Found the primary gene for Alternating Hemiplegia, a very rare neurological disorder

The discovery has been possible thanks to a large collaborative study, involving clinical centers and genetic laboratories in Europe and America, with the financial and logistical support of the patient organizations in Italy, France and the United States.

Verderio Superiore (LC), 30 July 2012. The Alternating Hemiplegia of Childhood (AHC) is a very rare neurological disease (1:1,000,000), chronic and severely disabling, characterized by the early onset of recurrent attacks of hemiparesis and tetraparesis, which are triggered by several factors such as physical stress, emotions or changes in temperature. In all patients there are also intellectual and motor disabilities of varying degree, 30% of the patients have also seizures.

The Italian patient association A.I.S.EA Onlus currently gathers 48 families with affected children affected, distributed throughout the whole country.

Alternating Hemiplegia of Childhood is a disease still very little known, poorly investigated and significantly under-diagnosed: in fact, since specific biological markers have never been available until now, the diagnoses are still made by the few medical experts of the disease, based exclusively on the clinical evaluation of the symptoms and by exclusion of other clinically similar diseases.

AHC is one of the many rare diseases not yet acknowledged by the Italian Government under the Ministerial Decree No. 279/01 for Rare Diseases, and it has not yet been granted an exemption code, necessary for the taking in charge of the affected patients by the National Health Service.

The collaborative genetic study in object, directed by a group of researchers at Duke University (Durham, NC), has finally discovered the genetic defect responsible for AHC.

The identified gene is ATP1A3 and encodes a protein functioning as sodium-potassium ion pump at the neuronal level. The gene discovery has been made possible through the application of the exome/genome sequencing, a very new technology that has recently revolutionized the research for genes responsible of many rare diseases.

The identification of the gene that causes AHC is the first important step towards the development of a drug effective and specific for the disease.

Indeed, some functional studies in this direction have already been launched, offering to the families affected by this terrible disease, in Italy and all over the world, a real hope for a better quality of life for their children.

This finding will also surely raise the awareness about AHC, in the scientific community, public institutions and society in general, especially regarding their ability to make new diagnoses more accurately. In fact, if on the one hand, the development of a new drug specific for this disease will necessarily require longer times and large investments in research, an immediate benefit is already obtainable, thanks to the development of a specific genetic test on the identified gene, to confirm the diagnosis in all the new suspected cases of AHC.
The availability of a specific test for AHC can drastically reduce the rate of wrong and late diagnoses that too often up to now have caused many patients to be treated with inappropriate medications.

Full details of the discovery have just been published by Nature Genetics, a prestigious international scientific journal.

Throw the initial sequencing of the exome of 7 patients the gene was identified by the researchers of the Duke University, and then, thanks to an impressive collaborative effort internationally sponsored and supported by the three main patient associations (in Italy, France and USA), the clinical centers and genetic laboratories from 13 different nations gathered to study further 95 patients, bringing to confirm the presence of causative mutations in the gene ATP1A3 in more than 75% of them. They are all de novo mutations, that’s to say present only in the patients and absent in all their parents.

For Italy, the Institute of Medical Genetics of the Catholic University in Rome participated in the study, with the organizational support of AISEA.

Financial support was provided not only by AISEA, but also by the French association AFHA, with which the Italian association is working closely for the development of the international research on AHC.

For this collaborative study, AISEA provided the most extensive follow-up case series, contained in the Biobank and the Clinical Register I.B.AHC.

The I.B.AHC project is fully funded and coordinated by AISEA, in collaboration with its Scientific Committee. Thanks to this project, the data and the biological samples of 38 patients were collected and are kept in the I.B.AHC Biobank and Clinical Register for Alternating Hemiplegia, available for any research on AHC undertaken in Italy and abroad.

The diagnoses of the patients participating to I.B.AHC are validated by the Scientific Committee of AISEA; the Biobank is hosted in the laboratories of the Scientific Institute E. Medea, Bosisio Parini (LC) and managed according to the I.B.AHC protocol, thanks to an agreement between the Institute and AISEA.

AISEA is also working closely with all the other patient associations abroad, to create an international alliance with the aim of supporting more and more effectively the collaborative research, which proved to be absolutely strategic to the achievement of this first great success of the finding of the genetic cause of AHC.

Until now all the costs for the research on AHC and the support to the families have been almost entirely borne by their associations, through their voluntary work and the generous donations from private citizens and small organizations.

We hope that this important finding and the consequent increased knowledge of the characteristics and the genetic causes of this disease can finally raise more awareness in the public institution, in the major research funders, and in the scientific organizations and pharmaceutical companies.

To all of them we ask for specific investments to support the next stages of the research necessary to get to the development of an effective drug for the AHC, and to promote a better health and social care for the affected people.
We heartily thank the researchers of the Institute of Medical Genetics, Catholic University of Rome (Prof. Giovanni Neri, Prof. Fiorella Gurrieri and Dr. Danilo Tiziano) for their important contribution to the finding of the gene of AHC.

Many thanks to our Scientific Committee (Dr. Giuseppe Gobbi, Dr. Tiziana Granata, Prof. Federico Vigevano, Prof. Giovanni Neri, Prof. Edvige Veneselli, Dr. Claudio Zucca, Prof. Maurizio Clementi) and our advisors (Dr. Nardo Nardocci, Prof. Fiorella Gurrieri, Dr. Renato Borgatti) for their continued collaboration in the development of the research on AHC; many thanks also to the managers appointed by A.I.S.EA for the I.B.AHC Biobank (Dr. Maria Teresa Bassi) and for the I.B.AHC Clinical Registry (Dr. Melania Giannotta and Dr. Elisa De Grandis).

To contact the association A.I.S.EA Onlus info@aiseaonlus.org

Links

Article published on Nature Genetics http://www.nature.com/doifinder/10.1038/ng.2358
“De novo mutations in ATP1A3 cause alternating hemiplegia of childhood”

I.B.AHC Biobank and Clinical Registry for Alternating Hemiplegia http://en.ibahc.org
Tools for the development of the research on this rare disease