

Giovanni Romeo



Personal Details

Name	Giovanni Romeo
Dates	1940
Place of Birth	Italy (Reggio Calabria)
Main work places	Genoa, Bologna
Principal field of work	Medical genetics
Short biography	See below

Interview

Recorded interview made	Yes
Interviewer	Peter Harper
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Edited transcript available	See below

Personal Scientific Records

Significant Record set exists
Records catalogued
Permanent place of archive
Summary of archive

Biography

Giovanni Romeo, born in Reggio Calabria, Italy, on May 29, 1940 holds the chair of Medical Genetics at the University of Bologna, his Alma Mater, where he moved back in 2002 after spending 8 years in Lyon, France (where he was Chief of the Unit of Genetic Cancer Susceptibility at the International Agency for Research on Cancer) and 10 years in Genoa (where he was Professor of Human Genetics at the University of Genoa Medical School and Istituto G. Gaslini, between 1986-1995). He was previously Associate Professor of Molecular Genetics at the University of Bologna Medical School (1978-86) and Lecturer in Genetics at the University of Naples and Group Leader of the Laboratory of Human Genetics at the International Institute of Genetics and Biophysics (I.I.G.B.) in Naples between 1972 and 1978. He was a visiting scientist at Stanford University (Laboratory of Prof. L.L. Cavalli-Sforza) in 1975-6 and trained at the Johns Hopkins Medical School, Baltimore, between 1968 and 1971. He graduated in Medicine in 1965 in Bologna where he went through his internship and residency in Pediatrics.

Together with Prof. V.A. McKusick he founded in 1988 the European School of Genetic Medicine (visit: www.eurogene.org<<http://www.eurogene.org>>) which has trained since then more than 5500 young human and medical geneticists from all over Europe and from other parts of the world (particularly from countries of the Southern rim of the Mediterranean sea basin and from the Middle East).

INTERVIEW WITH GIOVANNI ROMEO, 2nd JUNE, 2008

PSH. It's Monday June 2nd 2008 and I am talking with Professor Giovanni Romeo at the European Society of Human Genetics Meeting in Barcelona. Giovanni, just to start off, I can I ask you when you were born and where?

GR. I was born on May 29th 1940, in the South of Italy, in a beautiful city, Reggio Calabria, located just on the tiptoe of the Italian peninsula, in front of the straight of Messina. It is a city in the middle of the Mediterranean sea and I am a Calabrese by birth and by culture, having spent my childhood and adolescence there.

PSH. And may I ask, your family, were any of your family medical or scientific at all?

GR. My mother was a midwife and she died when I was five years old. So maybe her profession and her memory influenced my choice for medicine.

PSH. And your father?

GR. My father was in commerce and he was from Calabria while my mother was born in Romagna and studied in Florence. So I am a hybrid, genetically and culturally speaking..

PSH. From the North and South

GR. Yes, from the North and South

PSH. And have you had brothers and sisters too?

GR. Two older sisters, one lives in Reggio Calabria, the other in Bologna.

PSH. Can I ask, did you have any particular experience during your childhood or school that turned you in the direction of science or medicine?

GR. Yes I remember very well when I decided to go into medicine, I was about 15 years old. I was in High School and science was very attractive to me. In particular I was interested in biology.

PSH. Did you have good biological education in your later years at high school?

GR. I went through classic studies in High School and so I took 8 years of Latin and 5 years of Greek. Science therefore was not my major before Medical School but during my University years I fell in love with medical research. During my first year in Medical School I was attending the lectures of Prof. Olivo and was studying on a textbook of Histology written by the greatest medical researcher who was still alive at the time, Giuseppe Levi, who had been the mentor of Olivo. Levi died in 1964 and he had founded in Torino between the two world wars a leading research Institution where

Salvador Luria, Renato Dulbecco and Rita Levi Montalcini trained. So these three Italian Nobel Prize winners were students of Levi.

PSH. Remind me, in which University did you study?

GR. I studied at the University of Bologna Medical School. Levi was from the University of Turin. My professor of Histology was a student of Levi and his name was Oliviero Mario Olivo. He got me interested in research and I decided when I was in the third year of my Medical School that I would start working in a research Institute which was called General Pathology. At the time I was attracted by Biochemical Pathology, and this led me to the further choice of going into genetics. There was no formal training in medical genetics in Bologna at the time so I went into Paediatrics right after getting my medical degree. From there, after two years of internship in Paediatrics, I found out that the best place I could go for training in medical genetics was Johns Hopkins Hospital in Baltimore. The period I spent at Hopkins really represented the imprinting of my whole career in medical genetics.

PSH. When was it that you qualified in medicine?

GR. I qualified in 1965, and then in 1967 I took off for the States with my wife Isabella to go to Hopkins. From 1968 through '71 I was there, in the department of Paediatrics, and my mentors were Eph Levin and Barbara Migeon. The inspiring presence of Victor McKusick was felt very much at Hopkins and in 1968 I took the short course in medical genetics in Bar Harbor. Another European young geneticist attending that course was Albert de la Chapelle. Twenty years later together with Albert de la Chapelle, and many other European medical geneticists like yourself we started the first course in Medical Genetics in Sestri Levante which was modelled after the Bar Harbor course. Victor McKusick was again the leading figure and in a way the grandfather of this course which last year celebrated its 20th anniversary, always under the direction of Victor.

PSH. Can I ask, when you were at Hopkins, did you have a specific research project that you were doing, either with Victor or in Paediatrics?

GR. Yes I was working in Paediatrics and I was attending from time to time the Moore Clinic, but especially I was attending meetings like the first Birth Defects Conference organised by Victor at Hopkins. My research project was essentially in biochemical genetics. At that time it was not possible to do DNA studies in genetics. My mentor was a young assistant professor in Paediatrics, Ephraim Y. Levin, a very good teacher and I worked with him for almost two years on porphyrin biosynthesis and congenital porphyrias. In his laboratory we discovered among other things the enzymatic defect of Gunther disease, that is congenital erythropoietic porphyria. This was my first relevant publication in an international journal. Using the biochemical tools created by Ephraim Levin, who was also a very good biochemist, we found that Gunther disease was caused by a defect in uroporphyrinogen III cosynthetase. After that period, I moved into somatic cell genetics. I thought that I needed some specific training using the methods of human genetic analysis available at the time and therefore I started my second training at Hopkins with Barbara

Migeon. During this second postdoctoral period I became close with Barton Childs who was the inspirator of a lot of work in Medical Genetics at Hopkins. I should underline that I went through this long period of postdoctoral training with the motivation that eventually I wanted to go back to my country and do things there. And this was also the motivation which brought me to start the European School of Genetic Medicine in 1988.

PSH. What year did you go back to Italy?

GR. I went back to Italy in 1971.

PSH. Which kind of post did you return to?

GR. I was appointed Assistant Professor at the University of Naples at a time when Marcello Siniscalco became Professor of Human Genetics there. Naples, which is a wonderful city, had an excellent tradition in genetics. But it was difficult to get things done properly at that time there. I organised the lab of Biochemical Human Genetics in Naples but Marcello Siniscalco retired after two years and left Italy altogether. I was carrying on with my work which I had started with Barbara Migeon on Fabry disease. I had published a couple of papers and one in particular in Science on this subject during the period I spent in Barbara's lab. So I went on with this research interest but the working conditions in Naples were too difficult and after four years I left for a sabbatical, first with David Rimoin in L.A. in clinical genetics, and afterwards with Luca Cavalli Sforza in Stanford. During this latter period (between '76 and '78) I started my collaboration with Luca working on a project on cystic fibrosis. We published a few papers together and eventually I made again the choice to go back to Italy, this time to Bologna..

Going back to Bologna was my original purpose from the Hopkins time. I had the position of Associate Professor of Human Molecular Genetics for 8 years in Bologna where I started a laboratory and service of Neurogenetics which still exists in the Dept of Neurology. At the time I was working on Duchenne muscular dystrophy collaborating, among others, with Tony Monaco and Lou Kunkel. In 1985 I won the competition for full professorship in Genoa and the period which followed (1985-1995) was the most productive period of my career in Italy. I was working at the Gaslini Institute which is the largest Paediatric Hospital in Italy and for the first time I had the opportunity to build a strong group of young collaborators. Among the different clinical and molecular genetics projects I started in Genoa one was particularly successful and led to the identification of the major gene responsible for Hirschsprung disease. Hirschsprung was a difficult disorder to study at the time being what we call now a complex genetic disorder. To our surprise by studying families with recurrence of this disorder we found that the RET proto-oncogene was involved in at least 50% of familial cases. That was a very exciting result which led me to a turning point of my scientific interests.

Through the RET proto-oncogene my group got involved in the study of thyroid cancer, RET mutations being so prominent in Medullary Thyroid Cancer. Our contribution to the story of the RET oncogene and its associated disorders was widely acknowledged and this led to the offer from the International Agency for Research on Cancer in Lyon in 1995 to become head

of a newly established Cancer Genetic Predisposition Unit. I took this job not only because it allowed me to pursue my research interests on the RET oncogene but also to stay in close contact with Italy, Lyon being so close to Genoa. In particular I was interested in promoting the development of the European School of Genetic Medicine which was based at the time in Sestri Levante. Toward the end of that period in Lyon (2001), the offer came up eventually to go back to Bologna as Full Professor of Medical Genetics. Since my departure from Bologna in 1985, medical genetics had witnessed a complete stop due to internal politics within the Bologna School of Medicine and there was no teaching nor hospital service in medical genetics. I accepted the challenge because I consider Bologna my second hometown in Italy and I went back there with great enthusiasm and with the goal of building a strong medical genetics group. I believe I made it and I am here at this meeting in Barcelona with 10 of my best collaborators from Bologna I was able to recruit during these years.

I consider myself very lucky because at the end of my career I have been able to reach the goal I had since I left Italy in 1967 when I went to Hopkins. It has taken a lot of time to achieve this goal but this is often the case in my country. I have been able to recruit in Bologna the best collaborators I have ever had in my scientific career and this is also true for the group I left at the Gaslini Institute in Genoa which is now directed by Roberto Ravazzolo. This group is still working at the highest scientific level on some of the projects I started (for example the Hirschprung project led by Isabella Ceccherini and the CF project led by Gino Galletta)

PSH. Can I take you back now to the European School of Genetic Medicine?

GR. Yes, please

PSH. Tell me how did you first get the idea, was this from Bar Harbor, or was there some other influence?

GR. As I said in 1968 I was I was a student at the Short Course in Bar Harbor, and this was really an eye opening experience for me. I was still very young and I didn't know much about genetics. After my return to Italy I always kept good relations with Victor and with Hopkins, where I have a lot of friends. Eventually 20 years later the idea of a European Bar Harbor twin course became feasible because the Gaslini in Genoa (and in particular its Director, the late Prof. Paolo Durand) wanted me to do something for the visibility of the Institute in the field of Medical Genetics. Thus the School was born. After a few years I realized that postgraduate training was needed in Europe not only for medical genetics but also for other fields of genetic medicine. As an example when I was at IARC in Lyon, cancer genetics was the next obvious course to be organized. In 2001, when I was preparing myself to go definitively back in Bologna, I started thinking of a series of other courses which now represent different resources for the European School of Genetic Medicine, each led by its own directors and all organized by the European Genetics Foundation of which I am the President.

PSH: Remind me, what year was the first course?

GR: It was in 1988

PSH: And what led you to hold it in Sestri Levante?

GR: It happened by chance. The Gaslini Institute was very well known not only in Genoa but also in many surrounding small beautiful cities on the Riviera, among which Sestri Levante. There it was possible to rent very cheaply a castle (the Hotel dei Castelli) which became the venue of the School for several years, thanks to the help of the local Maresciallo dei Carabinieri, who was a friend of Prof. Paolo Durand

PSH: Am I right that the owner of the castle had had some problems with the law?

GR: One of the owners was in jail. The local Maresciallo dei Carabinieri , who knew everything that was going on in Sestri Levante, was able to help us because he was in touch with the judge of the tribunal of Milan, who was responsible for administration of the property of the castle.

PSH: It was a wonderful place for its atmosphere, to hold a course like that.

GR: Exactly, and that was the feature of those first years of the School. Sestri Levante was a magic place and the castle was the ideal venue where to convene students and faculty from all over Europe. As you certainly remember, the amazing thing was that in spite of language differences the students would really represent a very closely knit community and a lot of personal friendships and professional relationships started in this way in Sestri Levante. So it really was the experience of the School, and of that course in particular, which led to the idea of having a better, more efficient European Society of Human Genetics (ESHG). You might remember that the statute of ESHG was reformed just during those years.

PSH: And you became president of ESHG very soon after it was reformed.

GR: Yes. I was the first president democratically elected of ESHG. As you might remember, the president was not elected before my turn but he or she was appointed by a sort of club of old friends, which represented at the time the General Assembly of ESHG. So that was a real revolution for ESHG. I was not aware I would become president at the first ESHG meeting I attended in Corfu.

PSH: How many students were on the first Sestri course?

GR: Almost 100.

PSH: That's quite large for the beginning.

GR: Yes indeed, it was quite a success from the very beginning. This success was mainly due to the presence of Victor who represented the icon of the course but also to the fact that such a course was needed in Europe. Many other faculty, like yourself, Martin Bobrow, Malcolm Ferguson-Smith and

a lot of other European geneticists contributed to this success. Among the Americans Tom Caskey was teaching in the first course in 1988, and we convinced him to stay at the course for a full week, which was highly unusual for him.

PSH: Were there any special factors that made you move the location of the School?

GR: Well, little by little it became more difficult to do things in Sestri Levante, partly because of problems with the owners of the castle, as you mentioned. The venue in the castle became too expensive for us. We tried to keep the course in Sestri Levante and we found another venue close to the castle, in the peninsula of Sestri Levante. It was an old abbey (built in 1492) which, following our suggestion, the city council administration of Sestri Levante restructured creating a modern venue which however never became as efficient as we were expecting. So we were having a lot of logistic problems when the opportunity came up, at the time of my return to Bologna, to use a very efficient venue in Bertinoro di Romagna located 80 km south of Bologna. That was in 2001 and there was essentially no choice because we wanted a venue that could host several courses without having to re-organise every time everything as we were doing in Sestri Levante. My older son Guido, who had just graduated from University and who is now a scientific journalist, was responsible for all this organizational work in Sestri Levante. Bertinoro represented a big change and the School functions now almost automatically, because it is managed by the professional expert staff of the European Genetics Foundation. The venue in Bertinoro was also more compatible with the challenge I had accepted going back to Bologna where I had to start from scratch the new centre of medical genetics. This task has really taken most of my time since 2002.

PSH: Looking at the influence of Victor McKusick and his role in the School, is there anything you feel, apart from his just being there, that was a very special influence on the way the course developed.

GR: Yes, I think his experience in term of scientific and personal knowledge of the world of medical genetics was very useful in recruiting the faculty. In essence the experience of Bar Harbor was utilized by the European School of Genetic Medicine which has now its own new features. Most of the courses of the School are characterized by plenary morning lectures and afternoon workshops where students are divided in small groups. These workshops have been a success from the very beginning of the School. As an example, one workshop in the Medical Genetics course has been dedicated to linkage analysis using PC's. Through this and other interactive workshops the students are always exposed to some practical training in the use of informatics. The same is true for all the other types of workshops which are essentially based on group discussions with one or two faculty on a specific topic and the students like very much this type of interaction.

Victor left his mark on the development of the School for another reason. Five years ago, after my return to Bologna, a Catholic monastic order, called Servants of Mary, wanted to do something special for medical genetics

because they realized how much we can do in our field to help families struck by the occurrence of a genetic disorder. So they donated a huge piece of land in the most beautiful spot on the hills south of Bologna called Ronzano, located 3.5 km from the historic centre of the city, where there is a Hermitage of the same monastic order. In this location we have already established the temporary new venue of the School and we are building a new centre for the training in genetic medicine and for the public awareness of genetics. On May 13, 2005 in presence of Victor, of the Mayor of Bologna, of the Rector of our University, of the representatives of the monastic order and of many other people we dedicated the new center to Giuseppe Levi (the famous Italian medical scientist I mentioned before) and to Victor McKusick. So we have now in the world three centers or Institutes which are named after Victor McKusick. One is Baltimore, the McKusick-Nathans Institute; another is in Beijing, the third one in Bologna. Of course this is a big endeavor because the construction of the new venue will cost about 7.5 million €. The project has just been approved by the City Council Administration of Bologna and we are starting now the fundraising which is however quite difficult because of the economic situation in Europe and in the world. In three weeks, on June 24 2008, we are going to inaugurate the first laboratory of statistical genetics in the temporary venue of Ronzano-Bologna, that is in the same place where the new venue will be built. In the space we rent from the local Hermitage, 600 square meters in all, we are already organizing most of the courses of the European School of Genetic Medicine. I should mention that most of the work for establishing this temporary venue was done by my wife Isabella who has helped me a lot during all these years, in this like in so many other professional endeavors.

PSH: It's a wonderful achievement and I did not know all of that. Now we must finish soon. I've been asking everybody I've spoken with two questions and the first is. Is there a particular, either piece of work in terms of research or any other field of work that you yourself feel you can think of as your special achievement?

GR. As I said, a very productive period of my scientific career was in Genoa as documented by the mapping and identification of the RET proto-oncogene whose mutations are prominently associated with Hirschsprung disease as well as with Medullary Thyroid Cancer. But that was 20 years ago.... Now the last of my scientific project is being developed by the research group I was able to recruit in Bologna. What this group is achieving in Bologna is in a way the follow-up of the story of the RET proto-oncogene. We have developed a very interesting line of research studying a particular form of cancer frequent in the thyroid (but not only) which is called oncocytoma. This is essentially a type of tumor whose cells are full of mitochondria (so called mitochondria hyperplasia). This story has been so successful because in Bologna I could take advantage of a very efficient collaboration with some old friends (biochemists, cell biologists and neurogeneticists) who know a lot about mitochondria. With their help my group has been able to set up functional studies of the mitochondrial mutations we identified in oncocytomas. These are essentially nonsense or truncating mutations of the mitochondrial genome, affecting especially the mitochondrial subunits of complex I, and this represents a signature of this particular type of tumour.

We published the most relevant mutation data in PNAS last year. What I think is the most fascinating finding in this project is that at least one of these mutations recurs in a family. We have just described in a paper which is going to appear in Human Mutation the story of maternal inheritance of this mutation which would be lethal in homoplasmy, but is transmitted in heteroplasmy in the family and becomes homoplasmic in the tumor. I think this finding is going to have a more general significance in terms of genetic predisposition to cancer. So this the leading theme of research for my research group right now.

PSH: My final question, Giovanni, is: who do you feel has been the principal influence on your career in science and medicine?

GR: Well I think that all the persons who had the most profound influence on my scientific career are from Johns Hopkins. The first one is Eph Levin, who became a very good friend of mine and was very helpful to me. Barton Childs was the head of the genetics division in pediatrics at Hopkins at the time and his presence, together with that of Barbara Migeon, was very inspiring and very helpful. As I said, I was a postdoctoral fellow at Hopkins first with Eph Levin and later with Barbara Migeon. And of course there was Victor..... Victor was always a point of reference from the very beginning of my career in medical genetics and he best represents the imprinting that Hopkins left on my life.

PSH: Well thank you very much Giovanni, I am going to finish there. We could go on for a long time, but I am very grateful to you for sparing the time at such short notice.