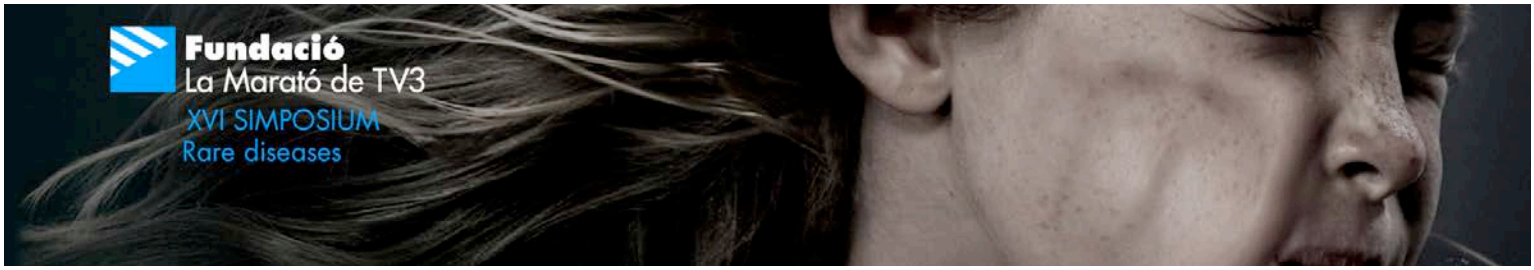

Clinical, genetic, epidemiological, pathophysiological and translational studies in spinocerebellar ataxias

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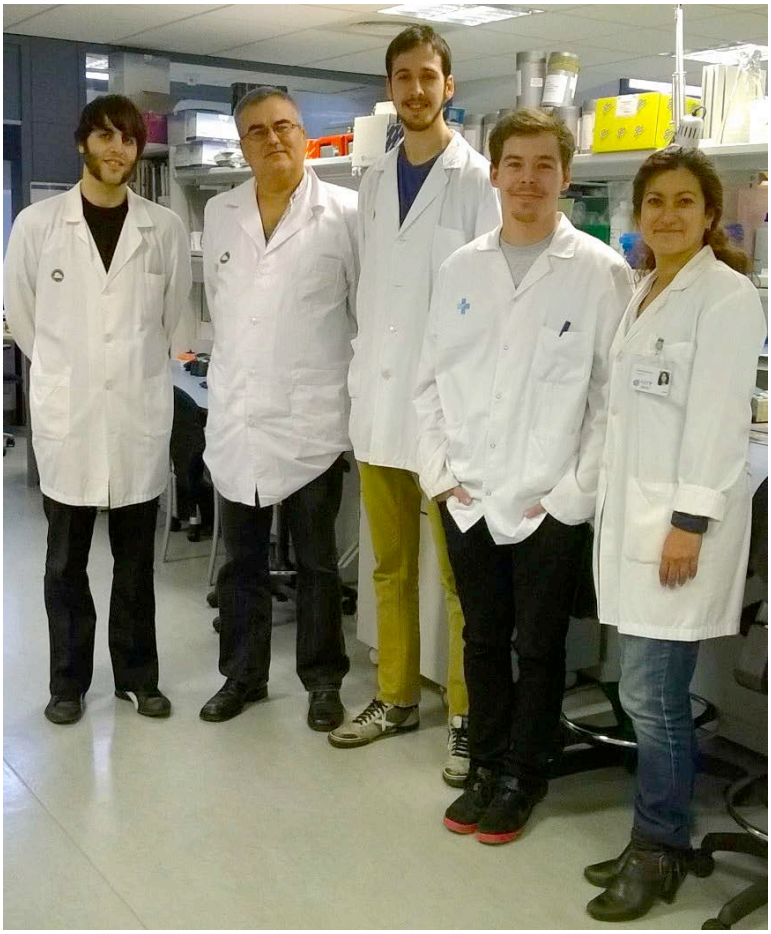

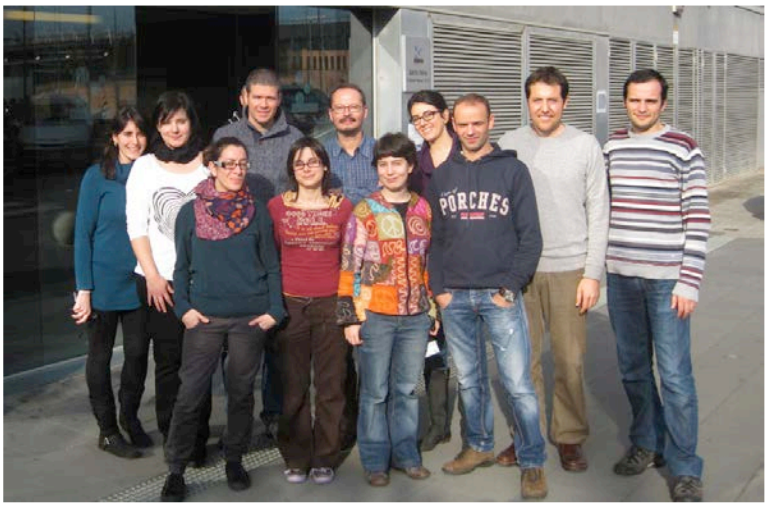
PORCHES

1. Project summary

The overall objective of the project is to implement a multidisciplinary approach to scientific research of spinocerebellar ataxias, including clinical, genetic, basic and translational aspects. To achieve this objective, a coordinated project is implemented in 5 different centres of excellence (IGTP, CSIC, IDIBELL, Hospital of Martorell, Hospital of Girona Dr. Josep Trueta). The research centres complement each other and bring both experience and human and material resources to achieve the objectives.

The specific objectives are the following:

1. To identify new genes and molecular deficits associated with spinocerebellar ataxias by using genetic, molecular and bioinformatics studies. To extend the molecular diagnosis in patients with ataxia pathology. To determine the incidence and prevalence of mutations in the general population. To implement phenotype-genotype correlations in all patients studied.

2. To characterise the molecular deficits and investigate the underlying neurodegenerative mechanisms in spinocerebellar ataxias. To obtain clinical, genetic, physiological and biochemical information in spinocerebellar ataxias (known as SCAS), a group of diseases of heterogeneous origin (hereditary or sporadic) characterised by progressive and irreversible impaired movement.

3. To identify and characterize new molecular pathways associated with spinocerebellar ataxias. To implement basic and translational research to obtain intrinsic knowledge of underlying neurodegeneration in spinocerebellar ataxias and into the molecular pathophysiological mechanisms, in particular in spinocerebellar ataxia type 1 (SCA1) among others. To transfer the knowledge acquired in the identification and implementation of therapies for spinocerebellar ataxias and other spinocerebellar neurodegenerations.

2. Results obtained

Objective 1:

1.1. We participated in the creation of a clinical registry of patients with spinocerebellar ataxias (SCAs) and their families in accordance with the following sub-objectives:

i. Patients participating in 4 clinical-genetic centres (Hospital Germans Trias i Pujol, Bellvitge Hospital, Dr. Josep Trueta Hospital and Hospital of Martorell) were recruited.

ii. A unified clinical research of the SCAs to document the clinical characteristics of patients included in the study protocol was defined and applied.

iii. Biological samples of ataxic patients from peripheral blood, urine, skin biopsy and autopsy tissues were obtained for clinical-genetic identification of biomarkers and basic and translational correlation studies.

1.2. A novel ataxia phenotype of dominant inheritance, SCA37, was identified and characterised. SCA37 is characterised by pure cerebellar ataxia in two Spanish families, although at least three additional families from the European continent are known to present with an identical phenotype. A unique feature in SCA37 is the presence of specific alterations of the vertical eye movements, which are pre-symptomatic signs of the disease.

1.3. New genetic factors associated with spinocerebellar ataxias have been identified. In particular we identified and located the genetic-molecular defect of SCA37 in the genomic region of 1p32. During the course of the project we identified the gene associated with SCA37 and we are in process of characterising the causative genetic defect. We extend these studies to the analysis of other patients with ataxia. Furthermore, we have identified 2 new causal genes and 12 mutations associated with ataxia phenotype previously not described. These findings enable us to identify new cellular and molecular mechanisms that produce ataxia and expand the number of ataxic patients with genetic diagnosis. We are researching the frequency of new ataxia subtypes identified in our population and the prevalence and epidemiology of the new mutations identified.

1.4. We have determined the incidence and prevalence of each mutation identified in the Catalan and Spanish populations. Known genes associated with spinocerebellar ataxia SCA were studied in a total of 1,909 cases with ataxia: 505 with familial and 1,404 sporadic origins respectively. In 200 family cases studied the causative mutations were identified. The causative mutations were not identified in any of the sporadic cases studied.

1.5. The phenotype-genotype correlations corresponding to all ataxia patients studied were established.

1.6. We are currently analysing the effects of the mutation in spinocerebellar ataxia type 37 (SCA37) in the SCA37 gene expression and pathophysiological mechanisms in post-mortem tissue from patients with the disease obtained through the neurological tissue biobank of the Hospital Clinic-IDIBAPS in Barcelona. Histology, immunohistochemistry, and electron microscopy studies in different regions of the affected nerve tissue obtained from post-mortem SCA37 patients clearly indicate a pure ataxia phenotype with exclusive cerebellar affectation. Furthermore, the neuropathological examination shows the presence of perisomatic granules (PSG) in the cerebellar neurons highlighting to glutamate receptor turn-over and regulation of such neurotransmitter as the subjacent physiopathological mechanism. These findings point to synaptic dysregulation as the underlying mechanism of neurodegeneration in SCA37. We are currently investigating this finding since this has not been previously described in any other type of ataxia.

Objectives 2 and 3:

We identified different molecular underlying mechanisms not associated previously with hereditary ataxia. We showed that the molecular route regulated by protein phosphatase type 2A (PP2A) activity is altered in early stages of cerebellar neurodegeneration. Characterisation of the identified alterations of this route enabled us to find altered substrates in the early processes involved during ataxia

neurodegeneration including mitochondrial metabolism, such as ATP production, oxidative stress, mitochondrial membrane potential and Ca^{2+} buffering capacity. These findings point to targets identified for modulating therapies and drugs and a few were tested in in vitro assays and in vivo studies with the aim of restoring the functionality of the altered cellular processes.

3. Relevance and possible implications

The description of a new genotype of spinocerebellar ataxia, SCA37 with features we have described for the first time has the following clinical implications:

1. It expands the diagnostic possibilities of autosomal dominant spinocerebellar ataxias (SCAs) that are not currently associated with a known genetic defect.

2. SCA37 is the first fully described SCA ataxia type in Spain and raises the need for new studies to determine its prevalence in our population, which should improve the efficacy of genetic studies in these diseases.

3. It allows the identification of risk carriers by identifying preclinical eye signs as clinical suspicion of SCA37 in young subjects of the studied families and in other families. This identification allows better definition of the strategy of genetic research in each individual and makes it more efficient. It also identifies a subgroup of patients with ataxia likely to start treatment in early stages of the disease before the classical cerebellar involvement is present.

4. Information on the prognosis and natural history of the disease by using profiling obtained during the monitoring of the clinical scale studied in a poorly prevalent rare disease. This is of great importance to patients and can be used as a historical control in future therapeutic trials.

5. Identification of a new locus of spinocerebellar ataxia has the following clinical implications:

i. It allows the identification of family members at risk for the disease before presenting preclinical signs.

i. It is the first step in the investigation of the implicated gene, already identified and characterised, and of future therapeutic options. In this regard we have made significant progress to understand the genetic and molecular basis of disease towards the implementation of specific therapies.

ii. It facilitates genetic counselling.

6. Identifying novel genes and genetic causative defects of ataxias opens new lines of research allowing the elucidation of the underlying physiopathological mechanisms for both its translation to clinical practice in the near future, and the identification of targets and molecular pathways, biomarkers, and the implementation of personalised specific treatments when they exist. As the targets and molecular pathways involved are common for most ataxias, the implemented studies are transferable to different types of ataxias and cerebellar degenerations.

7. In 2014, the "Functional Biology and Experimental Therapeutics Laboratory" in the Neurogenetics Unit at the IGTP was established with the aim of translating the results of the lines of research of the Unit to establishing functional assays for the identification of biomarkers and targets of therapeutic interest. The laboratory has been established to actively identify active compounds in screenings from different libraries either purchased commercially (US Food and Drug Administration, Dharmacon siGenome SmartPool, Prestwick Chemical Library, Chembridge, etc.), or obtained through collaborations with other research groups (mimetic peptides IQAC-CSIC) or industry. Transferability to clinical practice is envisaged in the medium term (three years) for those compounds proven in clinical trials (drug repositioning) and longer term (> 5 years) for those where biosafety tests type I need to be tested. To this aim we collaborate with the Medicinal Chemistry team at the IQAC-CSIC for modification and modulation of the active compounds identified in this project in order to transfer them

to pharmaceutical development. This group has proven experience in this type of studies.

8. An important component of this project, which is part of the Spanish Science and Technology Strategy, is the collaboration established with the private sector and industry, in this case with the Valencian company Sistemas Genómicos SL. As a result of the collaboration carried out since 2011 between the IGTP and IDIBELL groups and Sistemas Genómicos we have generated new genetic diagnostic tools, the neurogene 285® profile multigene panels, which prove very useful for early genetic diseases of study, such as ataxias among others, and enable an accurate diagnosis that complements clinical care, avoiding unnecessary additional testing, saving costs to the national health system and providing technology and innovation. This panel has been in commercial operation since the end of 2014. We are in the process of designing the panel for genetic diagnosis of lysosomal diseases, glycosylation, peroximal and creatine deficits, by genomic massive sequencing. This panel will be marketed by the end of 2015.

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Invited lectures

Invited Lecture A.Matilla-Dueñas: "Rare-Diseases Genetics in the era of Next-Generation Sequencing". First International Congress of Clinical Genetics and Genetic Counseling in Rare Diseases. Sevilla, Spain (2015).

Teaching A.Matilla-Dueñas: "actualització in Genètica Mèdica". Curs hospitalària formació, Hospital de Mataró, Barcelona, Spain (2015).

Teaching A.Matilla-Dueñas: "Genetics of neurological diseases: application of high-throughput genomics sequencing technology." Curso “Actualización en Genética Clínica”. Colegio de Biólogos de Cataluña. Barcelona, Spain (2015).

Invited Lecture Victor Volpini: "Neurodegenerative diseases in the evolutionary debate". Fundación Jiménez Díaz, Madrid, Spain (2015).

Invited Lecture Victor Volpini: "Advances in the field of neurodegenerative diseases: exome sequencing". VII International Conference on Rare Diseases and Orphan Drugs. Sevilla, Spain (2015).

Keynote Lecture A.Matilla-Dueñas: "Utility neurogene PROFILE® panel for the diagnosis of heterogeneous neurological diseases." Annual Meeting of the Spanish Society of Neurology, Valencia, Spain (2014).

Teaching A.Matilla-Dueñas: "Genetic study of ataxias: from genes to treatment". Training Course of the Commission for the study of degenerative ataxias and spastic paraparesias (CEAPED) of the Spanish Society of Neurology (SEN). Valencia, Spain (2014).

Invited Lecture FXGomis-Rüth: "Implicacions de la cristal·lografia de proteïnes en biologia/biomedicina". Research Institute of Hospital de la Santa Creu i Sant Pau, Barcelona, Spain. 13.2.2014.

Invited Lecture FXGomis-Rüth: "A 0.7 MDa multimeric proteinase inhibitor exhibits a unique Venus flytrap endopeptidase inhibitory mechanism". Conference on "Arthritis, Infections and Autoimmunity: Infections as an Ethiological Factor in Chronic Inflammatory Disease". Ustroń (Poland). 03/04/2014 - 09/03/2014.

Invited Lecture FXGomis-Rüth: "Infection and proteolysis: a molecular approach". University of Hamburg, Hamburg (Germany). 13.3.2014.

Invited Lecture FXGomis-Rüth: "Function minimal regulation in a metamorphic metallopeptidase". National Supercomputing Center, Barcelona, Spain. 9/5/2014.

Invited Lecture FXGomis-Rüth: "Reversible concentration-dependent oligomerization produces autoinhibition of a metamorphic metallopeptidase". The Protein Multiverse Conference, Madrid (Spain). 16.06.2014-17.06.2014.

Invited Lecture F.X.Gomis-Rüth: "Reversible concentration-dependent oligomerization Regulates metallopeptidase activity in a minimal". XVIII Gordon Research Conference on Proteolytic Enzymes and Their Inhibitors, Il Ciocco, Lucca (Barga) (Italy). 22.06.2014-27.06.2014.

Invited Lecture A.Matilla-Dueñas: "Deciphering new molecular pathways underlying spinocerebellar neurodegeneration: from genes to targets for therapy". University of Manchester, Manchester, UK (2014).

Invited Lecture A.Matilla-Dueñas: "Gene therapy based on adeno-associated virus (AAV) to treat Friedreich ataxia." Annual conference organized by FEDAES. Villagarcía de Campos (Valladolid), Spain (2014).

Invited Lecture Victor Volpini: "Atàxies hereditàries". Col.legi of Biòlegs de Catalunya, Barcelona, Spain (2014).

Invited Lecture Victor Volpini: "Genetic Counseling in Ataxias". Annual Conference of the Spanish Federation of Ataxias (FEDAES), Villagarcía de Campos, Valladolid, Spain (2014).

Teaching A.Matilla-Dueñas: "Genetic basis of neurological diseases. Application of new technologies for genetic diagnosis of heterogeneous diseases in Neurology". Curs "Advances in Human Genetics". Col·legi de Biòlegs de Catalonia. Barcelona, Spain (2014).

Invited Lecture A.Matilla-Dueñas: "Hereditary ataxias: from genes to therapy". IV Genetics and Disability Conference sponsored by the Royal Patronage on Disability and the Spanish Association of Human Genetics. Barcelona, Spain (2013).

Invited Lecture X.Gomis-Rüth: "Structural insights into the inhibitory mechanism of α2-macroglobulin". University of Halle / Wittenberg, Halle (Germany). 18.3.2013.

Invited Lecture X.Gomis-Rüth: "Processes Associated Proteolysis in cancer: a structural approach". Department of Molecular Biology, University of Salzburg, Salzburg (Austria). 8/4/2013.

Invited Lecture X.Gomis-Rüth: "Structural insight into the Venus fly-trap inhibitory mechanism of the 720-kDa proteinase pan-α2-macroglobulin tetramer". National Centre for Biotechnology, Madrid (Spain). 12.4.2013.

Invited Lecture X.Gomis-Rüth: "Structure of α2-macroglobulin, a Venus flytrap pan-protease inhibitor". XVII Gordon Research Conference on Matrix Metalloproteinases, XI, Il Ciocco, Lucca (Barga) (Italy). 19.05.2013-24.05.2013.

Invited Lecture Dr. X.Gomis-Rüth: "Structural studies of human α2-macroglobulin, a pan-protease inhibitor from blood". FASEB Science Research Conference on Proteases in Hemostasis and Vascular Biology, Sheraton Resort, Nassau (Bahamas). 02.06.2013-07.06.2013.

Invited Lecture X.Gomis-Rüth: "Structural insights into the Venus flytrap mechanism of inhibitory 0.7 MDa multimeric proteinase inhibitor". XIII Congress of the Spanish Society of Biophysics, Valencia, Spain. 19.06.2013-21.06.2013.

Invited Lecture X.Gomis-Rüth: "Structural biochemistry of metalloprotease regulation". Symposium de Biologie Structurale Institut de Biologie Structurale - IBS, Grenoble (France). 10.07.2013-12.07.2013.

Invited Lecture X.Gomis-Rüth: "At the interface of MS and MX: Structural insight into the Venus flytrap inhibitory mechanism of a multimeric 0,7MDa proteinase inhibitor".

International Symposium on the Frontier Between Cryo-EM and Protein Crystallography, Getxo (Bilbao), Spain. 03.10.2013-04.10.2013.

Invited Lecture I.deDiego: "Spinocerebellar ataxias and PP2A: a structural approach". IV Iberoamerican Conference on Movement Disorders: Spinocerebellar Ataxia and Parkinson's disease. Hospital Sant Pau, Barcelona, Spain. November 3-4, 2013.

Invited Lecture A.Matilla-Dueñas: "Neurogeneprofile 285 for genetic diagnosis of neurological diseases with genetic heterogeneity." XXVII Congress of the Spanish Society of Human Genetics (AEGH). Madrid, Spain (2013)

Invited Lecture C.Serrano Munuera: "SCA37: peculiarities of eye movements and definition of the phenotype". IV Genetics and Disability Conference sponsored by the Royal Council on Disability and the Spanish Association of Human Genetics. Barcelona, Spain (2013).

Invited Lecture Victor Volpini: "Genetic counseling in the medical practice." Menendez Pelayo International University. Santander, Spain (2013).

Invited Lecture Victor Volpini: "Hereditary ataxias: Genetic linkage analysis". VII National Congress of Clinical Laboratory. Bilbao, Spain (2013).

Invited Lecture A.Matilla-Dueñas: "Presentation of neurogene profile285® for genetic-molecular diagnosis of hereditary ataxias." Catalan Association of hereditary ataxias (ACAH). Barcelona, Spain (2013).

Invited Lecture A.Matilla-Dueñas: "Genetic diagnosis of neurological diseases with genetic heterogeneity: Neurogeneprofile 285". Annual Meeting of the Spanish Society of Neurology (SEN), Barcelona, Spain (2012).

Invited Lecture A.Matilla-Dueñas: "Spinocerebellar ataxias (SCAs): new modulators of ataxic phenotype and their application as therapeutic targets". Annual Meeting of the Spanish Society of Neurology (SEN), Barcelona, Spain (2012).

Invited Lecture A.Matilla-Dueñas: "Genetic diagnosis of neurological diseases with genetic heterogeneity: Neurogeneprofile 285". II International Symposium on Neurorehabilitation, Valencia, Spain (2012).

Teaching A.Matilla-Dueñas: "Neurobiology of movement". III Iberoamerican Course for the multidisciplinary study of movement disorders: Parkinson's Disease and Spinocerebellar ataxias. Lima, Peru (2012).

Teaching (Televideoconference) C.Serrano-Munuera, A.Matilla-Dueñas: "Spinocerebellar ataxia SCA37: clinical gene discovery". XVIII International Course in Neuroscience, Peruvian Institute of Neurological Sciences, Lima, Peru (2012).

Invited Lecture A.Matilla-Dueñas: "Ataxin-1 modulates protein phosphatase 2 (PP2) activity in spinocerebellar ataxia type 1 (SCA1) neurodegeneration". II Symposium IGTP-IMPPC. Badalona, Spain (2012).

Invited Lecture A.Matilla-Dueñas: "New scientific advances in spinocerebellar ataxias: characterization of a new subtype of dominant ataxia, SCA37, and a new molecular pathway involved in SCA1, the protein phosphatase PP2". Annual Conference organized by FEDAES. Villagarcía de Campos (Valladolid), Spain (2012).

Invited Lecture A.Matilla-Dueñas: "The launch of the National Scientific Registry of ataxias: a necessity." Annual Conference organized by FEDAES. Villagarcía de Campos (Valladolid), Spain (2012).

Invited Lecture X.Gomis-Rüth: "Recent advances in the structural biology of proteolysis and its regulation". Alumni Symposium - Protein Crystallography in Martinsried, itsa

Beginnings, Maturation, Dissemination, and no End; Max-Planck Institute of Biochemistry (Martinsried, Germany). 18.02.2012-19.02.2012.

Seminar X.Gomis-Rüth: "Structure of a2-macroglobulin". Joint Programme IBMB / IRB Structural and Computational Biology, Barcelona Science Park. 21.03.2012.

Invited Lecture X.Gomis-Rüth: "Insight into the molecular Venus flytrap: the structure of human methylamine-treated a2-macroglobulin". XVII Gordon Research Conference on Proteolytic Enzymes and Their Inhibitors, Il Ciocco, Lucca (Barga) (Italy). 17.06.2012-22.06.2012.

Invited Lecture X.Gomis-Rüth: "Structural biochemistry of proteolysis". Institute of Biotechnology, University of Helsinki, Helsinki (Finland). 03.09.2012.
Invited Lecture X.Gomis-Rüth: "Structural biochemistry of proteolysis in microbial virulence". Institute of Biochemistry, University of Gießen, Gießen (Germany). 11.10.2012.

Teaching A.Matilla-Dueñas: "II Course Neurogenetics for Neurologists" organized in collaboration with CIBERNED, CIBERER, SEN, and NEUROGENES. National Reference Centre for Attention to People with Rare Diseases and Their Families (CREER). Burgos, Espanya (2012).

Moderator Taula Rodona A.Matilla-Dueñas: "Framework for Addressing the Ataxias in Catalonia", organized by the Catalan Association of Hereditary ataxias (ACAH). Barcelona, Spain (2012).

Invited Lecture A.Matilla-Dueñas: "New cellular and molecular pathways of neurodegeneration in spinocerebellar ataxias". Annual Meeting of the Spanish Society of Neurology (SEN), Barcelona, Spain (2011).

Teaching A.Matilla-Dueñas: "Neurobiology of movement". II Iberoamerican Course for the multidisciplinary study of movement disorders: Parkinson's Disease and Spinocerebellar ataxias. Viña del Mar, Chile (2011).

Invited Lecture A.Matilla-Dueñas: "Clinical, Genetic, Epidemiologic and Translational Studies in the spinocerebellar ataxias: a multidisciplinary effort to investigate and treat ataxias". 1st Catalan Ataxia Conference organized by the Catalan Association of hereditary ataxias (ACAH). Barcelona, Spain (2011).

Invited Lecture Victor Volpini: "Genetics of the spinocerebellar ataxias". 1st Catalan Ataxia Conference organized by the Catalan Association of hereditary ataxias (ACAH). Barcelona, Spain (2011).

Invited Lecture Victor Volpini: "Bases of inheritance in monogenic diseases." In: “Fundamentals of Basic Genetics for Embryologists" Reprogenetics. ASEBIR VI Girona, Spain (2011).

Invited Lecture Victor Volpini: "Clinical and genetic heterogeneity of ataxias." Sistemas Genómicos Foundation. Valencia, Spain (2011).

Invited Lecture X.Gomis-Rüth: "Structural analysis of proteins by X-ray crystallography: overview and Its application to metallopeptidases". Department of Biochemistry and Molecular Biology, University of Valencia, Burjassot, Spain. 07.02.2011.

Invited Lecture X.Gomis-Rüth: "Recent advances in the structural characterization of metallopeptidases". X Gordon Research Conference on Matrix Metalloproteinases, Bryant University, Smithfield, Rhode Island (USA). 07.08.2011-12.08.2011.

Invited Lecture X.Gomis-Rüth: "Molecular evolution in metallopeptidases and their inhibitors". Department of Biotechnology, Chemical Institute of Sarria, Ramon Llull University, Barcelona, Spain. 18.11.2011.

Invited Lecture Dr. X.Gomis-Rüth: "Molecular evolution in metallopeptidases and their inhibitors". Biochemical Institute (Sonderforschungsbereich 877), Christian-Albrechts University of Kiel, Kiel (Germany). 22.11.2011.

Invited Lecture A.Matilla-Dueñas: "Pathogenic mechanisms of ataxias". Movement Disorders Study Group of the Spanish Society of Neurology (SEN), LXII Meeting SEN, Barcelona, Spain (2010).

Invited Lecture Victor Volpini: "Genetics of the cerebellar ataxias." First Iberoamerican Course for the study of movement disorders. RIVERMOV. Buenos Aires. Argentina (2010).

Invited Lecture Victor Volpini: "Ataxias: current genetic diagnosis and research beyond the paradigm". First Iberoamerican Workshop for the study of movement disorders. RIVERMOV. Buenos Aires. Argentina (2010).

Teaching A.Matilla-Dueñas: "Neurobiology of movement." I Iberoamerican Course for the multidisciplinary study of movement disorders: Parkinson's Disease and Spinocerebellar ataxias. Buenos Aires, Argentina (2010).

Invited Lecture A.Matilla-Dueñas: "The importance of networks as RIBERMOV to address scientific and medical challenges in Parkinson's disease and spinocerebellar ataxias". I Iberoamerican Workshop for the multidisciplinary study of movement disorders: Parkinson's Disease and Spinocerebellar ataxias. Buenos Aires, Argentina (2010).

Invited Lecture A.Matilla-Dueñas: "Molecular and cellular mechanisms in spinocerebellar ataxias". I Iberoamerican Workshop for the study of movement disorders: Parkinson's Disease and Spinocerebellar ataxias. Buenos Aires, Argentina (2010).

Invited Lecture A.Matilla-Dueñas: "Cellular and Molecular Pathways involved in Spinocerebellar Ataxias". Annual Conference organized by FEDAES. Villagarcía de Campos (Valladolid), Spain (2010).

Invited Lecture A.Matilla-Dueñas: "Spinocerebellar ataxia type 1 (SCA1): molecular pathways, pathogenic-mechanisms, and therapies". Annual International Conference of Euro-ataxia, Valladolid, Spain (2009).

Invited Lecture A.Matilla-Dueñas: "New research in dominant ataxia SCA1". Annual Conference organized by FEDAES. Villagarcía de Campos (Valladolid), Spain (2009).

Master theses

Kerrie Adrian Campbell, Master student of Molecular Biotechnology, IGTP, University of Barcelona: "Therapeutic treatment in a mouse model of Sanfilippo syndrome." In progress.

Alicia Hernández Pérez, Master in Biochemistry and Molecular Biology, IGTP, Autonomous University of Barcelona: "Study of mitochondrial dysregulation in the cerebellum of a mouse model of spinocerebellar ataxia type 1 (SCA1)". 09.2014

Ivan Domenech Mercadé, Master in Advanced Genetics, IGTP, Autonomous University of Barcelona: "Refinement and characterization of the genomic region 1p32 where the gene for spinocerebellar ataxia SCA37 is located". 07.2014.

Eudald Balagué Cabasés, Master in Biochemistry and Molecular Biology, IGTP, Autonomous University of Barcelona: "Study of the regulation of the regulatory mechanisms of ataxin-1 in PP2A activity." 09.2013.

Seró Mireia Torres, Master in Advanced Genetics, IGTP, Autonomous University of Barcelona: "genetic-molecular study of different subtypes of spinocerebellar ataxias". 07.2013.

Ainània Tecol Torres, Master in Genetics and Gnomish, GIBT, University of Barcelona: "genetic-molecular study of chorea acanthocytosis". 09.2013.

Queralt Caus Capdevila, Master in Neuroscience, IGTP, Autonomous University of Barcelona, Characterisation of the PPP1R2B and ANP32A Promoters and the role of ataxin-1, the protein associated with spinocerebellar ataxia type 1 (SCA1), in their regulation". 09.2013.

Mari Carmen García Guerrero, Master in Biochemistry and Molecular Biology, IGTP, Autonomous University of Barcelona: "differential for the study of motor and neuronal restoration grafting neural precursors in the mouse cerebellum SCA1 Proteomics". 09.2013.

Joel Puig Sadurni, Master in Advanced Genetics, IGTP, Autonomous University of Barcelona. "Molecular-Genetic Study of spinocerebellar ataxias: characterization of the region 1p32 in SCA37".

Carles Sanchez Riera, Master in Advanced Biotechnology, IGTP, Autonomous University of Barcelona. "Study of the expression of the leucine-rich acidic protein Anp32a in the brain of Alzheimer triple transgenic mouse". 07.2013.

Irene Garcia Ferrer. "Biophysical and biochemical characterization of synmetzin, a de novo designed minimal protease". University of Barcelona, 9.9.2011.

Mar Lopez Pelegrin. "Production and crystallization of putative metalloproteases from hyperthermophulic archaea". University of Barcelona, 22.7.2011.

Alba Peña Paris Master in Neuroscience, IGTP, Universitat Autònoma de Barcelona. "Molecular and proteomics studies in spinocerebellar ataxia type 1 (SCA1)". 09.2010.

Doctoral / PhD Theses

Eudald Balagué Cabasés, PhD Student in Neuroscience, IGTP, Autonomous University of Barcelona: "Gene therapy vectors based on adeno-associated virus (AAV) to treat a mouse model of Friedreich's ataxia." In progress.

Marc Corral Juan, PhD Student in Neuroscience, IGTP, Autonomous University of Barcelona: "Molecular Genetics of autosomal dominant ataxias: characterization of a new subtype spinocerebellar ataxia SCA37". In progress.

Carme Munuera Serrano, MD Neurologist, PhD in Medicine, Autonomous University of Barcelona. "Description of a new dominant spinocerebellar ataxia with altered vertical eye movements linked to a new locus". 03/11/2014. Cum Laude.

Sergio Trillo Muyo. "Structural and functional study of a protein inhibitor monodomain double-sided, sermetstatina, in complex with two peptidases of different kinds, subtilisin and esnapalisina". University of Barcelona, 31.5.2013. Cum Laude.
Tiago Oliveira Botelho. "Structural and functional studies on HmrA". University of Barcelona, 4.3.2011. Cum Laude.