



**6<sup>th</sup> INTERNATIONAL SYMPOSIUM  
ON DEVELOPMENT OF THE ENS:  
THE FIRST 1000 DAYS**

FERRARA (ITALY), St. ANNA HOSPITAL  
APRIL 24-27, 2022



**6<sup>th</sup> International ENS Symposium on the  
Development of the ENS: The First 1000 Days**

Ferrara (I) - April 24-27, 2022  
Conference Hall, St. Anna Hospital

**FINAL PROGRAMME**

**Sunday, April 24**

**AFTERNOON 4.30 p.m.**

**Plenary room**

4.30 p.m.      **Registration**

5.30 p.m.      **Welcoming Ceremony *Roberto De Giorgio***

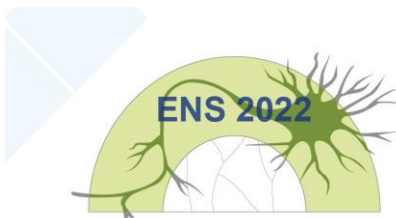
- Mayor of the City of Ferrara
- Rector of the University of Ferrara
- Dean of the Faculty of Medicine
- CEO of St. Anna University Hospital

Chairperson: *Roberto De Giorgio*

6.00 p.m.      **Keynote online - Lecture**  
Enteric Neurology: Challenges and Perspectives *Michael Schemann*  
*Discussion*

7.00 p.m.      **End of Session**

7.00 p.m.      **Welcome Cocktail Reception**



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### Monday, April 25

MORNING - 9.00 a.m. (Open coffee: 10.00 a.m.-11.30 p.m.)

#### Plenary room

##### ENS DEVELOPMENT

Chairpersons: **Nandor Nagy and Alan Burns**

9.00 a.m. New understanding on ENS development **Hideki Enomoto**  
*Discussion*

##### ORAL COMMUNICATIONS

9.20 a.m. EFFECTS OF SOX10 ON MURINE ENTERIC NERVOUS SYSTEM LINEAGE ALLOCATION  
**Avila Justin, Benthal Joseph, Southard-Smith Michelle**

9.30 a.m. JOINT SINGLE-NUCLEUS ATAC AND RNA SEQUENCING REVEAL CHROMATIN CLOSING AT  
DISTAL REGULATORY ELEMENTS DURING GLIAL-TO-NEURON DIFFERENTIATION  
**Guyer Richard, Bhave Sukhada, Stavely Rhian, Hotta Ryo, Goldstein Allan**

9.40 a.m. Epigenetic and environmental factors of neuronal lineage maintenance and survival **Robert  
Heuckeroth**  
*Discussion*

##### ORAL COMMUNICATIONS

10.00 a.m. SMOOTH MUSCLE DEPENDENT ENTERIC NERVOUS SYSTEM MORPHOGENESIS IN THE FETUS  
**Chevalier Nicolas, Amedzrovi Agbesi Richard J**

10.10 a.m. UNDERSTANDING THE DEVELOPMENT AND REGIONALISATION OF THE COLONIC ENTERIC  
NERVOUS SYSTEM.  
**Rahim Maryam, Lasrado Reena, Laddach Anna, Progatzy Franze, Kuehn Reimer, Pachnis  
Vassilis**

##### MOLECULAR PROFILING OF THE ENS

Chairpersons: **Nikhil Thapar and Vassilis Pachnis**

10.20 a.m. Neuronal lineages in the ENS **Michelle Southard-Smith**  
*Discussion*

10.40 a.m. Transcriptional profiling the ENS **Ulrika Marklund**  
*Discussion*

##### ORAL COMMUNICATIONS

11.00 a.m. NEUROGENESIS AND NEURONAL DIVERSITY IN THE ADULT ZEBRAFISH ENTERIC  
NERVOUS SYSTEM REVEALED USING RNA-SEQUENCING  
**Heanue Tiffany, Fourli Elina, Shapiro Michael, Boeing Stefan, McCallum Sarah, Obata Yuuki,  
Pachnis Vassilis**

11.10 a.m. RECONSTRUCTING ENTERIC NERVOUS SYSTEM LINEAGES AT SINGLE-CELL RESOLUTION  
**Laddach Anna, Chng Song Hui, Shapiro Michael, Progatzy Fränze, Kleinjung Jens, Pachnis  
Vassilis, Lasrado Reena**



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11.20 a.m. Neurobiopathology in zebrafish **Julia Ganz**  
*Discussion*

### ORAL COMMUNICATIONS

11.40 a.m. SHARED FEATURES OF ENTERIC CELL TYPES ACROSS SPACE, TIME AND SPECIES  
**Morarach Khomgrit, Techameena Prach, Marklund Ulrika**

11.50 a.m. SINGLE-CELL RNA SEQUENCING REVEALS MOLECULAR DIVERSITY OF ENTERIC GLIAL CELLS  
IN THE PEDIATRIC INTESTINE

**Windster Jonathan, Kuil Laura, Kakiailatu Naomi, Antanaviciute Agne, Sacchetti Andrea, Peulen-Zink Joke, Kan Tsung-Wai, Bindels Eric, De Pater Emma, Yousefi Soheil, Barakat Stefan, Kapur Raj, Meeussen Conny, Sloots Pim, Wijnen Rene, Melotte Veerle, Simmons Alison, Hofstra Robert, Alves Maria**

12.00 p.m. *Lunch*

**POSTER SESSION** (during lunch time) – with ‘Discussants’ (to entice interaction between audience and poster presenters)

Poster tour Discussants: **Pieter Vanden Berghe, Meenakshi Rao, Nandor Nagy, Elly Ngan, Gemma Mazzuoli-Weber**

**AFTERNOON - 2.00 p.m.** (Open coffee: 2.30 p.m.-4.30 p.m.)

### Plenary room

#### ENS STRUCTURE AND FUNCTION

Chairpersons: **Catia Sternini and Meenakshi Rao**

2.00 p.m. Neuron **Nick Spencer**  
*Discussion*

### ORAL COMMUNICATIONS

2.20 p.m. CHARACTERISATION OF SUBMUCOSAL NEURON CLASSES IN THE MOUSE SMALL INTESTINE  
**Wei Li, Morarach Khomgrit, Mikhailova Anastassia, Marklund Ulrika**

2.30 p.m. MECHANOSENSITIVITY OF ENTERIC NEURONES IN THE GUINEA PIG STOMACH  
**Mayr Sophia, Schliep Ronja, Mazzuoli-Weber Gemma**

2.40 p.m. Glia **Brian Gulbransen**  
*Discussion*

### ORAL COMMUNICATIONS

3.00 p.m. PROBING FUNCTIONAL HETEROGENEITY OF ENTERIC GLIA USING A NEW LIVE-IMAGING PARADIGM TO VISUALIZE CELL BEHAVIORS IN SITU

**Muppirala Anoohya, Anderson Michael, Rao Meenakshi**

3.10 p.m. GENETIC TARGETING OF CALCB-EXPRESSING ENTERIC NEURONS REVEALS REGIONAL HETEROGENEITY AND SEX-DEPENDENT FUNCTIONS IN VIVO

**Musser Melissa, Rutlin Michael, Grabowski Kathryn, Louis Adriell, Rao Meenakshi**

#### ENS AND ITS ENVIRONMENT



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Chairpersons: *Iain Shepherd and Jean Pierre Timmermans*

3.20 p.m. Glia and environmental factors **Werend Boesmans**  
*Discussion*

**ORAL COMMUNICATIONS**

3.40 p.m. ENTERIC GLIA MODULATE VISCERAL HYPERSENSITIVITY THROUGH THE CONNEXIN-43  
DEPENDENT SENSITIZATION OF TRPV1 NOCICEPTORS DURING INFLAMMATION  
**Morales-Soto Wilmarie**, McClain Jonathon, Tykocki Nathan, Gulbransen Brian

3.50 p.m. ENTERIC CHOLINERGIC NEURONS PARTICIPATE IN INTESTINAL HOMEOSTASIS BY  
REGULATING EPITHELIAL TUFT CELL LINEAGE SPECIFICATION  
**Fu Ming**, Kuruvilla Korah, Guan Peihong, Cailleux Frederic, Pierre Joseph, Gosain Ankush

4.00 p.m. Neuronal degeneration and regeneration **Subhash Kulkarni**  
*Discussion*

**ORAL COMMUNICATIONS**

4.20 p.m. MULTIPLE TYPES OF TISSUE-RESIDENT ENTERIC NEURAL PROGENITORS CAN BE TARGETED  
BY EXOGENOUS GDNF FOR THE TREATMENT OF HIRSCHSPRUNG DISEASE  
**Gary Alassane**, Soret Rodolph, Lassoued Nejia, Lefèvre Marie, Pilon Nicolas

4.30 p.m. ENTERIC NEURAL PLASTICITY DURING THE 24-HOUR CIRCADIAN CYCLE  
**Leembruggen Anita**, Nash Amelia, Stamp Lincon, Bornstein Joel, Hao Marlene

4.40 p.m. Extracellular matrix **Ankush Gosain**  
*Discussion*

**ORAL COMMUNICATIONS**

5.00 p.m. ENTERIC NEURONS EXHIBIT A REMARKABLE ABILITY TO REFORM NETWORKS AND  
REINNERVATE THE POSTNATAL INTESTINE  
**Stavely Rhian**, Rahman Ahmed, Bousquet Nicole, Pan Weikang, Guyer Richard A, Omer  
Meredith, Goldstein Allan M, Hotta Ryo

5.10 p.m. LOSS OF NDRG4 INDUCES INTESTINAL DYSMOTILITY AND CHANGES IN INTESTINAL CELL  
COMPOSITION IN ZEBRAFISH  
**Vaes Nathalie**, Kuil Laura, Kakiailatu Naomi, Bindels Eric M.J, Peulen-Zink Joke, Cheng  
William W, De Graaf Bianca M, Hofstra Robert M.W, Boesmans Werend, Alves Maria M,  
Melotte Veerle

5.20 p.m. **End of Session**



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**Tuesday, April 26**

**MORNING - 9.00 a.m.**

**Plenary room**

### CLINICAL CONSEQUENCES OF NEUROGASTROINTESTINAL DISEASE

Chairpersons: *Elena Bonora and Giovanni Barbara*

9.00 a.m. Hirschsprung disease *Allan Goldstein*  
*Discussion*

#### ORAL COMMUNICATIONS

9.20 a.m. BIALLELIC VARIANTS IN LIG3 CAUSE A NOVEL MITOCHONDRIAL NEUROGASTROINTESTINAL ENCEPHALOMYOPATHY  
*Bianco Francesca, Bergamini Christian, Lattanzio Giulia, Mazzoni Maurizio, Duijkers, Floor A. M, Taniguchi-Ikeda Mariko, Clavenzani Paolo, De Giorgio Roberto, Bonora Elena*

9.30 a.m. RET SIGNALING IN ENTEROENDOCRINE CELLS REGULATES GUT MOTILITY IN A SEX-DEPENDENT MANNER  
*Shepherd Amy, Feinstein Laurence, Sabel Svetlana, Rastelli Daniella, Mezhibovsky Esther, Matthews Lynley, Robinson Ariel, Gershon Michael D, Rao Meenakshi*

9.40 a.m. Novel understanding in the ganglionated Hirschsprung gut *Marthe Howard*

#### ORAL COMMUNICATIONS

10.00 a.m. PARKINSON MICE SHOW FUNCTIONAL AND MOLECULAR CHANGES IN THE GUT LONG BEFORE MOTORIC DISEASE ONSET  
*Gries Manuela, Christmann Anne, Schulte Steven, Weyland Maximilian, Rommel Stephanie, Martin Monika, Baller Marko, Röth Ralph, Schmitteckert Stefanie, Unger Marcus, Liu Yang, Sommer Frederik, Mühlhaus Timo, Schroda Michael, Timmermans Jean-Pierre, Pintelon Isabel, Rappold Gudrun, Britschgi Markus, Lashuel Hilal, Menger Michael, Laschke Matthias, Niesler Beate, Schäfer Karl-Herbert*

10.10 a.m. A SINGLE RET MISSENSE MUTATION IN HIRSCHSPRUNG'S DISEASE CAUSES INTESTINAL AGANGLIOSIS IN MICE THROUGH A DOMINANT NEGATIVE MECHANISM  
*Sunardi Mukhamad, Enomoto Hideki*

10.20 a.m. Syndromic Hirschsprung disease phenotypes: new genetic insights *Jeanne Amiel*  
*Discussion*

#### ORAL COMMUNICATIONS

10.40 p.m. IMPACT OF DISC1 PERTURBATION ON GASTROINTESTINAL FUNCTION  
*Tasnády Kinga Réka, Spaas Jan, Bon-Frauches Ana Carina, Vaes Nathalie, Sawa Akira, Brône Bert, Melotte Veerle, Boesmans Werend*

10.50 p.m. OPTOGENETIC STIMULATION OF CHOLINERGIC NEURONS: ROLE IN INFLAMMATORY BOWEL DISEASE  
*Rahman Ahmed, Stavely Rhian, Pan Weikang, Omer Meredith, Picard Nicole, Hotta Ryo, Goldstein Allan*



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- 11.00 a.m. Message from families of patients with Hirschsprung Disease  
**Eric Schnadig**, Founder and President of REACH (Research, Education & Awareness for Children with Hirschsprung Disease)
- 11.10 a.m. *Coffee break*

### Room A - AULA 1

#### PARALLEL SESSION – 9.00 a.m. – 10.30 a.m.

#### GISN SESSION - Neuroscience Glimps from Italy: the Experience of the “Gruppo Italiano per lo Studio della Neuromorfologia” (GISN)

Chairpersons: **Fabrizio Michetti and Alessandra Pacini**

- 9.00 a.m. **Lecture**  
Setting the clock: microbiota-gut-brain axis throughout the life **Claudio Nicoletti**  
*Discussion*
- 9.30 a.m. Enteric glia as bridging element between gut inflammation and visceral pain consolidation in rats **Elena Lucarini**  
*Discussion*
- 9.45 a.m. Obesity and enteric nervous system modulation: evidence from preclinical animal models  
**Ilenia Martinelli**  
*Discussion*
- 10.00 a.m. **Lecture**  
Impact of microbiota on S100beta in neurological disorders **Vincenzo Romano Spica**  
*Discussion*
- 10.30 a.m. End of Parallel Session

### Plenary room

#### STEM CELL TRANSPLANTATION IN ENTERIC NEUROPATHIES

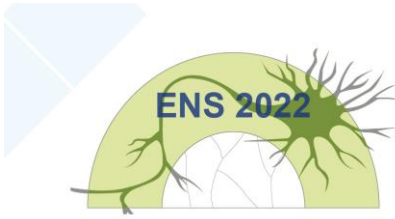
Chairpersons: **Marlene Hao and Karl-Herbert Schäfer**

- 11.30 a.m. Enteric neuronal stem cells **Ryo Hotta**  
*Discussion*

### ORAL COMMUNICATIONS

- 11.50 a.m. NEW INSIGHTS INTO GDNF-BASED TREATMENT OF HIRSCHSPRUNG DISEASE  
**Pilon Nicolas**, Soret Rodolphe, Gary Alassane, Lassoued Nejia, Yero Diaz Alexis, Zambito Oriana, Toufaily Chirine, Jenabian Ali, Sleno Lekha
- 12.00 a.m. DEVELOPING A NOVEL CELL THERAPY TO TREAT UPPER GI MOTILITY DISORDERS  
**Stamp Lincon**, Gwynne Rachel, Bergner Annette, Bornstein Joel, Myers Richard, Burns Alan, Hao Marlene
- 12.10 a.m. Enteric organoids **Maxime Mahè**  
*Discussion*

### ORAL COMMUNICATIONS



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- 12.30 p.m. SEQUELAE OF RESCUE SURGERY IN THE EDNRB-/- HIRSCHSPRUNG RAT  
*Furness John B, "Lei Enie, Adams Cameron D, Pustovit Ruslan V, Liew Jamie, HaoMarlene, Stamp Lincoln A, Burns Alan, Wykosky Jill*
- 12.40 p.m. GENERATION AND CHARACTERIZATION OF IMAGING-FRIENDLY hPSC-DERIVED ENS CULTURES  
*Kang Yi-Ning, Gogolou Antigoni, Moles-Garcia Emma, Fung Candice, W. Andrews Peter, Tsakiridis Anestis, Vanden Berghe Pieter*

12.50 p.m. *Lunch*

**POSTER SESSION** (during lunch time)

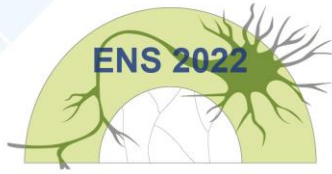
Poster tour Discussants: *Jean-Francois Brunet, Elena Bonora, Lincoln Stamp, Kulmira Nurgali*

**AFTERNOON - 2.15 p.m.**

**Plenary room**

Chairpersons: *Giancarlo Panzica and Marcello Costa*

- 2.15 p.m. **Keynote Lecture**  
Functional anatomy of the human insula and the von Economo neurons  
*Alessandro Vercelli*  
*Discussion*
- 3.15 p.m. **End of Session**
- 3.15 p.m. *Visit Ferrara*
- 8.00 p.m. **SOCIAL DINNER - LIFETIME ACHIEVEMENT AWARDS:** *Don Newgreen* Lifetime Achievement Award - *Robert Hofstra* Memorial Achievement Award



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**Wednesday, April 27**

**MORNING - 9.00 a.m.** (Open coffee: 10.00 a.m.-11.30 p.m.)

### Plenary room

#### ENS CHANGES DUE TO EARLY LIFE EVENTS

Chairpersons: *Michel Neunlist and Michael Gershon*

9.00 a.m. Anxiety and Depression *Kara Gross Margolis*  
*Discussion*

#### ORAL COMMUNICATIONS

9.20 a.m. EARLY LIFE ADVERSITY ALTERS ENTERIC NERVOUS SYSTEM DEVELOPMENT, GUT MOTILITY, AND VISCERAL SENSITIVITY  
*Najjar Sarah*, Hung Lin, Del Colle Evan, Israelyan Narek, Huang Zixing, Medina Melissa, Bernard Marguerite, Tonea Ruxandra, Juarez Daniel, Tong Yan, Gershon Michael, Margolis Kara

9.30 a.m. A NOVEL PURE PRIMARY CULTURE OF ENTERIC NEURONS TO STUDY THE EFFECTS OF GUT MICROBIOTA-DERIVED COMPOUNDS IN AUTISM SPECTRUM DISORDER  
*Caillaud Martial*, Paillé Vincent, Le Berre-Scoul Catherine, Andriantsitohaina Ramarason, Loussouarn Gildas, Neunlist Michel, Boudin Hélène

9.40 a.m. Microbiome neuronal interactions *Vassilis Pachnis*  
*Discussion*

#### ORAL COMMUNICATIONS

10.00 a.m. ROLE OF MICROBIOTA AND SEMAPHORIN 5A ON ENS CONNECTIVITY IN AUTISM SPECTRUM DISORDERS  
*Le Dréan Morgane Eileen*, Catherine Le Berre-Scoul, Justine Marchix, Jacques Gonzales, Michel Neunlist, Hélène Boudin

10.10 a.m. ENGINEERED LACTOBACILLUS PARACASEI PRODUCING PALMITOYLETHANOLAMIDE (PEA) PREVENTS COLITIS AND REDUCE ENTERIC GLIA-MEDIATED NEUROINFLAMMATION IN MICE  
*Esposito Giuseppe*, Seguella Luisa, Del Re Alessandro, Palenca Irene, Corpetti Chiara, Lu jie, Sanseverino Walter, Sarnelli Giovanni

#### POSTNATAL MATURATION OF ENS

Chairpersons: *Pieter Vanden Berghe and Kulmira Nurgali*

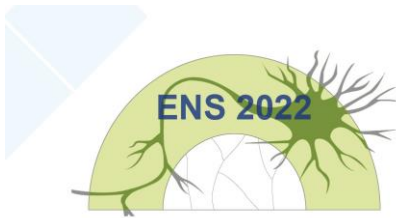
10.20 a.m. Brain and enteric connectivity molecules in postnatal development *Helene Boudin*  
*Discussion*

#### ORAL COMMUNICATIONS

10.40 a.m. EXAMINING THE EFFECTS OF AN ACUTE HIGH FRUCTOSE DIET ON LUMINAL SIGNALING IN THE MURINE ENTERIC NERVOUS SYSTEM  
*Fung Candice*, Tack Jan, Vanden Berghe Pieter

10.50 a.m. ACCELERATED GENERATION OF ENTERIC NERVOUS SYSTEM PROGENITORS AND NEURONS USING hPSCs





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**Gogolou Antigoni, Kang Yi-Ning, Frith Thomas J.R, Cooper Fay, McCann Conor J, Andrews Peter W, Vanden Berghe Pieter, Tsakiridis Anestis**

11.00 a.m. The gut environment as an important factor for ENS (re)-organisation **Conor McCann**  
*Discussion*

11.20 p.m. *Group Photo*

11.50 p.m. *Lunch*

**POSTER SESSION** (during lunch time)

Poster tour Discussants: **Nadege Bondurand, Hideki Enomoto, Catia Sternini, Toshihiro Uesaka, Paul H.K. Tam**

**AFTERNOON - 2.00 p.m.** (Open coffee: 2.30 p.m.-5.00 p.m.)

**Plenary room**

Chairpersons: **Vincenzo Stanghellini and Marcello Costa**

2.00 p.m. Where are we and where are we going with ENS Research **Simon Brookes**

2.40 p.m. **Award for the best abstract(s)** **Allan Goldstein and Roberto De Giorgio**

2.50 p.m. **Closing remarks (and where and when next meeting will be)** **Roberto De Giorgio and Allan Goldstein**

3.00 p.m. **End of Symposium**

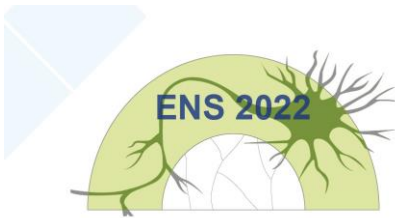
**Plenary room**

**SATELLITE SESSION – 3.30 p.m. – 5.30 p.m.**

**ENS NOMENCLATURE**

Group Coordinator: **Vassilis Pachnis**

**Participants: Julia Ganz, Michelle Southard-Smith, Ulrika Marklund, Marcello Costa, Michael Schemann, Nick Spencer, Allan Goldstein, Catia Sternini, Michel Neunlist, Pieter Vanden Berghe, Werend Boesmans, Brian Gulbransen, Subhash Kulkarni, Nadege Bondurand, Marlene Hao, Hideki Enomoto, Elly Ngan, Gemma Mazzuoli Weber, Karl-Herbert Schäfer, Conor McCann, Helene Boudin, Jean-Pierre Timmermans, Ankush Gosain**



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### **PRESENTATION**

ENS development is an ongoing process that does not end with embryogenesis. The ENS also undergoes postnatal growth and maturation, with the ability to respond to environmental influences after birth. This 6<sup>th</sup> International Symposium therefore expands our traditional concept of development to include ***“The first 1000 days: from conception to postnatal life.”*** This period is increasingly recognized as an emerging field of research with important consequences for both health and disease. It arises from understanding that normal and abnormal biology result from complex interactions between genetic and environmental factors starting as early as conception and continuing into postnatal life, with potential for long-lasting consequences, with even transgenerational impact.

Applying this concept to the “first 1000 days” of the ENS allows us to highlight the importance of understanding pre- and post-natal ENS development, its modulation and impact on its cellular surroundings, and the influence of multiple environmental factors (microbiota, nutrition, immunity, medications) during both embryonic and postnatal life. From a pathological point of view, such approaches could give us a better understanding of pathophysiologic mechanisms in congenital diseases of the ENS and also in diseases in which the ENS may be implicated later in life, including autism, neurodegenerative diseases, and functional bowel disorders. One could thus consider neurodegenerative disorders, such as Parkinson’s disease and Alzheimer disease, as conditions associated with abnormalities falling into the “1000-day paradigm”. Finally, this conceptual framework will allow us to introduce novel hypotheses and experimental approaches that can be applied for basic and translational research to broaden our understanding of enteric neuropathies and their impact on human health. Examples include applying novel imaging technologies, cell-based therapies, and computational biology to the study of the ENS. We look forward to taking this “1000 day” journey together as we welcome you to Ferrara and the 6<sup>th</sup> International Symposium.

### **CONGRESS VENUE**

Conference Hall  
St. Anna Hospital  
Via Aldo Moro, 8  
44124 Cona, Ferrara (Italy)

### **ORGANIZING SECRETARIAT**

**Delphi International Srl**  
Via Annibale Zucchini 79  
44122 Ferrara (Italy)  
Phone +39 0532 595011 Fax +39 0532 1934214  
[ens2022@delphiinternational.it](mailto:ens2022@delphiinternational.it)  
<https://ens-development-meeting.com/>