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Feature Article

The Mediterranean Institute for Life Sciences—An Attempt at Scientific Excellence in Croatia

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"Croatia—Mediterranean as it once was," this slogan (seen and heard in advertisements all around the world these days) professes Croatia's philosophy and orientation when it comes to its role in global tourism. Crystal clear sea, medieval Mediterranean culture, warm, simple-minded folk: this antithesis of the modern, fast-paced, high-tech world indeed does sell well. However, in the shadows of the ever-expanding, strategically important, moneymaking tourism, a different kind of endeavor is taking shape in Croatia, one that is significantly more forward-looking.

A few years ago in the city of Split, a port in the southern Adriatic and famous for the UNESCO-protected palace of the Roman emperor Diocletian, a molecular biology institute was founded with an explicit aim to try to bring world-class science to Croatia. Named for its geographical as well as ideological mark, the Mediterranean Institute for Life Sciences (MedILS) is currently undergoing a phase of major growth and expansion. Under the guidance of Prof. Dr. Miroslav Radman, a world-class geneticist known for his fundamental discoveries such as SOS-response in bacteria or DNA mismatch repair, the first generation of us, MedILS scientists, is aiming to position the institute into a recognizable player on the world's scientific scene.

In this essay, I will describe where MedILS as an institute is coming from and where it is going, focusing on the few quite unique basic ingredients that I hope will bring about its future success. From unrelenting emphasis on fundamental research in molecular biology to our ambition for MedILS to become the "Cold Spring Harbor" of Europe, our aims are set high. With significant financial support of Croatia's private business sector and strong collaborative ties with top-notch scientists from all around the world, the endeavor is posed for a quick start. The countdown has started, the first research groups have moved into the building, and this is the time of the Institute's greatest transformation and growth. Will it live up to its promises, remains to be seen. But, the times are undoubtedly exciting.

HISTORY, DEVELOPMENT, AND VISION

Already back in the early 70s, the Institute's founders' Prof. Dr. Marija Alacevic and Prof. Dr. Miroslav Radman had an idea of founding an interdisciplinary life-sciences institute somewhere on the beautiful coast of Croatia. Jokingly dubbed "The Warm Spring Harbor Laboratory," this ambitious brainchild of the two was envisioned to become a meeting point of different scientific cultures where a constant stream of high-quality biological workshops, symposia, and meetings would intermix with a powerful presence of strong research labs located on the premises. Inspired by the early-day genetics meetings at the original Cold Spring Harbor or the ferociously stimulating Gordon Conference meetings of the pioneering era of the 1960s and 1970s, MedILS was envisioned to be a place where world's top life-scientists come to meet, discuss, work together, and create novel science. The modern scientific landscape, being dominated by the big-money, publish-or-perish, grant-seeking orientation, indeed does sometimes overshadow the basic premises of fundamental research: simple curiosity, creativity, and time to think have become elusive qualities. And this is the gap that MedILS attempts to fill. After an almost 30-year long hiatus, the idea of the Institute started to materialize about 6 years ago, following the initiative of Prof. Dr. Hrvoje Kraljevic, a mathematician and at that time Minister of science in the Croatian government, who invited Prof. Radman to come to Croatia and make his ideas a reality. And today, a few years later, MedILS already looks the part needed to meet its original vision. Located in a beautiful spot on the coast of Adriatic, hidden in a thick grove of pine trees on the premises of the former Marshall Tito's villa, it has in 2007 officially started with workshops and symposia on the highest level together with basic, fundamental research in its laboratories (Fig. 1).

Implementing an ambitious development plan such as that of MedILS requires significant funds. The restoration of the old army barracks belonging to villa's complex into a modern

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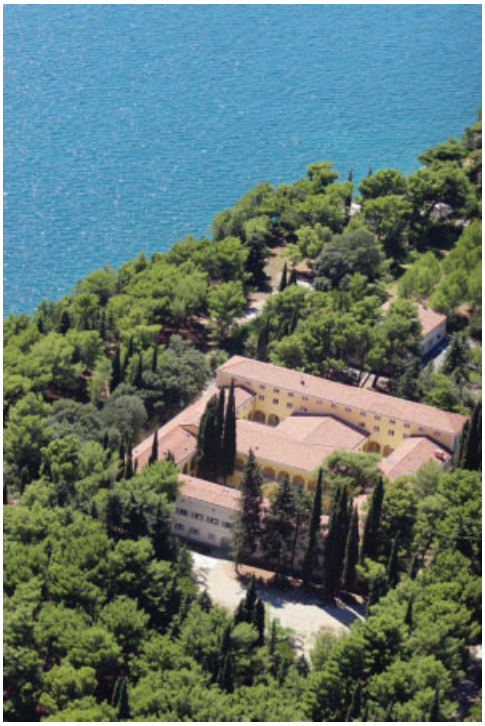

Figure 1. Arial view of MedILS.

laboratory building was originally funded by the Croatian government who also provided initial funds to help set up the laboratories. The second major injection of funding came in 2007, when the top 28 companies in Croatia vouched unconditional support for research at the Institute for the next 5 years, and important to say, with no strings attached. Recognizing the potential of basic research to transform the country on many levels (as well as plain good old publicity) these companies provided enough money to start running the Institute as a serious operation, hire some new faculty and further equip the labs. In addition, the importance of MedILS was recognized by the government of the City of Split by donating 12 standing scholarships to the students and postdoctoral fellows of the Institute. With the success and growth of the Institute, it is hoped that an additional segment of future support will come from the private domain. While MedILS' orientation and philosophy are strictly geared toward basic research, it is possible that over time some fruitful collaborations and ties with the more applied industrial and technological sector will be forged. Through direct creative input or more traditional consulting in branches such as biotechnology, the Institute could become the intellectual engine for the development of Croatia's industry in the more cutting-edge areas of technology. The paradigmatic relationship between the Silicon Valley and Stanford University is a great example to follow. The question whether this would be possible without compromising the Institute's firm dedication toward fundamental, basic research with no bounds set to limit its creative impulses and intellectual freedom, remains to be seen. While thus far the support from the business sector has played a major role in MedILS' development, it should be stressed that in addition the Institute does depend on outside grants and more standard ways to fund basic science. Therefore, in its future recruitment and expansions, the Institute leadership will pay particular attention to try to attract new faculty and group leaders, who will be competitive enough to attract their own funding.

SCIENCE AND CHALLENGES AHEAD

In terms of its recruiting philosophy so far, the Institute has emphasized the principle that the excellence of individual candidates is more valuable and relevant than their specific fields of research. A blend of quality people will always find ways to communicate and collaborate no matter what their backgrounds are, and in the process, quality science will emerge. Currently, there are seven different research groups at MedILS covering an eclectic range of disciplines from fundamental genetics to molecular biology of tumors to computational biophysics and bioinformatics. The group jointly led by Miroslav Radman and Ksenija Zahradka focuses on studying the mechanisms of adaptation to life under extreme conditions. In particular, they study the extremophile bacterium *Deinococcus radiodurans* which is able to withstand extreme doses of radiation and desiccation, deadly to the majority of other organisms. Extending further on the theme of life and death, the group led jointly by Ivan Kresimir Svetec and Francois Taddei, probes the mechanisms of death in yeast. By analyzing the phenotypical effects of knocking out one-by-one every single essential gene in *Saccharomyces cerevisiae*, they hope to find regularities and rules in the modes of cellular death, an area extremely attractive because of its ties to cancer. The group of Ivan Dikic and Janos Terzic meets the challenges of studying cancer head on. Their Molecular Biology of Tumors program utilizes a battery of molecular biology techniques and approaches to study the role of ubiquitin

Figure 2. MedILS contains laboratory space for about 100 scientists.

system in tumorigenesis. In a related fashion, the group of Fumiyo Ikeda focuses on probing connections between inflammation and cancer. The last group on the experimental front, that of Dimitri Krainc and Janos Terzic, uses a combination of modern genomics and proteomics approaches to tackle the fundamental origins of several major neurodegenerative diseases such as Parkinson's and Alzheimer's diseases. Furthermore, the institute is aiming to develop into a major center for bioinformatics, computational biology and biophysics. These disciplines, undoubtedly important in modern molecular biology research, provide an added benefit that they are not highly expensive to fund. The group of Anita Krisko and Ivo Sbalzarini focuses on the bioinformatics of bacterial cells. Currently, their focus goes in the direction of looking for the ways in which environmental adaptations of different species of archea and bacteria are encoded in their proteomes. Finally, the group of Bojan Zagrovic uses major computational resources to study the structure and dynamics of biomolecules. One of the founders of the distributed computing project Folding@Home, Bojan Zagrovic aims to set up the second control center of the Folding@Home network (currently numbering more than 250,000 processors), next to Stanford University.

A cursory glimpse at the current scientific roster at MedILS reveals an important peculiarity that more than a half of the group leaders engaged there have permanent positions at world's top institutions such as Necker Institute, Goethe University, Harvard University or ETH Zurich. Namely, the idea that MedILS would be a focal point, a node in the global academic network is directly reflected in its current structure: in most of the groups, one of the group leaders is a recognized scientist with permanent basis abroad, who, together with a coleader permanently in Split, runs an outpost of his lab on the location in Split. Frequent visits and modern means of communication do indeed facilitate such modus operandi, but it should be emphasized that in the near future we expect further additions of four independent leaders with permanent location in Split.

Despite the initial successes, MedILS is still at its inception and many challenges lie ahead of us. First and foremost, the Institute is still at about 20–25% of its optimal capacity and there is plenty of room for growth and expansion (Fig. 2). Securing competitive startup packages and recruiting strong, independent group leaders who will be permanently stationed in Split and be able to obtain the majority of their own funding in the international scientific arena is probably our top prerogative. The Institute has international ambitions and recruiting non-Croatian group leaders is a part of our policy; recent recruitment of Dr. Fumiyo Ikeda from Japan is a first move in this direction. In its further growth, MedILS will be guided by the international Scientific Advisory Board consisting of the professors Nenad Ban (ETH, Zurich), Pascale F. Cossart (Pasteur Institute, Paris), Axel Ulrich (Max Planck Institute, Martinsried), Wilfred F. van Gunsteren, (ETH, Zurich), Jean-Claude Weill (Hospital Necker, Paris), Ari Helenius (ETH Zurich), and Roger L. Williams (MRC, Cambridge). Second, further equipping the labs, consolidating the supply channels for consumables (sometimes not a trivial task in Croatia!), and creating a fully productive research environment is another challenge, which should be overcome within the next year or two. Third, if MedILS is to make an impact on the international scientific stage, it should be more than a sum of its parts. With the optimal size of about 100 scientists on premises, it is too small to just be a collection of 10 or so research groups. Finding common denominators between the existing groups, starting collaborations, and further recruiting in a strategic fashion is something that we will pay attention to in the period to come. Final, recruiting top-notch students from Croatia and abroad is an important element if MedILS is to succeed. Our focus on interdisciplinary-minded all-rounders, biologists who are not afraid of math or programming or physicists who are actually stimulated by the "dirtiness" and complexity of biological systems, is something that we will not shy away from. The hope is that through the creation of a unique intellectual atmosphere, such population will be naturally drawn to apply.

This article was opened up with a quote of a catchy soundbite coined by the tourist officials of Croatia. I would like to close it off with a paraphrase: "MedILS—Mediterranean as it should be": multicultural, open, focused on exploration and growth, ready to integrate and assimilate, creative, forward-looking. All of these attributes of Mediterranean could be, and hopefully will be, applied to the science at MedILS as well. You too are invited to participate.