

**4th International Meeting**  
**HIRSCHSPRUNG DISEASE AND RELATED**  
**NEUROCRISTOPATHIES**

**Sestri Levante (Genoa), April 22-24, 2004**

**Nunziata Centre - Mediterranean Foundation**  
**Via Portobello, 14**

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**Thursday, April 22, 2004 - Morning**

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- 08.30      Opening ceremony and Authorities  
**Dott. Biasotti** (Liguria Region President), **Ing. R. Levaggi** (Regional Health Councillor),  
**Dott. U. Serra** (President of Giannina Gaslini Institute), **Ing. B. Musso** (Vice-President of Gaslini Foundation), **Prof. L. Moretta** (Scientific Director of Giannina Gaslini Institute), **Dott. A. Lavarello** (Mayor of Sestri Levante)

**History of dysganglionoses**

- Chairmen:    **V. Jasonni**  
                  **R. Ravazzolo**
- 09.00      **J.L. Grosfeld**  
                  Historical presentation of Hirschsprung disease and its management
- 09.30      **G. Romeo**  
                  History and perspectives of the molecular genetics of Hirschsprung disease
- 10.00      Coffee break

**Development of Enteric Nervous System**

- Chairmen:    **J.A. Tovar**  
                  **A. Di Benedetto**  
                  **G. Martucciello**
- 10.30      **M.D. Gershon**  
                  Colonisation of the colon: molecular guidance molecules that help migrating enteric neuronal precursors to find where they belong in the bowel
- 11.00      **V. Pachnis**  
                  Coordinate control of enteric nervous system development by multiple signalling pathways
- 11.30      **J.F. Brunet**  
                  PHOX2 B and the ontogeny of autonomic reflex circuits
- 12.00      **W.J. Pavan**  
                  Functional genomic analysis of neural crest development
- 12.30      **K.H. Schaefer**  
                  Expression of neuronal, glial, and stem cell markers during human enteric nervous system development

12.50 Lunch

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### Thursday, April 22, 2004 - Afternoon

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#### Molecular genetics in Hirschsprung disease (I)

Chairmen: **A. Chakravarti**  
**R. Ravazzolo**

- 14.30 **S. Lyonnet**  
Multigenic Hirschsprung and syndromic variants of Hirschsprung
- 15.00 **M. Goossens**  
Molecular genetics of syndromic Hirschsprung disease: SOX10 and ZFHX1B (SIP1) molecular defects
- 15.30 **R. Hofstra**  
Mapping putative mutations as the major contributor to the development of sporadic Hirschsprung disease to the RET genomic sequence between the promoter region and exon 2
- 16.00 **A. Mc Callion**  
Comparative functional genomic approaches of Hirschsprung
- 16.30 Coffee break

#### Molecular genetics in Hirschsprung disease (II)

Chairmen: **S. Lyonnet**  
**G. Romeo**

- 17.00 **P. Tam**  
Ret haplotype in Chinese Hirschsprung patients
- 17.30 **To be announced**  
PHOX2 B as candidate gene for Hirschsprung disease
- 18.00 **J. Amiel**  
Molecular and developmental bases of congenital central hypoventilation syndrome (Ondine's course)
- 18.20 **I. Ceccherini**  
Genetic variants and molecular pathogenesis underlying Hirschsprung disease and congenital central hypoventilation syndrome
- 18.50 **I. Shepherd**  
Positional cloning of the zebrafish ENS mutant lessen

#### Evening Chakravarti's keynote lecture

- 21.00 - 21.45 **A. Chakravarti**  
Are RET mutations necessary and sufficient for Hirschsprung disease?

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## Friday, April 23, 2004 - Morning

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### Intestinal dysganglionoses

- Chairmen: **A.M. Holschneider**  
**P.L. Lelli-Chiesa**  
**M. Lima**
- 08.00 **P. Puri**  
Variant Hirschsprung's diseases
- 08.30 **W. Meier-Ruge**  
Pathological findings in Colonic Motility disorders
- 09.00 **H. Kobayashi**  
What exactly is "hypoganglionosis"
- 09.20 **J. Sutcliffe**  
Are we comparing apples with oranges? Interstitial cells of Cajal reporting in human disease
- 09.35 **A. Pini Prato**  
4 years experience with Solo-RBT in the diagnosis of intestinal dysganglionoses
- 09.50 **A.M. Holschneider**  
Clinical relevance of Dysganglionoses with special regard to Intestinal Neuronal Dysplasia
- 10.20 Coffee break

### Intestinal Neuronal Dysplasia

- Chairmen: **W. Meier-Ruge**  
**A. Barabino**  
**G. Martucciello**
- 11.00 **M. Hatano**  
Animal model of IND
- 11.25 **R. Kapur**  
Hox 11L1-null mice and other rodent models of intestinal pseudo obstruction
- 11.50 **W. Coerdts**  
Quantitative morphometric analysis of the submucous plexus in age-related control groups
- 12.05 **H. Kobayashi**  
IND: primary or secondary disorder
- 12.25 **S. Borghini**  
Molecular studies on HOX11L1
- 12.40 **Y. Sato**  
The search of a novel gene responsible for Hirschsprung disease and related neurocristopathies
- 12.55 Lunch

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## Friday, April 23, 2004 - Afternoon

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### Concurrent sessions -Room A and Room B:

#### Room A - Paper presentations - Development and molecular genetics

Chairmen: **I. Ceccherini**

**R. Hofstra**

14.10 **G.D.H. Croaker**

Screening of GFRalpha1, and limited screening of RET in Hirschsprung's disease confirms the importance of polymorphisms in disease susceptibility

14.25 **S. Moore**

Combined associations of RET and EDNRB in sporadic Hirschsprung disease

14.40 **G.M. Burzynski**

Identification of an unknown functional disease variant with a dosage-dependent effect in HSCR: sequencing the 5' region of the RET locus

14.50 **M.G. Borrello**

Biological effects of the dual phenotypic janus mutation of the RET co-segregating with both multiple endocrine neoplasia type 2 and Hirschsprung's disease

15.00 **C. Carniti**

Experimental models for the study of the RET mutations responsible for Hirschsprung's disease

15.10 **A. Burns**

Analysis of the role of RET as a dependence receptor during enteric nervous system development

15.20 **N. Bondurand**

Control of ENS differentiation by ET3 and SOX10

15.30 **J.M. Delalande**

Investigation of the signalling mechanisms utilised by sacral neural crest cells during development of the enteric nervous system in the chick embryo

15.40 **K.K. Chan**

Abnormal enteric ganglia development in transgenic mice with ectopic expression of mutant SOX10 in the vagal neural crest

15.50 **V.C.H. Lui**

Sonic Hedgehog (SHH) regulates the proliferation, migration and differentiation of the enteric neural crest stem cells (NCSCS) in gastrointestinal tract

16.00 Coffee break

#### Room A -Poster view and discussion - Development and molecular genetics

16.20 **J.B.M.G. Verheij**

Hirschsprung database: a useful tool for clinical and genetic studies in Hirschsprung patients and their families

**P. Zordan**

In vivo strategy for the analysis of the mouse RET gene promoter region

**I. Matera**

Role of PHOX2B frame-shift mutations and polyalanine expansion in congenital hypoventilation syndrome

**P. Griseri**

Nucleotide variants associated with a rare RET haplotype might affect post-transcriptional regulation

**F. Puppo**

Chromatin conformation identifies evolutionary conserved non-coding elements modulating tissue-specific RET gene expression and likely involved in human disease

**F. Lantieri**

Hirschsprung disease and associated haplotypes of the RET proto-oncogene in the Italian population

**G. Martucciello**

In vivo inoculation of neural crest derived neuroblasts

**A. Brizzolara**

Histochemical study of Dom mouse enteric nervous system

**Room A - Unified session - Proposal of International Guidelines on "criteria for classification and diagnosis of dysganglioneses "**

Chairmen: **J. Grosfeld** (JPS Editor-in-Chief)  
**J.A. Tovar** (JPS European Editor)

17.30 Participants:  
**W. Meier-Ruge, P. Puri, G. Martucciello, A.M. Holschneider**

**Room B - Satellite Workshop on pathology (multifocal microscopy available for live discussion)**

Chairmen: **W. Meier-Ruge**  
**C. Gambini**

14.10 Participants:  
**W. Meier-Ruge, R. Kapur, P. Puri, G. Martucciello, A. Sementa, C. Gambini, H. Kobayashi, W. Coerd**

16.00 Coffee break

**Room B - Paper presentations - Clinical session**

Chairmen: **G. Amici**  
**A. Leggio**  
**G. Riccipetioni**

16.20 **S. King**  
Slow Transit in Children: an update from the Royal Children's Hospital in Melbourne

16.30 **G.D.H. Croaker**  
A new technique suggests frequent abnormalities in heart rate control in Hirschsprung's disease (HSCR)

16.40 **A.S. Brooks**  
Evidence that Goldberg-Shprintzen and Mowat-Wilson Syndrome are different disease entity: a clinical and molecular study

16.50 **T. Balducci**  
Distribution of interstitial cells of Cajal and NOS immunohistochemistry in Hirschsprung disease: our experience

16.57 **G. Li Voti**  
Anorectal malformation associated to Hirschsprung disease, mesenterium

- commune and unilateral renal agenesis
- 17.04 **E. Ferrucci**  
Topical application of isosorbide dinitrate in patients with persistent constipation after pull-through, for Hirschsprung disease
- 17.14 **L. Migliazza**  
Primary transanal endorectal pull-through for rectosigmoid Hirschsprung's disease: results in 14 cases
- 17.24 **S. Chatterjee**  
A new concept in definitive surgery for total colonic aganglionosis
- 17.30 **D. Jovanovic**  
Modified operation for Hirschsprung disease: a report of 222 cases
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**Saturday, April 24, 2004**

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### **Surgical treatment of Dysganglionoses**

- Chairmen: **J.A. Tovar**  
**P. Puri**  
**V. Jasonni**
- 08.00 **A. Coran**  
Enterocolitis associated with Hirschsprung disease: a clinical-radiological and histopathological characterisation
- 08.25 **J.A. Tovar**  
Swenson operation
- 08.40 **G. Martucciello**  
Soave operation
- 08.55 **J.L. Grosfeld**  
Long term follow up for Duhamel operation
- 09.10 **L. De La Torre**  
Transanal endorectal pull-through
- 09.25 **K. Georgeson**  
Laparoscopic Endorectal pull through
- 09.40 Coffee break

### **Workshop on surgical treatment of dysganglionoses\*\*\***

- Chairmen: **A.M. Holschneider** (Editor of European Journal of Pediatric Surgery)  
**G. Romeo**  
**V. Jasonni**
- 10.00 Participants:  
**A. Coran, A. El-Hadidi, L. De La Torre, J.L. Grosfeld, K. Georgeson, G.A. MacKinlay,**  
**G. Martucciello, G. Mattioli, P. Puri, P. Tam, J.A. Tovar**  
\*\*\*Each Author will briefly present his own experience (5 to 7 minutes).

The meeting will be subsequently held in an interactive way (questions and answers for each lecturer)

Special topic: Redo surgery in Hirschsprung disease

- Chairman: **M. Rivosecchi**
- 12.00 **A. Coran**  
Redo operations for Hirschsprung disease
- 12.25 **V. Jasonni, R. Ravazzolo, C. Gambini**  
Final Remarks
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**Scientific Secretariat**

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**Scientific Committee**

**V. Jasonni, R. Ravazzolo, I. Ceccherini, C. Gambini, G. Martucciello**

**Organizing Secretariat**

**M.C. Cogorno - M. Aloe**

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