EXAMPLE OF A SUCCESSFUL R&D COLLABORATION:
THE RIBERMOV LATIN-AMERICAN NETWORK ON
MOVEMENT DISORDERS.

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Director Functional and Translational Neurogenetics Unit
RIBERMOV Coordinator
Genetics Section Editor “The Cerebellum”
Health Sciences Germans Trias (IGTP)
Universitat Autònoma de Barcelona
Badalona (Barcelona), Spain
What is RIBERMOV?

www.ribermov.org
Clinical:
- Clinical Registry of patients.
- Unified Clinical Research Protocol.
- Biological Samples.
- Clinical-Genetic correlations.

Epidemiological:
- Estimate incidence and prevalence of studied diseases.

Genetics:
- Develop and implement new tools to facilitate diagnosis.
- Identify and characterise underlying genetic and molecular causes.

Translational:
- Identify and characterise new molecular pathways.
- Elucidate pathophysiological mechanisms.
- Translate the new knowledge to implement therapies.
To standardize methodologies to implement clinical and interventional studies.

To generate a record of clinical information with natural histories and to collect DNA samples for each registered individual.

To analyze the epidemiological impact and risk factors for these diseases in each participating country.

To provide genetic diagnosis and counseling as preventive measures.

To carry out familiar studies using genetic linkage, disequilibrium, and association analysis to identify new disease causal deficits.

To complement clinical investigations with basic research studies aimed to elucidate the underlying physiopathological molecular mechanisms.

To identify new risk factors including modifier genes aimed at understanding the clinical variability with direct towards the prognosis.

To identify new molecular pathways and biomarkers using molecular tools of structural biology, proteomics and transcriptomics studies to assist the diagnosis, prevention, and the design and development of effective therapeutic strategies.
1. To promote **Clinical Research**. To standardize methodologies in order to implement clinical, epidemiological and interventional studies. Information systems will be implemented to include the Hospital records of clinical information with natural histories and epidemiological data. DNA samples for each registered individual will be collected and a BioBank for Biological samples was created for the study of these pathologies.

2. To analyze the **epidemiological impact**, the prevalences, and risk factors for these diseases in each participating country.

3. To implement **diagnosis and genetic counseling** as preventive measures. Family studies were carried out using genetic linkage, disequilibrium and wide association studies to identify new disease genes and causal deficits. Modifier genes were also identified. Genotype-phenotype correlations were performed for causal molecular defects and potential neurophysiological biomarkers.

4. To complement clinical studies with **basic research** aimed to increase our knowledge of the underlying physiopathological molecular mechanisms. New risk factors including modifier genes were identified to explain the clinical variability with subsequent applications for the prognosis.
5. To identify new **molecular pathways and biomarkers** using molecular tools, structural biology, proteomics and transcriptomics studies to increase our knowledge of the underlying mechanisms to assist in diagnosis, prevention, and the design and establishment of therapeutic strategies.

6. To promote the design and establishment of **pre-clinical and clinical assays**.

7. To **promote training and exchange of specialists**, the **transfer of knowledge and technology** among the participating countries in the various disciplines of Clinical, Epidemiology, Genetics, and Basic Research. European standards were implemented in the Ibero-American participating groups for genetic and clinical protocols as well as in the regulations on consent and confidentiality in data processing, and for the usage and shipment of biological samples.

8. To generate a **website and an interactive platform** for the exchange and dissemination of knowledge, results, ideas, and for discussing projects or needs of each group and that of other groups in Latin-American countries.
# RIBERMOV Activities

<table>
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<th>Activities</th>
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<td>Meetings</td>
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<td>Training: 4 RIBERMOV TC</td>
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<td>Workshops</td>
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<td>Extra-mural grant funding</td>
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4 fellowships to attend III RIBERMOV TC in Lima, Peru, September 2012:

1. Raphael Machado de Castilhos (Brasil)
2. Juan Cristobal Núñez Fuster (Chile)
3. Denny Almaguer Gotay (Cuba)
4. Isabel Alonso (Portugal)
Scientific Meetings
XVIII Curso Internacional de Neurociencias,
Sociedad Peruana de Neurología, Agosto 2013
1\textsuperscript{ST} Bilateral Workshop CUBA-SPAIN, March 2011
IV International Symposium on Hereditary Ataxias

Themes in IV International Symposium on Hereditary Ataxias

1. Preclinical and Clinical Trials in SCA2 Patients and Other Polyglutamine Diseases.
2. Neuropharmacogenetics.
3. Neurodegenerative Diseases due to Proteinopathies: From SCA2 to Other Related Conditions (Huntington Disease, Amyotrophic Lateral Sclerosis, Parkinson Disease, Alzheimer Disease, Prion Diseases).
4. Neurochemistry and Immunology as Therapeutic and Diagnostic Tools for Hereditary Ataxias.
7. New Ataxias Electrophysiological Biomarkers.
9. Ethical and Psychological Aspects in the Diagnosis of Neurodegenerative Diseases.
10. Neuroinformatic and Neurosciences.
11. Hereditary Ataxias Seen Through the Experience of Patients and Relatives.
4th International Symposium on Inherited Ataxias, Varadero, Cuba, June 2011
AWARD RAFAEL ESTRADA in memoriam
Varadero, Cuba 2011

Los 5 premiados con el presidente del Jurado

Jonas Saute (Brasil) recibiendo el premio
TÍTOL: OXIDACIÓN DE DOPAMINA Y NEURODEGENERACIÓN DE NEURONAS EN LA ENFERMEDAD DE PARKINSON.

PONENT: PROF. JUAN SEGURA AGUILAR
PROGRAMA DE FARMACOLOGÍA CLÍNICA Y MOLECULAR, UNIVERSIDAD DE CHILE,
RED IBEROAMERICANA MULTIDISCIPLINAR PARA EL ESTUDIO DE LOS TRASTORNOS DEL MOVIMIENTO (RIBERMOV)-CYTED

DATA: DIVENDRES 11 MARÇ 2011

HORA: 12.00

LLOC: AULA POLIVALENT,
INSTITUT D’INVESTIGACIÓ EN CIÈNCIES DE LA SALUT GERMANS TRIAS I PUJOL (IGTP)

HOSTE: DR. ANTONI MATILLA, NEUROCIÈNCIES,
COORDINADOR RIBERMOV
Congreso Europeo de Neurociencias,
Barcelona,
Julio 2012

Congreso Internacional de Huntington,
Septiembre 2013
Visit to the National Institutes of Health, USA, May 2013

Annual Meeting of the American Neurology Society, San Diego, USA, 2013
Scientific Achievements
Laura Bannach Jardim, MD, PhD

e-mail: ljardim@hcpa.ufrgs.br

Médica.
Professora do Departamento de Medicina Interna, da Faculdade de Medicina da Universidade Federal do Rio Grande do Sul.
Chefe do Serviço de Genética Médica do Hospital de Clínicas de Porto Alegre
Coordenadora da Rede Neurogenética da UFRGS.

Áreas de interesse:
Neurogenética, Erros Inatos do Metabolismo e Aconselhamento Genético.
Atua principalmente em pesquisa clínica, sobre os seguintes temas: doenças neurogenéticas, como as ataxias espinocerebelares, e doenças neurometabólicas, como as esfingolipídoses e a adrenoleucodistrofia ligada ao X.
Ancestral Origin of the ATTCT Repeat Expansion in Spinocerebellar Ataxia Type 10 (SCA10)

Teresa Almeida¹, Isabel Alonso¹, Sandra Martins², Eliana Marisa Ramos¹, Luísa Azevedo², Kinji Ohno³, António Amorim²,⁴, Maria Luiza Saraiva-Pereira⁵, Laura Bannach Jardim⁵, Tohru Matsuura³, Jorge Sequeiros¹,⁶, Isabel Silveira¹*
Ataxia Rating Scales—Psychometric Profiles, Natural History and Their Application in Clinical Trials

Jonas Alex Morales Saute · Karina Carvalho Donis · Carmen Serrano-Munuera · David Genis · Luis Torres Ramírez · Pilar Mazzetti · Luis Velázquez Pérez · Pilar Latorre · Jorge Sequeiros · Antoni Matilla-Dueñas · Laura Bannach Jardim · On behalf of the Iberoamerican Multidisciplinary Network for the Study of Movement Disorders (RIBERMOV) Study Group

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Abstract We aimed to perform a comprehensive systematic review of the existing ataxia scales. We described the disorders for which the instruments have been validated and used, the time spent in its application, its validated psychometric properties, and their use in studies of natural history and clinical trials. A search from 1997 onwards was performed in the MEDLINE, LILACS, and Cochrane databases. The web sites ClinicalTrials.gov and Orpha.net were also used to identify the endpoints used in ongoing randomized clinical trials. We identified and described the semi-quantitative ataxia scales (ICARS, SARA, MICARS, BARS); semi-quantitative ataxia and non-ataxia scales (UMSARS, FARS, NESSCA); a semi-quantitative non-ataxia scale (INAS); quantitative ataxia scales (CATSYS).
The APOE ε2 Allele Increases the Risk of Earlier Age at Onset in Machado-Joseph Disease

Conceição Bettencourt, PhD; Mafalda Raposo, BSc; Nadiya Kazachkova, PhD; Teresa Cymbron, PhD; Cristina Santos, PhD; Teresa Kay, MD; João Vasconcelos, MD; Patrícia Maciel, PhD; Karina C. Donis; Maria Luiza Saraiva-Pereira, PhD; Laura B. Jardim, PhD; Jorge Sequeiros, MD, PhD; Manuela Lima, PhD

Arch Neurol. 2011;68(12):1580-1583
Short communication

Lrrk2 p.Q1111H substitution and Parkinson’s disease in Latin America

Ignacio F. Mata\textsuperscript{a,b,*}, Gregory J. Wilhoite\textsuperscript{c}, Dora Yearout\textsuperscript{a,b}, Justin A. Bacon\textsuperscript{c}, Mario Cornejo-Olivas\textsuperscript{d}, Pilar Mazzetti\textsuperscript{d}, Victoria Marca\textsuperscript{d}, Olimpio Ortega\textsuperscript{d}, Oscar Acosta\textsuperscript{e}, Carlos Cosentino\textsuperscript{f}, Luis Torres\textsuperscript{f}, Angel C. Medina\textsuperscript{g}, Carolina Perez-Pastene\textsuperscript{h}, Fernando Díaz-Grez\textsuperscript{h}, Carles Vilariño-Güell\textsuperscript{c,i}, Pablo Venegas\textsuperscript{j}, Marcelo Miranda\textsuperscript{j,k}, Osvaldo Trujillo-Godoy\textsuperscript{l}, Luis Layson\textsuperscript{l}, Rodrigo Avello\textsuperscript{m}, Elena Dieguez\textsuperscript{n}, Victor Raggio\textsuperscript{o}, Federico Micheli\textsuperscript{p}, Claudia Perandones\textsuperscript{p}, Victoria Alvarez\textsuperscript{q}, Juan Segura-Aguilar\textsuperscript{d}, Matthew J. Farrer\textsuperscript{c,i}, Cyrus P. Zabetian\textsuperscript{a,b}, Owen A. Ross\textsuperscript{c}
Online First

New Subtype of Spinocerebellar Ataxia With Altered Vertical Eye Movements Mapping to Chromosome 1p32

Carmen Serrano-Munuera, MD; Marc Corral-Juan, BSc; Giovanni Stevanin, PhD; Hector San Nicolás, BSc; Carles Roig, MD, PhD; Jordi Corral, BSc; Berta Campos, PhD; Laura de Jorge, BSc; Carlos Morcillo-Suárez, PhD; Arcadi Navarro, PhD; Sylvie Forlani, MD, PhD; Alexandra Durr, MD, PhD; Jaime Kulisevsky, MD, PhD; Alexis Brice, MD, PhD; Ivelisse Sánchez, PhD; Victor Volpini, MD, PhD; Antoni Matilla-Dueñas, PhD
New Subtype of Ataxia Identified

Apr. 29, 2013 — Researchers from the Germans Trias i Pujol Health Sciences Research Institute Foundation (IGTP), the Bellvitge Biomedical Research Institute (IDIBELL), and the Sant Joan de Déu de Martorell Hospital, has identified a new subtype of ataxia, a rare disease without treatment that causes atrophy in the cerebellum and affects around 1.5 million people in the world.

Related Topics

Health & Medicine
- Today's Healthcare
- Diseases and Conditions
- Personalized Medicine

Mind & Brain
- Alzheimer's
- Disorders and Syndromes
- Stroke

Articles
- Rett syndrome
- Neurology
- Huntington's disease
- Traumatic brain injury
- Transmissible spongiform encephalopathy
- Multiple sclerosis

Related Stories

Dysfunction in Cerebellar Calcium Channel Causes Motor Disorders and Epilepsy (Mar. 21, 2013) — A dysfunction of a certain calcium channel, the so-called P/Q-type channel, in neurons of the cerebellum is sufficient to cause different motor disorders as well as a special type of epilepsy.

New Genetic Disorder of Balance and Cognition
Targeted Exome Sequencing
NEUROLOGICAL DISEASES: 400 genes
(Neurogene Profile®)

MYASTHENIAS
NEUROPATHIES
- Demyelinating
- Axonal
- Intermedium
- AD, AR, LX

88 GENES

ATAXIAS
LEUCODISTROPHIES
- Spinocerebellar
- Episodic
- Spastic
- Telangiectasia
- Friedreich
- Syndromic

99 GENES

DEMENTIAS
ALS
PARKINSON TREMOR
- Late Onset
- Early Onset
- Dementia with Parkinsonism

PARAPLEGIAS
- AD
- AR
- Syndromic

89 genes

DIOSTROPHIES
MIOPATHIES
- Emery-Dreyfuss
- Waist
- Distroglycans
- D Merosin

- M. Disproportion fiber
- Miotubular
- Nemalinic
- Minicore

74 genes
ALGORITHM FOR THE GENETIC DIAGNOSIS OF INHERITED ATAXIAS

**AUTOSOMAL DOMINANT**
- EXPANSION DETECTION: SCAs 1, 2, 3, 6, 7, 10, 12, 17, 36, DRPLA

**AUTOSOMAL RECESSIVE**
- GAA EXPANSION: Friedreich Ataxia

**MULTIGENE PANEL**
- ATAXIAS: 99 GENES

**X-LINKED INHERITANCE**

**NEGATIVE**

**EXOME SEQUENCING**
- RESEARCH
ALGORITHM FOR THE DIAGNOSIS OF INHERITED NEUROPATHIES

MLPA: 5 genes
Negative

MULTIGENE PANEL CMT: 88 genes
Negative

NEUROLOGICAL DISEASES

EXOME SEQUENCING
RESEARCH
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<th>METHODOLOGY</th>
<th>SAMPLE</th>
<th>SYMPTOMS</th>
<th>INHERITANCE</th>
<th>ANALYSED GENES</th>
<th>MUTATED GENE</th>
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<th>GENETIC DIAGNOSIS</th>
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<td>ATAXIA</td>
<td>AR</td>
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<td>Het. c.9938delC (Exón 10) p.Pro3313Glnfs*11</td>
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<td>AT-2</td>
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<td>CACNA1A</td>
<td>CACNA1A</td>
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<td>SCAS/15/26/29?</td>
<td>AD</td>
<td>ATAXIAS PANEL</td>
<td>ITPR1</td>
<td>Het. c.4218C&gt;G (Exón 32) p.Glu1406Gln</td>
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<td>AR</td>
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<td>ATM</td>
<td>Homo c.11991C&gt;G (Exón 7) p.Leu400Pro</td>
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<td>ATAXIA WITH OCULOMOTOR APRAXIA</td>
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<td>ATAXIAS PANEL</td>
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<td>Compound Het. c.6679C&gt;T (Exón 4B) p.Arg2227Cys</td>
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<td>Compound Het. c.771C&gt;G (Exón 5) p.His257Gln</td>
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<td>ATAXIA, HEARING LOSS, EARLY MENOPAUSE</td>
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<td>EXOME</td>
<td>C100RF2</td>
<td>Compound Het. c.85C&gt;T (Exón 1) p.Arg29*</td>
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<td>ATAXIA, SPASTIC PARAPLEGIA, MYOCEROTIC TREMOR</td>
<td>AR</td>
<td>EXOME</td>
<td>RNF170</td>
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**Familia AT-9**

- I:1
- I:2
- II:1
- II:2
- II:3

**Familia AT-10**

- I:1
- I:2
- II:1
- II:2
- II:3
- II:4
- II:5

* = affected individual
LIMITATIONS

1. Heterogeneity in resources in participating groups
   - Funding resources
   - Human resources
   - Methodologies, etc

2. Different country regulations:
   - Biobank
   - Biological samples
   - Consentment forms for Genetics studies
   - Patient Data Protection
   - Intellectual Property
   - Etc.
CONCLUSIONS

1. Latin-American Collaborative Networks and Projects are needed and welcome

2. More Funding and Resources to Latin-American Groups to make them possible

3. Identify problems and limitations to overcome them

4. Successful interactions

5. Training is highly benefited: human resources

6. Translation and Exploitation of Results

7. Collaboration with Industry

8. Latin-American groups are very well trained, very eager to collaborate, but have limitations and resources and funding.
Barcelona, Spain, 2013
Thank you for your attention!!