Interview of Dr. Dimitris Stellas, Associate Researcher, Institute of Chemical Biology (ICB/NHRF)

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Mr. Stellas, you are returning to the Institute of Chemical Biology (ICB/NHRF) ten years after completing your postdoctoral research here. How do you feel about this return?

It is a great pleasure and honor for me to return to the NHRF and offer from my new post, as an associate researcher, having done a 10-year postdoctoral training course at other institutes in Greece and abroad. The ICB/NHRF consists of very remarkable people at all levels and positions, who create a very good atmosphere of help and cooperation as well as a work environment really pleasant to work at.

Talking about returns, you joined ICB/NHRF having recently arrived from the USA, where you were a Fellow at NCI/NHI. Tell us about your experience there.

The level of Greek universities and research centers is very high, but to be able to compare, we should have a measure of comparison. I think NCI/NIH will always be a measure of comparison for me. I have indelibly imprinted in my memory the welcome of the president of NIH, Dr. Collins, who said that it is an honor for NIH to have us in its resources, but it should also be an honor for us to work at an institute that has contributed much to science and has so far led to 160 Nobel Prizes! I could say a lot about my experience at NCI, not only about the purely scientific part but also about behaviors or staff guidance, etc. Yet, I

would prefer to try to apply them instead of just talking about them. I will only mention the great breakthrough of cancer immunotherapy and the logic of immunotherapy with autologous transplanted or not T lymphocyte transplantation, which began with Dr. Rosenberg in Building 10. I was also impressed by how united and organized they were during the challenge of COVID-19 pandemic, with almost universal participation from all research teams, for the common good. Finally, I would like to mention 2-3 points that have to do with the operation of the institute. A very important element of the research taking place in NIH/NCI is the direct connection of the laboratory with the clinic and the patients. There is an endless, fruitful dialogue and exchange of views between scientists with completely different interdisciplinary specializations aimed at an in-depth understanding of the disease at the molecular and systemic levels to achieve a cure for patients. This connection seems to be less meticulous in our country. Another thing worth mentioning, apart from science, is that NIH has intramural funding, in other words, it self-finances its researchers and favors collaborations with each other. Thus, it invests in its research resources, and judging by the result, this model seems to be effective.

So what made you come back to Greece? What was the motivation?

I will answer you with the Homeric phrase: *'ὡς οὐδὲν γλύκιον ἧς πατρίδος οὐδὲ τοκήων'* which means *'There is nothing sweeter than home and parents'*. Of course, there were many motives for me to decide to return, not financial ones, as one would imagine. I have always considered it a duty of mine to help my country, but the fact that I knew the good work environment of ICB/NHRF, which helps us all to thrive, played a significant role in my decision to return. Finally, I believe that ICB/NHRF has a great advantage, which fits very well with my mentality of exchanging views between different specialties (interdisciplinary), for the benefit of patients. ICB/NHRF is the only Institute in Greece that theoretically covers all stages of preclinical research, as it is staffed with research teams involved: 1. In identifying a potential drug target, usually a gene product, 2. In design and in synthesis of new bioactive compounds against the drug target, 3. In *in vitro* assessment of activity and selectivity, and 4. In preclinical studies of toxicity and activity *in vivo*, while the direct clinical benefit of a therapeutic approach for the patient can be predicted through humanized animal models, which I am called upon to develop.

Where does your research mainly focus on within ICB/NHRF? What are your research goals?

Identification and confirmation of therapeutic goals/diseases and biological evaluation of targeted bioactive molecules-drugs. The title says it all, it leaves no doubt as to what the

team's scope will be. I'm kidding of course. My research at ICB/NHRF will focus mainly on the study of cancer immunotherapy. To this end, I will try to develop 'humanized' mouse models. What is this; Based on individualized treatment, many researchers use immunocompromised animals (without a functioning immune system), in which they place part of the patient's tumor orthotopically in the corresponding tissue of origin. These models are now abandoned because they do not take into account the interaction with the immune system at all, a factor that is crucial for the course of the disease. So, we will develop models in which the endogenous immune system of the experimenter will be replaced by the patient's immune system and after incorporating part of the patient's tumor, they will develop the tumor in the corresponding tissue, with the tissue of origin. Such an approach is particularly attractive because it allows the study of combined therapeutic approaches such as a combination of chemotherapy and immunotherapy and provides conclusions that can be translated directly into the clinic for the benefit of the patient. The team will also develop immunosuppressive cancer models, which will be used by ICB researchers and collaborators to study the properties of the bioactive compounds they synthesize, whether it is a toxicity study or an activity study. I will also continue to deal with pancreatic cancer and breast cancer, trying to develop and implement innovative therapies, such as autologous transplantation of specially modified T lymphocytes (CAR-T) or modified NK (CAR-NK) cells. Finally, being influenced by SARS-COV-2 era, and the experiments I did in NIH, under the guidance of Dr. Pavlakis, if the circumstances allow, I would like to study the cellular immunity that we may have developed against the virus.

In conclusion, what do you think about the landscape of research in Greece, in terms of means and opportunities for young scientists? What are the difficulties to be faced?

The research landscape in the country is changing for the better. HFRI (ELIDEK) has been established in recent years and is very important in our country. New funding programs (research-innovation) were also announced and constitute another effort to support local research. Anything else needed? Of course! For example, it is a bit rich that the previous service of colleagues is not recognized in terms of salary, due to a poorly written law. For me, not even half of the 10 years of postdoctoral service were recognized, it's like I finished my university yesterday! But let's not keep saying what needs to change, I may need a whole volume to list them. Let's keep in mind that things are going in the right direction and given the country's economic conditions, I think we are on the right track. Of course, we must become competitive and harmonized with international standards. For this purpose, we need both "hands" and "minds", but also sustainable funding. Unfortunately, to produce a project, an innovative idea itself is not enough, we must have the consumables, the staff and the logistical infrastructure (instruments and facilities) to achieve them. Everyone should help on this, the state, the private sector, and ourselves.

Only cooperatively will we succeed. I hope we stand our ground during the COVID-19 pandemic.