

## Funding of a Medical Research Institute in a Small Country: 15 years of Instituto de Patologia e Imunologia Molecular da Universidade do Porto (IPATIMUP)

This is an interview with Prof Manuel Sobrinho-Simões, the Director of the Institute of Molecular Pathology and Immunology of the University of Porto (IPATIMUP), Porto, Portugal. The interview was prepared for this Pathology thematic issue, by Prof Ivan Damjanov, from the University of Kansas School of Medicine, Kansas City, Kansas, USA. The interview deals with the funding and the growth of IPATIMUP, which became, within 15 years from its inception, one of the leading biomedical research institutions of Portugal. The interview touches upon the logistical, political, financial, and personnel-related problems they encountered during these 15 years. It illustrates some of the dilemmas and questions faced by scientists in Porto, which are also relevant to scientists in other small countries.

My name is Ivan Damjanov and I am 64 years old. I graduated from the Zagreb University School of Medicine in 1964. Since 1974 I have been living in the United States, but as much as possible, I have tried to keep in touch with my colleagues in Croatia. Currently, I am a professor of Pathology at the University of Kansas School of Medicine. I also serve on the Advisory Board of the *Croatian Medical Journal*.

Last year I persuaded Prof Matko Marušić, Editor-in-Chief of the *Croatian Medical Journal*, to publish my interview with Prof Manuel Sobrinho-Simões, Professor of Pathology at the University of Porto School of Medicine, Porto, Portugal. Prof Sobrinho-Simões is also the Director of the Instituto de Patologia e Imunologia Molecular da Universidade do Porto (IPATMUP), a medical research institute which he founded 15 years ago. The interview deals with the problems related to building a research institute in a small country, a topic which is quite relevant to small scientific communities.

For the sake of full disclosure, I would like to declare that I have known Prof Sobrinho-

Simões for more than 25 years (see Fig. 1). I serve on the Overview and Advisory Board of IPATIMUP, but I do not receive any monetary compensation for my services. I happen to be a great fan of Dr Sobrinho-Simões and his crew at IPATIMUP and firmly believe that we all could learn from their experience.

### Building and Funding the Institute

**ID:** Thank you for agreeing to give this interview to the *Croatian Medical Journal*. Could you tell our readers a few words about yourself?

**MS-S:** I was born in Porto in September 1947. My father was a professor of biochemistry at the Medical School of the University of Porto. My grandfather, as well as my great-grandfather, was a general practitioner in Arouca, a small village in northern Portugal. Many relatives on my mother's side of the family, including my great-grandfather and my mother's brother, were general practitioners in Bombarral, a small village in southern Portugal. I am mentioning all these details to explain why I did not consider any other possibility but to be a physician and to remain in Portugal.

I was attracted to clinical medicine and I enjoyed studying the etiopathogenesis of diseases as well as laboratory work, so I decided early to devote my life to academic medicine and to become an anatomic pathologist. I received my M.D. degree from the Medical School of Porto in 1970 and eight years later the doctorate in medical sciences. I did my post-doctoral training in the Norwegian Cancer Research Institute/Radium Hospital in Oslo from 1979 until 1980.

Early in my career, I became involved in the activities of the European Society of Pathology (ESP), because I thought that that forum could help my peripherally located country to become more involved in the European scientific community. Slowly, I rose through the ranks and became the Chairman of the Advisory Council, General Secretary and, finally, the President of the ESP in 1999. I held this position for two years.

In the 1980s, through ESP I was involved in creating the European School of Pathology in Turin and the European Course on Cellular Pathology in Lyon. Later on, I was involved in the creation of the Krakow, Moscow, and Ankara branches of the European School of Pathology. In October I will inaugurate, together with Prof Bussolati, the fourth branch of the School in Craiova, Romania. Needless to say, it would be very nice to establish a branch of the European School of Pathology in Zagreb.

**ID:** Even though you had numerous invitations to move to other parts of Europe or the Americas, you decided to stay in Portugal. Was that a difficult decision?

**MS-S:** Through a retrospectoscope everything seems easy! In real life it was not that easy. I guess I liked my small world too much – Portugal, the city of Porto, beach of Ancora, mountains in Arouca, my large family with grandparents, aunts, cousins, my “tribe,” my students, my friends. These interpersonal links, the roots that keep me anchored to Portugal are probably nothing more than emotional ties and a reflection of my possessive character – nevertheless they kept me in Portugal for good, and I do not regret staying. It has been a rich and fulfilling life.

**ID:** Do you think you made the right decision?

**MS-S:** I guess so. However, there were moments when I had my doubts. Things move

slowly in Portugal. Since you are from Croatia you will probably understand. I guess I should not say more.

**ID:** When did you decide to build IPATIMUP?

**MS-S:** We got the idea in 1989, shortly after we finished organizing the European Congress of Pathology in Porto. The photograph of you and me standing in Coimbra (Fig. 1) reminds me of those days. We realized that the momentum generated by the Congress could help us mobilize the internal forces and obtain sufficient public support for a research institution mainly devoted to human pathology.



**Figure 1.** The earliest picture of the two of us we could find. Manuel Sobrinho-Simões stands to the right and Ivan Damjanov to the left. The picture was taken in Coimbra, the oldest University town in Portugal, in 1989, during the 12th European Congress of Pathology. The proceeds of this Congress were used as the seed money for the Institute.

**ID:** To have an idea is fine, we all have them, but how did you manage to find the money to build the Institute? Could you identify the crucial steps from the formulation of the idea to the opening of IPATIMUP? Teach us how to make dreams come true!

**MS-S:** We used the profit realized from organizing the European Congress of Pathology as the seed money. It was not a large sum, but it was a nice “down payment,” or if you want to call it a “start-up” fund. It helped us negotiate with the Dean of the Medical School and the Chairman of the Pathology Department. Most importantly, it showed them that goal-directed investment could be initiated with relatively small funds. At the same time, we began negotiating the future legal framework of IPATIMUP with the Rector of Porto University. The idea was to build a non-profit pri-

vate institution of public utility, which would be relatively independent of the politics of the University. We convinced him to set aside 10,000 square meters of land in the University campus near the Medical School, and that's the place where we started building the Institute (Fig. 2).



**Figure 2.** The IPATIMUP under construction in 1993 near the University Hospital (white building).

Once we began and the foundations were laid, we named our Institute, in keeping with the trends of 1990s, an institute for molecular pathology and immunology. In 1990, we applied, together with the University of Porto, to the European Union Developmental Programme, which was designed to help the establishment of research institutions in Portugal. Our grant application received a favorable review in 1992, and we started building the Institute in 1993. It took us four years to even start laying the foundations! The IPATIMUP was completed in three years and we moved into the new home in the summer/fall of 1996 (Fig. 3).

The first group of scientists consisted of pathologists, basic researchers, and clinicians interested in cancer. All of us were full-time employees of the University of Porto. Shortly thereafter, we were joined by a team of population geneti-



**Figure 3.** The construction of the IPATIMUP was completed in 1996.

cists from the Faculty of Sciences of the University of Porto. The labs were equipped with the donations from several private and public institutions, especially from the Lisbon based Calouste Gulbenkian Foundation. In 2000, the same process was repeated. Using our own seed money, we applied together with the University of Porto to the European Developmental Programme and we were granted money to build the second part of the Institute.

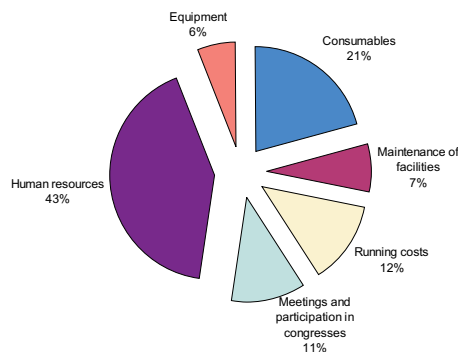
**Present Time**

**ID:** Please briefly describe the Institute that you have built in Porto.

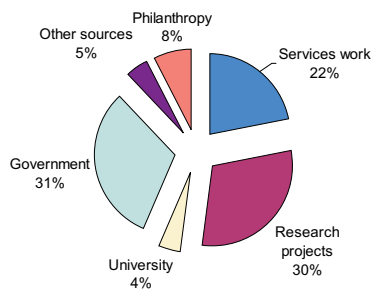
**MS-S:** The Institute covers 4000 square meters and has three floors: the ground floor with research laboratories and other support research facilities; the first floor with the routine labs and diagnostic service rooms (e.g. doctor's offices for fine needle aspiration cytology or paternity tests), library, computer rooms, auditorium, administrative area, and meeting rooms for the outreach program; and the third floor with housing offices and meeting rooms.

**ID:** How does IPATIMUP function at the moment? Does it have its own budget? How firmly or loosely is IPATIMUP attached to the Medical School and the University?

**MS-S:** In 2004, IPATIMUP has received about 3,400,000 Euros. The different expenses and the sources of our revenues are summarized in Fig. 4 and Fig. 5. As you will see, about one fourth of the revenue comes from diagnostic work (cytology, histopathology, molecular pathology, paternity tests, and forensic genetics) and about 1/3 from the Pluriannual Contract (5+5 years)



**Figure 4.** Expenses of the IPATIMUP, 2004.



**Figure 5.** Income of the IPATIMUP, 2004.

with the Ministry of Science and Universities. The remainder comes from research projects and contracts with the industry (30%), from the University of Porto (4%), and from philanthropic sources (8%). The support from the Medical Faculty, as well as from other Faculties of the University of Porto that are members of the General Assembly of IPATIMUP (Sciences, Biomedicine, Pharmacy, Dentistry, and Nutrition), is provided in human resources. Please notice that 25 of the 44 individuals who hold doctoral degrees work in the Institute without pay. The salaries of these 25 professors (including mine) are paid by their respective Faculties. The papers published by the 25 professors are credited to both the IPATIMUP and their respective Faculties. The costs of the Institute in 2004 are summarized in Fig. 4. Due to the link to the University, the percentage for human resources in the overall costs is reasonable (43%) and I think not excessive. This dual funding is the only way that we could have a world class Institute in a relatively small country like Portugal. I think that Croatia should also consider this approach to funding research institutes.

**ID:** You were the Chairman of the Department of Pathology at the University Hospital. You gave up that position and now you are a full time Director of IPATIMUP. Why did you resign from the position at the University Hospital?

**MS-S:** Because I was not able to perform both jobs in a satisfactory way and because I had somebody (my long time collaborator and a senior pathologist, Dr Fátima Carneiro) who would be a much better Chairman of the Hospital than I had ever been. Nevertheless, I kept an office in the Hospital, I still participate in teaching of medical students and residents, and hold the title of professor of pathology. Thus, I have the right to partici-

pate in the affairs of the Medical School, which is very important for collaborative projects and for assuring the support of the University for IPATIMUP.

**ID:** This means that you still have responsibilities at the Medical School. Is this good or just "a necessity of life?"

**MS-S:** It is very good for both institutions. For instance, due to the link to IPATIMUP, the Department of Pathology gets credit for the scientific production of IPATIMUP, which is for Portuguese conditions considered to be "stellar." I am not sure whether it is really "stellar," but the bottom line is that the Department of Pathology accounts for 30% of all publications of the Porto Medical Faculty in international peer reviewed journals. This is ten times more than one would expect from the number of professors and assistants in the Department of Pathology, who represent only 3% of the total faculty. Also, medical students appreciate us coming to teach them. Furthermore, it is important for the pathology residents and junior faculty to have an opportunity to do quality research in an institute that is closely linked with the Medical School. The advantages of these close links between the Medical Faculty/ University Hospital and IPATIMUP are too numerous to be listed here.

**ID:** Do other members of the Institute also have dual appointments? Is their primary loyalty with the Department of Pathology or IPATIMUP? Where do they spend more time?

**MS-S:** Most of the members of the Department of Pathology have, like me, a dual appointment. To dispel misunderstandings, this actually means two jobs and just one salary! Basically, we have three types of faculty members. In the first group we have pathologists, like me and Dr Fátima Carneiro, who divide their time more or less equally between the two institutions (8.30-13.30 Medical Faculty/Hospital followed by another "shift" from 14.30-20.30 at IPATIMUP). The second group consists of professors like Dr Leonor David who have decided to relinquish their hospital position and work full time at IPATIMUP; or professors like Dr Fernando Schmitt who were hired from the beginning to spend their time exclusively at IPATIMUP and only occasionally go over to the Medical School, where they teach senior medical students and participate in postgraduate courses. Finally, the third group of IPATIMUP members

comprises hospital based professors like Drs José Manuel Lopes, Elsa Fonseca, and Isabel Amendoeira, who work predominantly as diagnostic pathologists, and visit IPATIMUP for 1-2 hours every day or only periodically. Each member has his or her own priorities, but as far as I am concerned, I feel equally loyal to IPATIMUP, Medical School, and the Hospital.

### How We Do It in Porto

**ID:** Please describe briefly the scientific organizational structure and the main functions of IPATIMUP?

**MS-S:** The IPATIMUP has a board of directors, which is elected every three years by the General Assembly (chaired by the Rector of the University). The members of the General Assembly are private foundations, such as the Portuguese American Foundation for Development (FLAD), public institutions such as the City Hall of Porto and the Commission for the Development of Northern Portugal, and national non-governmental institutions such as the Portuguese Red Cross and the Portuguese League Against Cancer. There is a Finance Committee chaired by FLAD and an International Advisory Board composed of seven internationally renowned scientists known for their contributions to human pathology, oncobiology, and population genetics. We are glad that you are one of our Advisory Board members.

The most important decision that I had to make as the Director of IPATIMUP was, without any doubt, the selection of external advisory and supervisory bodies. The credibility of the entire Institution and its employees depended on that decision. Accountability, transparency of all proceedings, and professional honesty guaranteed by external supervisors chosen for their integrity, international reputation, and accomplishments are in my opinion essential for all research institutions, but are especially critical for the institutes in small countries like Portugal.

**ID:** How did you decide what to study in your Institute?

**MS-S:** From the first days we decided to devote our work to solving biomedical problems that are important for our country. Thus, we decided to study the etiopathogenesis of some types of cancer that are prevalent in Portugal, such as gastric cancer, thyroid cancer, and breast cancer.

We deal with sporadic and familial conditions and we pay particular attention to the diagnosis of preneoplastic disorders. After having invested in research in the pathology and genetics aspects of cancer research we are now investing a lot in cell biology. A consequence of the research activities is that we do a lot of graduate teaching and training (Master Courses in Oncobiology and Molecular Medicine and a Doctoral Course on Biomedicine, together with the Porto Biomedical Institute and several Faculties devoted to basic sciences). We also have a fantastic outreach program involving teachers and students of elementary and secondary schools in Northern Portugal (Fig. 6) and we perform diagnostic services.



**Figure 6.** Youngsters attending courses at the IPATIMUP during summer holidays of 1997.

**ID:** How much does it cost to do all this?

**MS-S:** It costs about 3 million Euros per year.

**ID:** Where do you find the money? Does the European Union help?

**MS-S:** I have already detailed the main revenue sources of IPATIMUP. For practical purposes we think it is good to try to keep a balance that can be best described as: 1/3 from the Government and the University, 1/3 from services and contracts, and 1/3 from research projects and philanthropy.

The European Union has helped a lot in getting the building under the roof, and is still important for many of the functions of the Institute. For scientists from a small country like Portugal, it is extremely difficult to win funds at the European level. European projects are designed for mega-institutions and for meganetworks, and for us it is

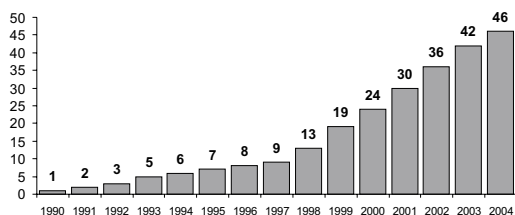
relatively difficult to become a part of those. Nevertheless, we decided that we must try and, accordingly, we are considering joint ventures. Most importantly, we are collaborating with the two other Biomedical Institutes of Porto and with several European institutions that are, like us, focused on cancer research using a translational approach.

**ID:** What are your priorities and how do you allocate the funds?

**MS-S:** We have established, with the help of North American specialists, the Research Strategic Plan of IPATIMUP for the period 2002-2007. According to this Plan, our priority is to excel in translational research on human cancer, with primary emphasis on gastric cancer. The funds are allocated by the Board of IPATIMUP to achieve this objective.

**ID:** Besides the research, the Institute has an educational function. Please give us first some facts. How many students have so far received their advanced degrees at IPATIMUP?

**MS-S:** On average, 12 students get a Master's degree and 4 to 6 PhD students get a doctoral degree every year. In Fig. 7 one can see that the number of PhD degrees obtained every year since the inception of the Institute has been rising.



**Figure 7.** Number of doctorates (PhD equivalent, cumulative) awarded at the IPATIMUP from its inception.

**ID:** You also provide pathology services for the oncologists in Porto and northern Portugal. Can research and service work be combined? What are the advantages and disadvantages of this approach?

**MS-S:** Research and service work can be combined provided the latter is kept within a balanced frame and the Institution does not turn into a private "for profit" laboratory. For us, the services have been an extraordinarily important source of income. These funds represent a finan-

cial buffer, safer and more predictable income than the government monies. Furthermore, these diagnostic pathology services are a good source of human tumor material and give credibility to the concept of "translational research." It also helps us to maintain contact with other countries. For example, we receive consultation and challenging and interesting cases from other parts of Portugal, but also from most European countries and Brazil.

This diagnostic activity gives us visibility and provides "ammunition" for talks with the ever important politicians. It is much easier to explain them the benefits of proper pathologic diagnosis of cancer than the significance of various *Drosophila* genes, as you very well know!

The diagnostic services are directed by Dr Fernando Schmitt, a Brazilian doctor, who has used this material for numerous studies and has earned for himself as well as for IPATIMUP a lot of visibility and credibility in Portugal and Europe. Fernando is the President of the Portuguese Society of Cytopathology. (Isabel Amendoeira, another member of IPATIMUP, is the Vice-president of the Portuguese Society of Pathology). He is also involved in the activities of the European Society of Pathology. We all strongly believe that all members of IPATIMUP must be socially engaged both at the local, national, and international level.

We consider the diagnostic services to be an integral part of IPATIMUP and, like research, we want them to be accredited by external organizations. Thus, our Unit for Cytopathology and Histopathology will hopefully be accredited next month by the American College of Pathologists (ACP). We have planned this accreditation for years and hope that IPATIMUP will become the first ACP-accredited laboratory not only in Portugal but also among the first in Europe. We believe that this will show our customers and the public in general that quality is important to us and that we want to be as good as possible.

The diagnostic service work and our prominence on the medical scene in Porto are crucial for recruitment of young scientists. We want them to stay with us rather than to go abroad, and therefore we are actively recruiting the best biomedical students into our graduate programs. Recently, we have managed to attract trainees from other countries as well, especially from Brazil, Spain, Western Europe, Portuguese speaking Af-

rica and even some Eastern European Countries (Bulgaria, Poland, Russian Federation) and China.

### Accomplishments – Time to Brag

**ID:** Scientific output. How do you measure it?

**MS-S:** Basically, through the number of articles published in international peer-reviewed journals.

**ID:** How do you know whether anybody cares about your group in Porto or abroad?

**MS-S:** Let me be honest. We would like to get as much recognition abroad as possible, but the main function of IPATIMUP is to promote science locally and have an impact on our citizens. If you work continuously, some awards and recognitions will ultimately come. At the local level, the scientific community of Portugal has honored IPATIMUP by bestowing the 2002 award for the life time achievement upon me. I was very honored by that award, which would not have come without the contributions of my collaborators (Fig. 8). I think that all my collaborators took it as recognition of our 15 year long effort to place science performed in Porto on the international map.

**ID:** Do you think that you have had a measurable impact on anybody outside of Portugal?

**MS-S:** I do not know whether we have had any impact but at least we publish in high impact biomedical journals, and *eo ipso* you could assume that somebody is reading our papers and



**Figure 8.** The members of the Institute, celebrating the Pessoa's Prize that was awarded to IPATIMUP in 2002. This national award was named in honor of the great Portuguese poet Fernando Pessoa, who died in 1935.

that we might even have some international impact. We also know we have some impact because many IPATIMUP scientists are invited to give lectures and advanced courses abroad, and some of our papers were accompanied by important editorials. Some of our members received awards in international competitions. For example Drs Fátima Carneiro and Raquel Seruca received the Benjamin Castelman Award from the United States and Canadian Academy of Pathology in 2002.

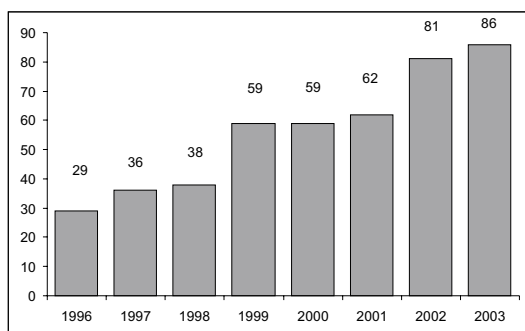
Through IPATIMUP and the international recognition of our research, pathology has become one of the most sought-after residencies in Porto. I became most acutely aware of how prestigious it became to enter a pathology residency only after several sons and daughters of my esteemed clinical colleagues applied to become pathologists. In Portugal, it has been a long tradition that sons and daughters become members of the same specialty as their fathers. I am not sure why young doctors want to become pathologists, but I take it as a compliment that they are breaking ranks with their parents and joining us!

**ID:** How important is it for you to publish in high impact journals? Maybe you could tell us how you play that "citation impact factor" game? A brief introduction about the IF would also be welcome.

**MS-S:** As you know, medical journals may be ranked by their impact factor, a unit designed by Garfield and his collaborators at the Institute for Scientific Information (ISI) in Philadelphia. Being listed in the *Current Contents*<sup>®</sup> can also be a measure of the quality of a journal. It is a matter of prestige for a journal to be indexed in this bibliographical database, as is, to my understanding, also the *Croatian Medical Journal*. Please, convey my congratulations to the Editors. Almost no medical journal in Portugal is and I guess that there are not many Croatian journals indexed either. Please excuse me if I am wrong.

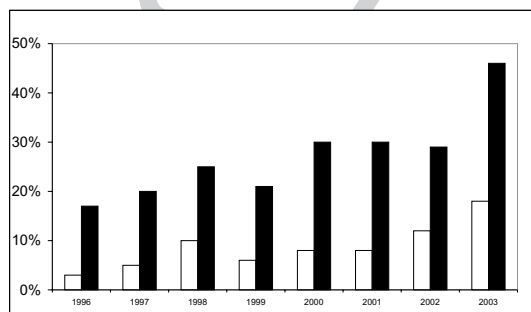
Impact factor (IF) measures how often articles from a given journal are cited by others, but that I do not need to repeat this for the readers of the *Croatian Medical Journal*. The more prominent the journal the higher is its impact factor. For example Nature has an impact factor of 30.979, Journal of Pathology 4.6, Ultrastructural Pathology 0.9. The highest ranked Portuguese journal has an IF lower than 0.5.

In order to achieve international recognition, we decided to publish our papers almost exclusively in *Current Contents*® journals (Fig. 9). Our approach to medical publishing takes into account the IF of the journals where we plan to submit the manuscripts. We feel that the IF provides a quality assurance, and could be used as an external measure of the quality of our papers.



**Figure 9.** Scientific papers (cumulative numbers) from the IPATIMUP published over the years in the journals indexed in the *Current Contents*® database.

At the end of each year, we count the IPATIMUP papers that were published in peer reviewed journals. A graphic presentation of our results, I hope, speaks for itself (Fig. 10). We have arbitrarily divided the journals where these papers were published into three groups: top journals that have IF over 6.0, journals with medium impact factor (over 3.0) and those that have an impact factor below 3.0. I am very pleased and proud of the fact that more and more of our papers are accepted in high impact journals. We are quite pleased with this trend but hope that we could do even better.



**Figure 10.** Scientific papers published in two groups of journals indexed in the *Current Contents*® database and sorted according to their impact factor: impact factor >6 – open bars, and impact factor 3-6 – closed bars.

**ID:** These data are impressive. Are there any other signs of recognition bestowed on the members of IPATMUP?

**MS-S:** You obviously want me to brag! But I think it was you who told me once that modesty is an overrated virtue, if virtue at all. OK, I will do it but I hope that your readers will not misjudge me as a braggart. Also, please remember that all awards given to the Director are recognition to the entire staff and that the entire region or Portugal takes pride when our work is recognized.

Over the last few years, members of IPATIMUP have been elected to the editorial boards of 15 international peer reviewed journals. We have strong representation in the European Society of Pathology and in its Working Groups, in the European School of Pathology, European Course on Cellular Pathology, European Association for Cancer Prevention, European Association for Cancer Research, just to mention a few.

**ID:** Congratulations. In my mind, your achievements could be quite favorably compared to those of your soccer club FC Porto, but I am sure that as a Porto-fanatic you do not share my opinion. If FC Porto has a public visibility 10, what is the public visibility score of IPATIMUP? Do the people of Porto know that you exist at all?

**MS-S:** We have been repeatedly considered the best known research institute in Porto, and one of the best known research institutes in Portugal. IPATIMUP has received several awards and we are grateful to Porto City Hall, Red Cross, TVs, newspapers, and Artists Associations who bestowed these honors upon us. Yes, we think that all that publicity has done wonders for us and that most citizens of Porto know something about our Institute. Maybe less than about football club Porto, but I am sure that in Croatia you cannot compare soccer and science either.

**ID:** Finally, how do you see your legacy? What are your main accomplishments?

**MS-S:** To have contributed to the creation of an Institute that is alive and well and to have helped a dozen young men and women in my country to get further than I have ever dreamed to go.

**ID:** Would you have done it otherwise?

**MS-S:** For me there were no alternatives and thus I think that the answer is no.



**ID:** Any advice for Croatian biomedical scientists and doctors before Croatia enters the European Union?

**MS-S:** They should join hands and efforts, and establish both national and international networks. Science requires team-work, contacts, and support groups. Science cannot exist in a vacuum. Science has no borders. Good science must be recognized internationally as such by your peers and that's why I think that it is important to introduce external, independent evaluations at every level. It has helped us a lot and I am sure that it will give credibility to your efforts as well.

**ID:** Do you think that this interview could help in that respect?

**MS-S:** Of course, especially if it generates discussions. The most important thing is to have open discussions about all the problems and all plans that you might have. In a collegial atmosphere – for starters I could send you a bottle of Port-wine or a case of our *vinho verde* with my best wishes.

**ID:** A bottle of Dalmatian *Dingač* or *Postup*, my favorite Croatian red wines, would probably do. Until then, thank you for your time and hope to see you soon in Zagreb or along the Adriatic coast.

Institute of Molecular Pathology and Immunology of the University of Porto  
(Instituto de Patologia e Imunologia Molecular da Universidade do Porto)

<http://www.ipatimup.pt/>

Rua Dr. Roberto Frias, s/n

4200-465 Porto - Portugal

Phone: +351 22 5570700

Fax: +351 22 5570799

E-mail: [ipatimup@ipatimup.pt](mailto:ipatimup@ipatimup.pt)