an audience. He did not miss anything that I did; he and my husband became known as "my two minders" in my social circle because I never went anywhere without them.

In March 2017 my Dad started complaining of his head "not being right". He attended his GP about it on several occasions, but nothing he was given medication wise worked for him. His head "not being right" got worse and worse for him, and he became extremely withdrawn and didn't want to go out and do the things that he used to enjoy doing like going for a Costa coffee with me while we put the world to rights, or going out for a meal with his friends at his favorite Italian restaurant.

On October 19, 2017, at approximately 3 p.m., I got a frantic call from my mother saying that my Dad had had a heart attack and she had called an ambulance. It wasn't a heart attack; he had suffered a grand mal seizure and then had another one in the hospital when he was taken for a CT scan, so he was sedated and given anti-seizure medication via an IV. The CT scan showed nothing, so he was sent home the next day with *epilim* medication and was told he would see a neurologist.

My Dad paid privately to have an MRI scan as he was convinced that he had a brain tumor, but this also showed nothing untoward. A neurologist concluded that he had temporal lobe epilepsy with no known explanation for the onset of it. Every time he tried to switch medication for it, he became extremely ill, so he ended up going back onto *epilim*. Over the course of 2 years, his mobility declined rapidly, his memory declined, and he became increasingly confused and aggressive—his personality completely changed. He was no longer my Dad.

Lisa and her Dad enjoying a cup of coffee.

I insisted on a second opinion from a different neurologist in September 2019, and in December 2019 we were told that my Dad likely had motor neurone disease with associated dementia. However, before that was given as my Dad's formal diagnosis, the second neurologist said he wanted to run a range of blood tests. They were done in December 2019, and on January 8, 2020, we were told that my Dad didn't have motor neurone disease with associated dementia but what he actually had was CASPR2 antibody encephalitis, and although he would never be as he was, his condition was treatable.

I had never heard of it so I researched this condition online and came across the Encephalitis Society charity in the UK. They helped me get my Dad in front of Professor Sarosh Irani at the John Radcliffe Hospital in Oxford who first identified the CASPR2 antibody as being a cause of encephalitis.

Professor Irani arranged to admit my Dad to the John Radcliffe Hospital for further tests, a series of plasma

...I have gained an incredible new perspective on life. I have a lot of hope for the future.

Lisa and her parents.

exchange treatments, and autoimmune therapy treatment via steroids. My Dad was released from the hospital just before the lockdown came in for coronavirus, and although I have not been able to see him in person we have kept in touch via video calls on Facebook messenger.

I'm pleased to say that my Dad is now improving massively as a result of his treatment. His mobility has improved, and he is now only using a stick to help him walk, and has improved a bit cognitively. However, he still has memory problems, aggression at times and he has strong obsessions about certain things that he homes in on, and nothing can placate him. For example, he is obsessed with not catching coronavirus and washes his hands multiple times a day and insists on wiping them with antibacterial wipes.

My Dad is forever changed because of CASPR2 antibody encephalitis, but we are SO grateful to the NHS in the UK for finally getting to the bottom of what was wrong with him even if it took almost three years. Learning to navigate my Dad's new normal has been very upsetting and difficult, and it sometimes feels like I have assumed the role of a parent with him and he is a small child. This has been particularly hard for me to come to terms with, but I am so happy and so grateful that he is still with us. Without his actual diagnosis, I am sure that his symptoms would have been put down to motor neurone disease with associated dementia and he would be in a care home now. The experiences I've had over the last three years with my Dad has led me to work on writing a book

...I have gained an incredible new perspective on life. I have a lot of hope for the future.

called "Encephalitis Daughter" which I hope will be a resource for patients who are also diagnosed with autoimmune encephalitis and for their families who will have to learn to navigate a "new normal" for their loved one. I am also a born campaigner; I am trying to raise as much awareness as possible of autoimmune encephalitis and the importance of early diagnosis and intervention for a good outcome with treatment.

Lisa and her Dad.

If anyone reading this would like to reach out to me about my story, I can be found on Twitter as **@cybergeekgirl** or message me via **hello@cybergeekgirl.co.uk**.

I am always happy to talk to anyone who has been diagnosed with autoimmune encephalitis and their families to share my experiences.

The work undertaken by the AE Alliance and others supporting this rare disease is so important to those diagnosed with AE and their caregivers. Thanks to these efforts, my Dad and our family don't feel alone and know we have support when we need it.

AEA in the Community

Research Network Recap

On May 5, 2020—Giving Tuesday Now—AE Alliance rolled out the AEA Research Network. The network unveiling featured webinars by Dr. Eric Lancaster; Dr. Stanley Naides and Dr. Iswariya Venkataraman; and Dr. Sean Pittock. They spoke about the latest developments and challenges in AE research.

We raised $17,562 for the Research Network, which includes a generous matching contribution by Bob Given, an AE survivor and strong proponent of AE research efforts. Research is critical to understanding the disease process and developing specific treatments for AE. AE Alliance continues to work closely with the Medical Advisory Board and Clinicians Network to ensure these research dollars generate a long-lasting impact.

Learn more: aealliance.org/researchnetwork

Join the network: classy.org/campaign/aea-research-network/c282099

Ohio Support Group Meeting

Dr. Stacey Clardy

On June 20, AE Alliance hosted the virtual OH Support Group Meeting, which was also open to our Texas and New York groups. We had the pleasure of hearing Dr. Stacey Clardy (University of Utah) speak passionately about her approach to AE care, research, and the importance of sharing our AE journeys with our local, state, and national representatives. We need to get our voices heard! After her presentation, Dr. Clardy took a lot of time to answer questions from our members. Members enjoyed coming together as a group to support each other and felt empowered by Dr. Clardy's presentation.

Clinical Trials: A Step-by-Step Guide

Clinical trials ensure treatments are safe and effective. Each step helps answer different questions about the treatment.

Step 1: Preclinical Study

Learning how a treatment works in test tubes and animals to determine potential safety and effectiveness.

Step 2: Application Period

Researcher submits an Investigational New Drug (IND) application to the FDA for a proposed clinical trial.

Step 3: Phase 1

Involves the fewest participants. Makes sure the therapy is safe and determines the correct dosage.

Step 4: Phase 2

More participants. Researchers look for favorable or useful effects while monitoring safety.

Step 5: Phase 3

The longest phase with the most participants. Proves the therapy has the desired result while being safe.

Step 6: FDA Final Approval

FDA review teams thoroughly examine all submitted drug data and make a decision regarding approval. From start to finish, the clinical trial process takes many years. However, the FDA has various ways to accelerate the process for some therapies.

AE Facts

4,000
people get diagnosed with AE each year in the United States

1 in 100,000
people develop AE each year (globally)

55%
of AE patients are admitted to the ICU

12-35%
relapse rate in AE patients

>25
autoantibodies discovered to date

6%
mortality rate in AE patients

Challenges Faced by AE Patients & Their Families

Misdiagnosis or no diagnosis	Physicians not familiar with full spectrum of AE	Imperfect diagnostic testing	AE care requires a team of specialists
AE poses a heavy financial burden	Logistical challenges in accessing specialists	Complicated care schedules & medication regimes	AE has a big impact on the psychological well-being of all involved

No specific treatment protocols available

No FDA-approved treatments

Limited number of clinical trials available

How to Change the Course of AE

Patients and caregivers have unique perspectives on the benefits and risks of potential new medicines and are able to provide valuable insights on their disease, available treatment options, and their outcomes. Patients and caregivers play an integral part in advancing AE research.

AE Alliance

AE Alliance has a broad international base of physicians and researchers on the AEA Medical Advisory Board and Clinicians Network. The Research Network unites patients, survivors, caregivers, and others interested in AE. The network works across the board to push AE research forward.

aealliance.org/researchnetwork

Become a Monthly Donor

Monthly giving means strong and steady monthly funding that AE Alliance can count on and plan for, allowing AE Alliance to make meaningful long-term commitments to families in need, physicians, and researchers. You simply decide on an affordable amount that meets your budget and your desire to help.

Give Now

Research Corner

The ExTINGUISH Trial

We are excited to report that in the ongoing effort to improve patient care, three of our AEA Physician Scientists (with input from many of our physicians in the AEA), have designed a Phase 2b clinical trial for NMDA-R encephalitis – meaning it is past stage 1 where the first safety and tolerability work is done, and instead this trial will be focused on determining and quantifying efficacy of the medication(s).

The trial has received the initial support of the NeuroNEXT Clinical Trial Network group, which is a large network of medical centers in the US that can effectively handle large clinical trials. The clinician scientists, along with the support of the NeuroNEXT Network, have submitted the trial proposal to the National Institutes of Health (NIH) for review, and were assisted by the AEA in reviewing the proposal and providing a patient advocate to participate in the trial design process. NIH will review the Trial in the coming months to determine if they will fund this proposal. **We at AEA are hopeful that NIH will realize the importance of funding a large, multicenter trial to advance both the understanding and treatment of this common form of autoimmune encephalitis.**

The Lead Investigators on the proposed study are:

- Stacey L. Clardy MD PhD, University of Utah + Salt Lake City VA
- Maarten Titulaer MD PhD, Erasmus University Rotterdam
- Gregory Day MD, Mayo Clinic Jacksonville

The NeuroNEXT Clinical Trial Network (with over 25 sites in the United States) was integral in helping to design the trial, including input from many AEA-member Neurologists at those sites.

It is A Phase-2b, Double-Blind, Randomized Controlled Trial to Evaluate The Activity and Safety of Inebilizumab in Anti-NMDA Receptor Encephalitis and Assess Markers of Disease.

Short title: "The ExTINGUISH Trial" (Acronym stands for: Encephalitis Treatment with Inebilizumab for NMDAR andGUIdance on Serum + CSF biomarkers to predict Health outcomes)

More About the ExTINGUISH Trial Proposal

N-methyl-D-aspartate receptor (NMDAR) encephalitis is one of the most common causes of autoimmune encephalitis, with prevalence exceeding herpes encephalitis in industrialized nations. NMDAR encephalitis typically affects patients ages 10-50, causing prominent psychiatric symptoms associated with declining consciousness, seizures, movement disorders, and life-threatening dysautonomia. Intensive care, including cardiorespiratory support, is required in up to 75% of cases.

The diagnosis is confirmed by the detection of IgG autoantibodies against the central nervous system NMDAR in the cerebrospinal fluid. Despite the severity of the illness, NMDAR encephalitis is a treatable neurological disease, with retrospective case series establishing the benefit of off-label intravenous steroids and immunoglobulins. These treatments are presumed to work through effects on IgG NMDAR autoantibody levels in the CSF, although prospective data informing predictors of treatment responses are limited.

Various off-label therapies have been proposed as "second-line" treatments in NMDAR encephalitis. The majority of second-line treatments target circulating B-cells with various degrees of blood-brain penetrance and efficacy, and poor consensus on the timing, dose, and route of candidate agents' delivery.

High-quality evidence is needed to direct the treatment of NMDAR encephalitis. Inebilizumab is a promising therapeutic monoclonal antibody for the treatment of NMDAR encephalitis. This humanized monoclonal antibody against the B-cell surface antigen CD19 was recently shown to be safe and efficacious in treating neuromyelitis optica spectrum disorder—another antibody-mediated disorder of the central nervous system.

Compared to other off-label B-cell depleting therapies, such as rituximab, inebilizumab depletes CD20+ B-cells and CD20- plasmablasts and plasma cells, resulting in robust, broad, and sustained suppression of B-cell expression.

The ExTINGUISH Trial will plan to randomize 116 participants with moderate-to-severe NMDAR encephalitis to receive either inebilizumab or placebo in addition to first-line therapies. Patient outcomes will plan to look at measures of disability, neuropsychological tests, bedside cognitive screening tools, quality of life/functional indices, and outcome prediction measures. Clinical data will be combined with quantitative measures of NMDAR autoantibody titers and

biomarkers in spinal fluid and blood to learn about biological contributors to outcomes, and to evaluate for biomarkers that may serve as early predictors of good outcomes in future clinical trials in NMDAR encephalitis.

The results of The ExTINGUISH Trial will immediately impact patient care, as well as facilitate the design and implementation of future clinical trials in patients with autoimmune encephalitis.

Thank you, Dr. Clardy, Dr. Titulaer, and Dr. Day for this groundbreaking work!

Odense Autoimmune Encephalitis Research Group: Q & A with Dr. Morten Blaabjerg

Dr. Morten Blaabjerg leads the Odense Autoimmune Encephalitis Research Group in Denmark, and he is a member of the AEA Clinicians Network. The Research Group aims to increase the understanding of autoimmune encephalitis to provide the best possible treatment for patients.

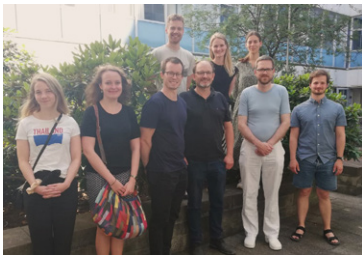
Can you tell us more about your professional background?

I am a consultant neurologist at the Department of Neurology, Odense University Hospital, Denmark, and a professor in neurology at the University of Southern Denmark. I started doing neurobiological research more than 20 years ago during my medical studies, where I investigated the regulation of glutamate receptors (e.g., NMDA and mGluRs) in stroke models. In particular, we were interested in the regulation of NMDA receptor internalization (which later was found to be the pathological mechanism in anti-NMDAR encephalitis). After seeing my first AE patients, I was fascinated by these conditions, where early and correct diagnosis and treatment makes a huge difference. My interest was further strengthened by the fact that the underlying mechanisms were similar to those I investigated previously.

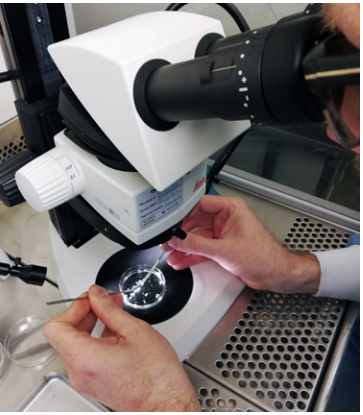
When was the Odense Autoimmune Encephalitis Research Group founded? What is the mission of the group?

We officially founded the group in 2018, though some of the members had been engaged in AE research for several years before this. Our strategy is to do translational neuroscience research, meaning to answer relevant clinical questions using both clinical and basic neurobiological methods. Our interest is to determine:

1. WHAT are the mechanisms causing AE;
2. HOW are the patients best treated;
3. WHAT is the outcome (e.g., long-term symptoms, QoL, etc.).



The Odense Autoimmune Encephalitis Research Group. From top left: Christian Winterberg, Mette Nissen, Anna Amalie Ellerup. From bottom left: Mette Blok-Andersen, Silke Funch, Mattias Gamre, Morten Meyer, Morten Blaabjerg and Matias Ryding. Not pictured: Sebastian Storm, Christine Nilsson and Martin Wirenfeldt.



Organotypic hippocampal rat slice cultures

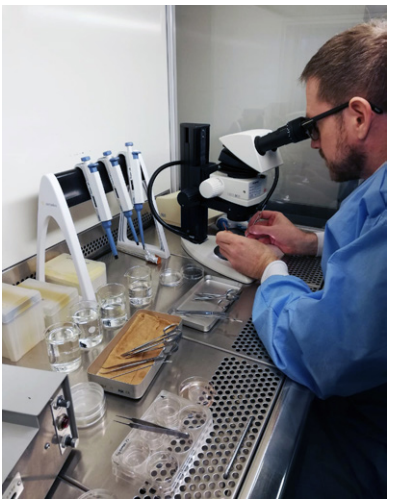
Besides clinical studies, this involves animal models, tissue models, and cell models.

There are not many groups that solely focus on AE. Was there a particular reason or motivation to start this group?

Since AE syndromes are evolving at an astonishing pace, and patients are still misdiagnosed, resulting in delayed treatments and outcomes, we feel that AE needs our full attention. In Denmark, we have useful registries, and therefore we know precisely how many patients are diagnosed and which hospitals are involved. This information allows us to do nation-wide studies, which we believe will benefit the field. Moreover, we think that our neurobiological and translational approach will help improve understanding of AE's underlying mechanisms and lead to the discovery of novel potential treatments.

Could you elaborate on the research you are currently doing? Could you dive more deeply into human stem cells used as a model for AE?

Currently, we are collecting data on all Danish AE patients in a research database. This data includes symptoms at onset and during the disease course, information on clinical work-up, treatment and outcome, and a timeline between symptom onset, admission to hospital, and initiation of relevant treatment. With this study, we aim to describe our national cohort and investigate the potential delays in treatment and diagnosis to increase awareness among doctors.



Prof. Dr. Morten Blaabjerg

In the lab, we currently work with an animal model of anti-NMDAR encephalitis, where we investigate a potential new treatment that has shown promising effects in cell cultures. Recently we also started to use stem cells as a model. With these cells, we are able to generate unlimited numbers of human neurons with the obvious advantage that these neurons are closer to the real situation than neurons derived from rodents that are normally used. Using this model, we are currently investigating the cellular pathological effects of AE antibodies.

How are you funded?

We obtain all our funding from private funds or larger research funding agencies.

AEA thanks Dr. Blaabjerg for the important work he and Odense Autoimmune Encephalitis Research Group conduct.

To learn more, please visit **www.encefalit.dk**

BETPSY project

Prof. Jérôme Honnorat dedicates his work to the diagnosis and the treatment of patients with autoimmune encephalitis or paraneoplastic neurological syndromes. He is also a member of the AE Alliance Clinicians Network.

Autoimmune encephalitis (AE) and paraneoplastic neurological syndromes (PNS) are rare neuroimmune syndromes with a wide range of clinical presentation but without pathognomonic clinical sign facilitating the diagnosis. Although rare, the diagnosis of AE or PNS is essential because, despite severe neurological symptoms, patients can be cured by appropriate immunotherapy. Autoantibodies highly specific of AE and PNS has been described in the serum and cerebrospinal fluid of the patients and can be used as biomarkers of the disease.

However, if some autoantibodies are now well-characterized and industrial kits have been developed to detect them, in numerous cases of highly suspect AE or PNS no specific autoantibodies are identified leading frequently to inappropriate treatment. Furthermore, as the mechanisms of AE and PNS is still unknown, treatments are not optimal and in some cases inefficient. There is no prognosis biomarker able to predict the patient's sensitivity to immunotherapy and there are only a few clues to know how the immune system can provoke the neuropsychiatric symptoms observed in the patients.

The aim of the BETPSY project is to better characterize AE and PNS patients to identify new diagnostic and prognostic biomarkers and develop new diagnostic tools. As the French reference center on AE and PNS since 2007, we developed a national network able to construct an exceptional collection of clinical data and biological samples of these very rare diseases. Our cohorts are a unique opportunity to identify new autoantibodies as biomarkers, but also genetic and HLA haplotyping specificities influencing patient's evolution as well as tumor specificities leading to immune responses.

Our biological collection will also be an opportunity to improve the sensitivity and the specificity of existing tests developed by EUROIMMUN already on the market. At the end of the project, other academic consortiums or industrial companies could use the collections. Obviously, our project will benefit patients with AE and PNS leading to a better and early diagnosis, as well as treatment improvement. Finally, we will also improve our knowledge of the possible role of the immune system in other neurological diseases.

Jérôme Honnorat is Chair of the Department of Neuro-Oncology at the neurological hospital, Hospices Civils de Lyon, Team leader of the "Synaptopathies and Autoantibodies (SynatAc)" at the Institute NeuroMyoGene (UMR INSERM U1217, CNRS 5310), and coordinator of the French reference center on paraneoplastic neurological syndromes and autoimmune encephalitis. His main scientific interests include gliomas treatment, immunotherapy, biomarkers, paraneoplastic neurological syndromes, and autoimmune encephalitis. His main work consists in the description of the clinical specificities of patients with autoimmune encephalitis and paraneoplastic neurological syndromes and the interest to detect specific autoantibodies as biomarkers of these diseases and as tools to understand synaptic functions.

Thank you Prof. Honnorat, for the important work you and your colleagues are doing.

To learn more, please visit **www.rhu-betpsy.fr**

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