**The ATP1A3 in Disease Symposium: How did it start and why it is important for AHC**

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*www.atp1a3-disease-symposium.org*

We are delighted and grateful to see the 10th meeting of the Symposium taking place as part of the 10-year anniversary event in Edinburgh 19-21 October 2022.

In the early 2012 several research teams in Europe, in the USA and in Japan were racing to find the genetic causes of AHC. Thanks to the favourable research landscape, shaped during the preceding years by the joined efforts of AHC family organisations, clinicians and geneticist, each team was equipped with a collection of clinically characterised AHC blood samples that allowed them to apply the newly available WES technology and the trio sequencing approach. Soon, the news for breakthrough results by the USA-led team started to spread. Two publications, in Nature Genetics (Heinzen et al.) and in Lancet Neurology (Rosewich et al.), came out on line on July 29th 2012, followed later by the publication on the Japanese patients (Ishii et al.). In all studies, heterozygous pathogenic mutations in the *ATP1A3* gene were identified in the majority of the tested AHC patients. These publications could finally prove the uniform genetic basis of AHC. Importantly, heterozygous mutations in the *ATP1A3* gene had already been described eight years earlier as the cause of an adult-onset movement disorder, rapid-onset dystonia parkinsonism, RDP (Carvalho Aguiar et al. 2004).

Now, the path to designing new effective medical treatments tailored to AHC seemed open. It was evident that if we wanted to understand how *ATP1A3* mutations can cause neurological disease, we have to better understand the role of ATP1A3 (and generally, of Na+/K+-ATPase) at the molecular and cellular level. We needed therefore to engage new relevant scientific and clinical expertise in the ongoing AHC research and we knew that the best way to do that was through scientific meetings. In June 2012 ENRAH took the initiative and, together with the Duke University group led by David Goldstein, decided to organise a Symposium. There was no time to look for public funding , but we had to keep up the momentum of the breakthrough research going.

Moreover, we were very excited that some excellent research on ATP1A3 / Na+/K+-ATPase has already been produced over the years by various disciplines in this field. We started reaching out and invite people the day after the first publications appeared on line at the end of July 2012. The response that came was absolutely amazing, there was a high interest expressed by everyone contacted and new topics and research teams were added by the day. On August 20th we were ready to announce the Symposium in Brussels on 10 and 11 December 2012 .The Agenda, included 1) the recent findings of *de novo* mutations in *ATP1A3* causing AHC2) clinical phenotypes studies in AHC 3) mutations in *ATP1A3* causing RDP 4) functional studies of *ATP1A3* mutations causing RDP 5) animal and cell models for ATP1A3 pathology. We will skip here the details on the challenges for the organisation the following three months, but it is important to acknowledge the financial support received for the Symposium from the AHC family organisations, that was critical to realize this meeting.

Sixty six participants from fifteen countries attended the Symposium in Brussels December 2012. These included scientists, clinicians and parents from AHC associations, and guests from the European Commission DG Research. What happened in Brussels is probably best described by one of our guests, who wrote us: “*I have enjoyed to see this close cooperation between patient representatives and the scientific world. I have never experienced this kind of cooperation in this extent before.”*

At the closing of the Symposium we knew that this was rather a beginning, something we have to keep going and growing. Today, it is really amazing to see this long list of meetings and novel physicians, basic scientists, patients and family organizations joining at every meeting:

- Symposium ATP1A3 in Disease: *From gene mutations to new treatments*

Basil & Co Brussels Louise Seminar, Brussels, Belgium, 10 - 11 December 2012.

- Second Symposium on ATP1A3 in Disease: *Genotype/Phenotype Correlations, Modelling and identification of potential targets for treatment*

Catholic University School of Medicine, Rome, Italy 23 -24 September 2013.

- Third Symposium ATP1A3 in Disease: *Genotype/phenotype correlations, modelling and identification of potential targets for treatment*

de Lunterse Boer &Conf. Center De Werelt, Lunteren, The Netherlands, 29-31 August 2014.

- 4th Symposium on ATP1A3 in Disease: *A Collaborative Effort of Advocates, Researchers and Clinicians to Set the Stage for Treatment Trials*

Double Tree Bethesda Hotel Conference Center, Washington DC, USA, 27-29 August 2015.

- 5th Symposium on ATP1A3 in Disease

UCL Institute of Neurology, London WC1N 3BG, United Kingdom, 24-26 August 2016.

- 6th Symposium on ATP1A3 in Disease

Palace Hotel Tachikawa, Tokyo, Japan, 21-22 September 2017.

- 7th Symposium ATP1A3 in Disease

Robert H. Lurie Medical Research Center, Chicago, USA, 13-14 October 2018.

- 8th Annual Symposium on ATP1A3 in Disease: *Moving towards the light*

Grand Hotel Reykjavík, Iceland, 3-4 October 2019.

- 9th Symposium on ATP1A3 in Disease (ON-LINE)

Karolinska Institutet & University Hospital, Stockholm, Sweden, 23-24 September 2021.

Each of these meetings has contributed in its unique way to the Symposium and we are grateful to all organisers and participants. We think this sets the basis for a community, who tries to join forces for our common goal: End ATP1A3 related diseases!