MARA GIORDANO

Born in Rome
Current position: Associated Professor in Medical Genetics (MED/03)
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Education
1989- Degree in Biological Sciences at the University of Pavia (110/110 Cum Laude).
1994- Specialisation in Genetics at the University of Pavia (50/50)
1999- PhD in Human Genetics at the University of Torino.

Fellowship and contracts
1991-1993 Fellowship by "Fondazione per le Biotecnologie"
1993-1994 CEE fellowship at the INSERM 91 (Creteil, Paris France)
1994-1998 PhD Fellowship (University of Torino)
1998-2000 Fellowship by AISM (Multiple Sclerosis Italian Association)
2000-2005 Research assistantship (Assegno di Ricerca) by University of Eastern Piedmont
Current position
2006- to date Associate professor in Medical Genetics (Eastern Piedmont University)

Research Experiences
1987-1990 Laboratory of Human Genetics, University of Pavia (Italy) directed by Prof. S. Benerecetti Santachiara: she was involved in research projects concerning the study of mitochondrial DNA polymorphisms in Human populations.
1990-1991 Laboratory of Plant Genetics, University of Pavia (Italy) directed by Prof. R.Cella: working on a research project concerning identification of a novel DNA-methyltransferase in rice cultured cells.
1991-1992 Laboratory of Human Genetics directed by Prof. P. Momigliano Richiardi University of Torino
(Italy): involved in the study of HLA polymorphisms in the Italian population and in the study of mutations involved in Myotonic Dystrophy.
1993-1994 Laboratory of Biochemistry and Genetics, INSERM 91 Creteil (Paris, France), directed by Prof. M. Goossens: working in a research project on the identification of new mutations involved in autosomal
recessive Retinitis Pigmentosa
1994-1997 laboratory of Human Genetics, University of Torino (Italy), directed by Prof. P. Momigliano
Richiardi: mainly involved in the search for mutations and polymorphisms involved in Growth Hormone
Deficiency and in the characterization of functional variants.
1997 (from July to October) Laboratory of Human Genetics directed by Prof. Luca Cavalli-Sforza, University of Stanford (CA, USA),: during this stage she learned a newly developed technique (Denaturing High Performance Liquid Chromatography; DHPLC) to identify polymorphisms in a Multiple Sclerosis candidate region.
1997 to 2005 Laboratory of Human Genetics. During this period she was mainly involved in the search for

genes contributing to multifactorial diseases (Multiple Sclerosis and Celiac Disease) and in the identification of variations causing Growth Hormone Deficiency.
2005 to date Laboratory of Human Genetics: she is on the behalf of a research group working on the Genetics of Growth Disorders and Renal Diseases composed of two PhD students, three post-docs,two fellows and four students preparing their thesis.
Research activity

Current projects for which she is the PI of the Unit:

-Ricerca Finalizzata Bando 2012 (Ministero della Salute): Vitamin D deficiency and obesity after kidney
transplantation: multicenter study on gene-environment interactions leading to "complex-phenotypes" in a human system associated with cardiovascular events and graft rejection.
(RF-2011-02351876).

-Bando Regionale 2014 a sostegno di progetti di ricerca industriale e/o Sviluppo sperimentale sulle malattie Autoimmuni e Allergiche. “Caratterizzazione immuno-infiammatoria di alcuni ceppi di lattobacilli con sviluppo di un nuovo prodotto probiotico indicato nelle allergie (PRONTALL). Scientific role in the project. Evaluation of the epigenetic modifications (DNA methylation) induced by probiotic administration in patients with allergic rinhitis.

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- **Diagnostic activity:**

Coordination of execution of about 900 molecular diagnoses (index cases) at the laboratory of Human Genetics of the University of Eastern Piedmont in Novara for the following pathology:
-Intellectual Disability
-Growth
-Renal Diseases

Teaching Activities:

At the School of Medicine of the University of “Piemonte Orientale (UPO)”
-from 2006 to 2010: Course of “ Diagnostica Molecolare” , Corso di Laurea in Biotecnologie
-from 2006 to 2010: Course of Disegno Sperimentale, Corso di Laurea in Biotecnologie
-from 2006 to 2009 : Course of Tecniche di Diagnostica Molecolare, Corso di laurea specialistica in Biotecnologie
-from 2006 to 2009 Course of Basi Molecolari delle Malattie, Corso di laurea specialistica in Biotecnologie
-from 2009 to 2014 Course of Genomica Funzionale Corso di laurea specialistica in Biotecnologie Mediche
-from 2014 to date Course of Functional Genomics, Master Degree in Medical Biotechnolgies, Università del
Piemonte Orientale
-from 2002 to date Course of Tecniche di Analisi Genetica, Corso di laurea in tecnico di Laboratorio Biomedico
-from 2010 to date Course of Genetica con Elementi di Laboratorio, Corso di laurea triennale in Biotecnologie presso l’Università del Piemonte Orientale

Academic responsabilities:

-President of the "Commission Conto Terzi" of Department of Health Science (UPO)
-Component of the ECM University Commission (role: progettista)
-Component of "Research Commission" of Department of Health Science (UPO)
-Coordinator of Erasmus Project and International Relationship at the School of Medicine of University of
Eastern Piedmont
-Vice Director of the Master Degree in Medical Biotechnologies (Course in English)

Current Research Projects:

Identification of novel genes involved in Growth Disorders

Research over the last 20 years has led to the elucidation of the genetic aetiologies for a relative small number of patients with short stature with or without pituitary hormone deficiencies. Although the exponentially increasing advances in our understanding in the genetic of growth led to the identification of numerous monogenic causes of growth disorders most of the patients with short stature and correlated disorders remain with an explained aetiology and without a correctly addressed therapeutic programme.
This project is aimed to the identification of novel genes involved in growth defects and the final goal is the creation of a robust sequencing platform including genes causing Short Stature to be used in the diagnostic workflow. These genes are identified through different main steps. 1) Patients have been selected with different form of Short Stature including all the familial cases and patients with the most severe form of short stature, thus higher likelihood of having a monogenic disorder. 2) First, the selected patients are screened by a customised aCGH platform to identify patients bearing pathogenic CNV and possibly to identify novel dosage sensitive genes that will be included in the final gene panel.
The genes in which mutations will be identified through the described workflow and for which the potential role in the pathology will be supported by functional studies, will be screened in all the patients not analysed in the previous steps and in patients that will be recruited during all the project duration .

Identification of novel regulatory region of the SHOX gene
Short stature is defined as a condition in which the height of an individual is more than 2 SD score (<-2 SDS) below the mean for age and sex and is estimated it affects about 3% of children in the world.
Patients in which the cause underlying short stature is not detectable through standard diagnostic procedures are referred as Idiopathic Short Stature (ISS) and they constitute a heterogeneous group. The best known monogenic cause of ISS is the haploinsufficiency of the SHOX gene (Short Stature Homeobox-containing) located at the tip of the short-arm of both X and Y chromosomes within the pseudoautosomal region 1 (PAR1). Point mutations and deletions of SHOX and/or its enhancers have been found in about 10% of ISS patients.
This project is aimed to the screening for SHOX mutations, deletions and duplications a cohort of ISS patients through standard procedures (MLPA and direct sequencing of the exons and the intron-exon junctions) and to analyze through a custom designed arrayCGH platform with high resolution in PAR1 those patients tested as negative through the standard methods in order to find out novel candidate regions with potential enhancer activity. A SurePrint G3 Custom CGH 8x60K platform (Agilent Technologies) was designed using the tool Agilent SureDesign (https://earray.chem.agilent.com/suredesign/). The array has a very high resolution within the PAR1

region (about 8000 probes with a 350 bp average probe spacing), a high resolution in the X chromosome (about 10 kb) and a low resolution backbone. ArrayCGH experiments were performed according to manufacturer's instructions.
Up to now we screened about 450 ISS patients and we could identify a SHOX mutation in 7% of them, according to previous studies. Fourty four patients tested negative for mutations have been analysed throught the custom CGH array. We have identified a potential novel enhancer sequence and we are currently analyzing the functional activity of this sequence

Identification of imbalances in Neuropsychiatric pediatric patients

This project is aimed to the identification of imbalances in patients with neurodevelopmental disorder and intellectual disability through high density arrayCGH. Up to now we recruited 250 Neuropsychiatric patients that have been analysised with aCGH. In the 20% of them we identified likely causative deletion/duplication of which about 50% correspond to known microdeletion/microduplication syndromes. In several patients however the rearrangement is not clearly related to the disorder and the scope of the project is to study the role of the involved genes.