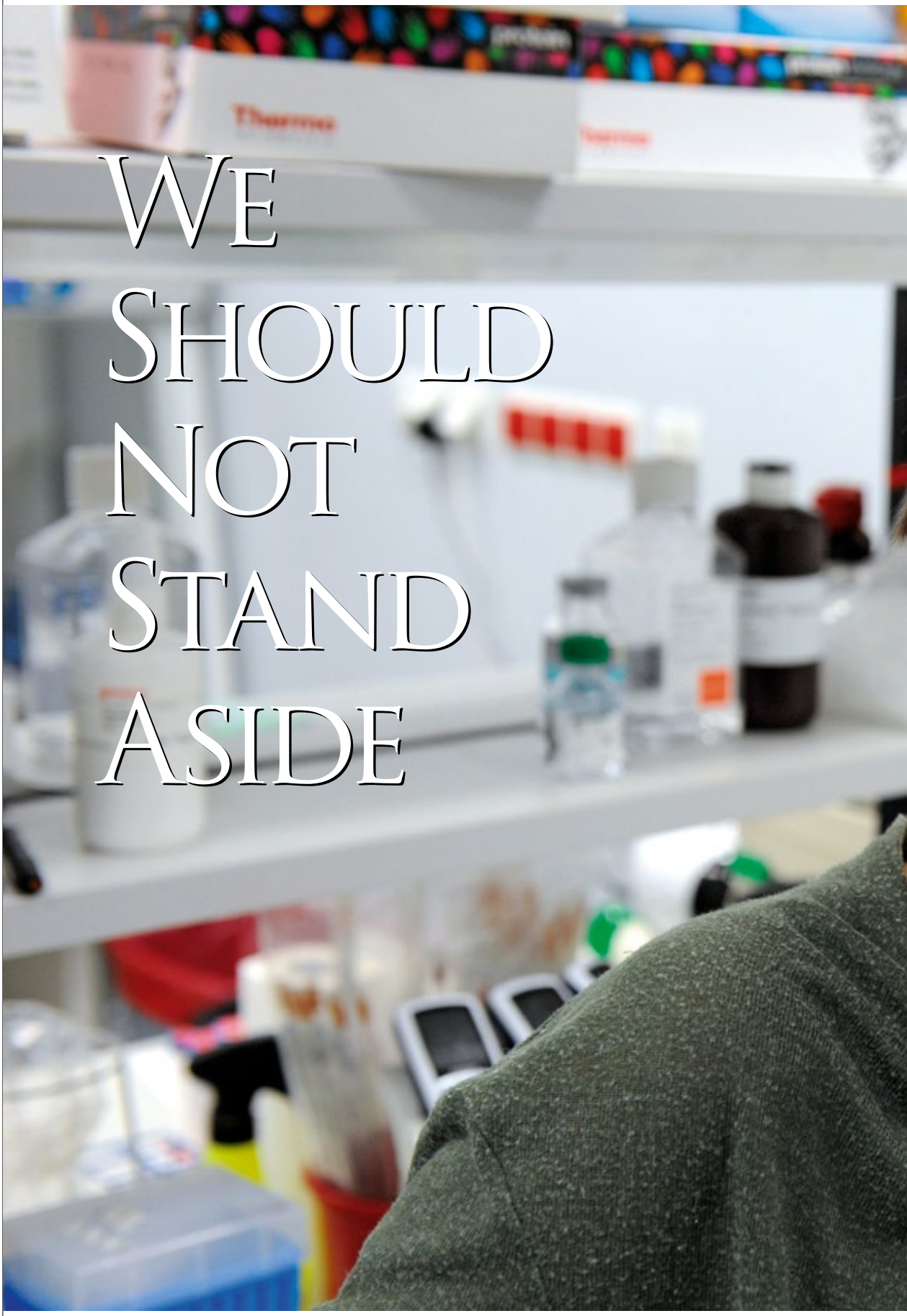
We Should Not Stand Aside



JAKUB OSTAŁOWSKI

Magdalena Winiarska, PhD works at the Department of Immunology at the Medical University of Warsaw. She is this year's recipient of a grant from the European Research Council (ERC) for the project "Searching for novel strategies improving cancer immunotherapy (STIMUNO)."

Dr. Magdalena Winiarska from the Warsaw Medical University discusses what we know and don't know about cancer, the importance of exchanging ideas in science and the meaning of success

ACADEMIA: I'll just ask you straightaway: when will we have a cure for cancer?
MAGDALENA WINIARSKA: A "moonshot" project has been recently launched in the United States, promising to send cancer off into oblivion soon... Of course, we know this is not how things will really happen. I think our goal should be for cancer to become a chronic disease, which is already happening in many cases. Many people with cancer can lead good quality lives for a relatively long time. One scientist who contributed to developing a drug for bone marrow cancer commented that, paradoxically, after this product was brought to market, the percentage of patients with chronic myelogenous leukemia actually increased. Why? Simply because this drug allows patients to function better and live longer, so statistically the number of patients suffering from this type of cancer increased in the population. This example shows that we should consider redefining the term "cure." When it comes to cancer, the kind of therapeutics we're looking for are not likely to actually cure it.

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This does not sound very optimistic.
Of course there are treatments that do lead to a complete cure. A treatment may work so effectively that no cancer cells can be detected with currently available diagnostic tools. But that doesn't mean tumor cells do not remain hidden in the body. Our cancer detection capabilities are quite limited. This is also why in many cases it is difficult to say whether a patient has been cured. There was one interesting case, where a woman suffering from melanoma was thought to be cured after the appropriate treatment. She died from a different cause and her kidneys were taken for transplantation, but both patients who received them ended up developing melanoma.

Was the disease imprinted in her body's history?
It could be that those cells never actually disappeared but the immune system had them under control, stopping the disease from recurring. Transplant patients have weakened immune systems, which of course may contribute to the development of cancer. The cancer cells, however, were in this case probably transplanted along with the kidneys. But it's possible that we often live with cancer cells, or cells with DNA mutations, developing in our bodies. Although we have many mechanisms designed to repair such mutations, our immune system must be battling against mutated cells that have failed to repair DNA damage.

So we shouldn't think of cancer solely as a tumor that can be cut out or a growth that develops within an organ?
No. Even if the immune system manages to keep mutated cells under control, a tumor can still develop in our body. Cancer cells have various sneaky ways of avoiding the immune system. Tumor cells can also attract immune cells and reprogram them to support cancer growth instead of fighting it. As part of our ERC grant, we aim to identify novel strategies that cancer cells use to escape from the immune system and examine the exact mechanisms of this process.

So you don't actually know what you're looking for.
Well, I do know, a bit. I have my assumptions, but I can't reveal anything yet.

The topic is very broad and many research centers are studying it. Is this a kind of competition?
If two different research teams discover a similar phenomenon, it only supports that the conclusion is rather universal. I have recently learned to appreciate working with other research teams. It also gives an opportunity to know what others are interested in. Building this type of an interactive network is one of the best aspects of doing science. It is better to be part of this ongoing exchange than to stand aside.

Are there many centers looking into metabolic changes in the tumor microenvironment?

In fact, thousands of them. Scientists have recently reached the conclusion that tumor creates a very heterogeneous environment. It is not just the cancer cells, but also the cells that surround them, immune cells that have just been recruited and reprogrammed to support the "dark side," so to speak, as well as many other factors. Sometimes a tumor is even described as an organ with a life of its own, characterized by a completely different metabolism, a different blood supply, and in addition all this depends on what kind of tissue the tumor developed on.

So there are many unanswered questions.
Very much so. What happens in the tumor microenvironment? How do cancer cells behave? How do they affect and change the environment? These are all still unexplored areas. The popular opinion is that a tumor consists of cancer cells. Nothing could be further from the truth.

What do you plan to do with the ERC grant?
We have already begun research within this project. When you apply for such a grant, you don't start from scratch. You have to support the idea with preliminary results showing the potential of your research. Many things have to be done in the preparatory phase. You can have thousands of ideas, but you need to know which one of them makes sense and is feasible. You need to determine whether you will honestly be able to confirm or reject the hypothesis. If you can reject it based on credible evidence, this is also very valuable. But as for me, these days I've been dealing mainly with administrative work.

You don't miss the lab?
I do, a little bit. But I also realize that there's a very difficult balance to strike. Doing experiments is extremely time-consuming. It's not just about coming to the lab, pouring liquids, peering under the microscope, adding some reagents. In order for an experiment to be useful, you need to plan it wisely, and to do that, you have to read the literature, figure out exactly what you need. Then run the experiment, gather the results, analyze them, and think about the next step. The experimenting itself is only small part of research. I am aware that I would not be able to do it myself anymore. I have a team running the experiments and my role is to help at the initial stages and later in analyzing and interpreting the results. Also, my role as a person applying for grants and seeking funds is very important.

What types of samples does your team use for physical experiments?
Typically, these are established tumor cell lines that multiply in vitro. So we can grow them in vitro, in plastic culture dishes.

So these are not cells from patients?
A "cell line" is a culture of established cells with specific characteristics. There are thousands of them, easily available from special banks. If they are human cell lines, they are derived from patients, either from excised tumors or isolated from the blood of leukemia patients. Cell lines can also be derived from murine tumors (from mice). Established tumor cell lines serve only as a simplified model of the tumor. But we also have primary cells at our disposal, which we obtain in collaboration with clinicians. After receiving the ethics committee's approval for research, we also use these materials for experiments.

Getting back to the lab: will you also use the grant to purchase lab equipment? Have you gotten ideas from other places as far as what could be useful to streamline the process?
I am not planning on buying any major equipment. We are generally able to satisfy most of our own needs ourselves, as they aren't overly demanding. There are many PAS institutes in the Ochota Campus area in Warsaw that are well equipped, so we can always make use of them. What we are mainly lacking is better know-how and expertise. Immunotherapy and immuno-oncology are not widely studied fields here on the campus, or in Warsaw, or in fact in Poland. We do not have specialized research centers dedicated to immune-oncology. Scientists working for example at Harvard Medical School, even though their labs may look poor compared to ours, with old benches and old freezers, get to work next door to someone who won a Nobel Prize for work in tumor immunology, or next to the world's best proteomics specialist. We need know-how and expertise much more than equipment or money for reagents. I see great potential in collaboration between people who do research in immunotherapy or immunology. Discussions help stimulate ideas for larger interdisciplinary projects. In my opinion, this is what is most lacking. It's a problem for Polish science.

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What is the reason for this? Is it because students don't choose this direction, as it's a difficult topic?

Polish science needs students, but most of all it needs outstanding and experienced researchers. There is no problem with recruiting a good student or even PhD student. The problem is finding professionals. It is nearly impossible to find an experienced post-doctoral fellow who has spent some time abroad. It is even more difficult to find top-notch immunotherapy specialists. Why? Poland is not an attractive place for anyone but Poles. The people who come here with experience from abroad are usually Poles returning home. We are not attracting other outstanding specialists who might choose to live here and could help propel us further in this field.

They're not even tempted by scholarships and the chance to work on interesting research projects?

We can try to increase salaries and scholarships to attract top-level scientists. But still, when someone is good and has the opportunity to work for example in Heidelberg, where a whole institute is dedicated to cancer research, he will choose to go there, even if the salary is lower. Because he knows he will be part of an institute that is shaping the future of immunotherapy.

> I don't necessarily see obtaining a grant as success, but as a chance to invest in the team and to discover something.

So it's a vicious circle?

Somehow yes, because no one in Poland is at the forefront of cancer research. We are trying, but we are nowhere near that scale. I do want to point out, however, that there are plenty of absolutely brilliant Polish scientists who, if we were to offer them good conditions and stable funding, would return. There are well-known Polish researchers in the world, many of them based in the United States. If they all returned to Poland, it would propel us very far forward. But convincing them is a challenge. They will not even be tempted solely by a good salary, thought it would indeed have to be sufficiently high.

What we are still missing is the scientific environment, where researchers can have constant contact and be able to consult on a regular basis. I can of course go somewhere and discuss the problem with someone personally, but usually if I have a research question and I am looking for a solution, there is almost no one who might help me.

Yet despite these difficulties, you still manage to achieve success.

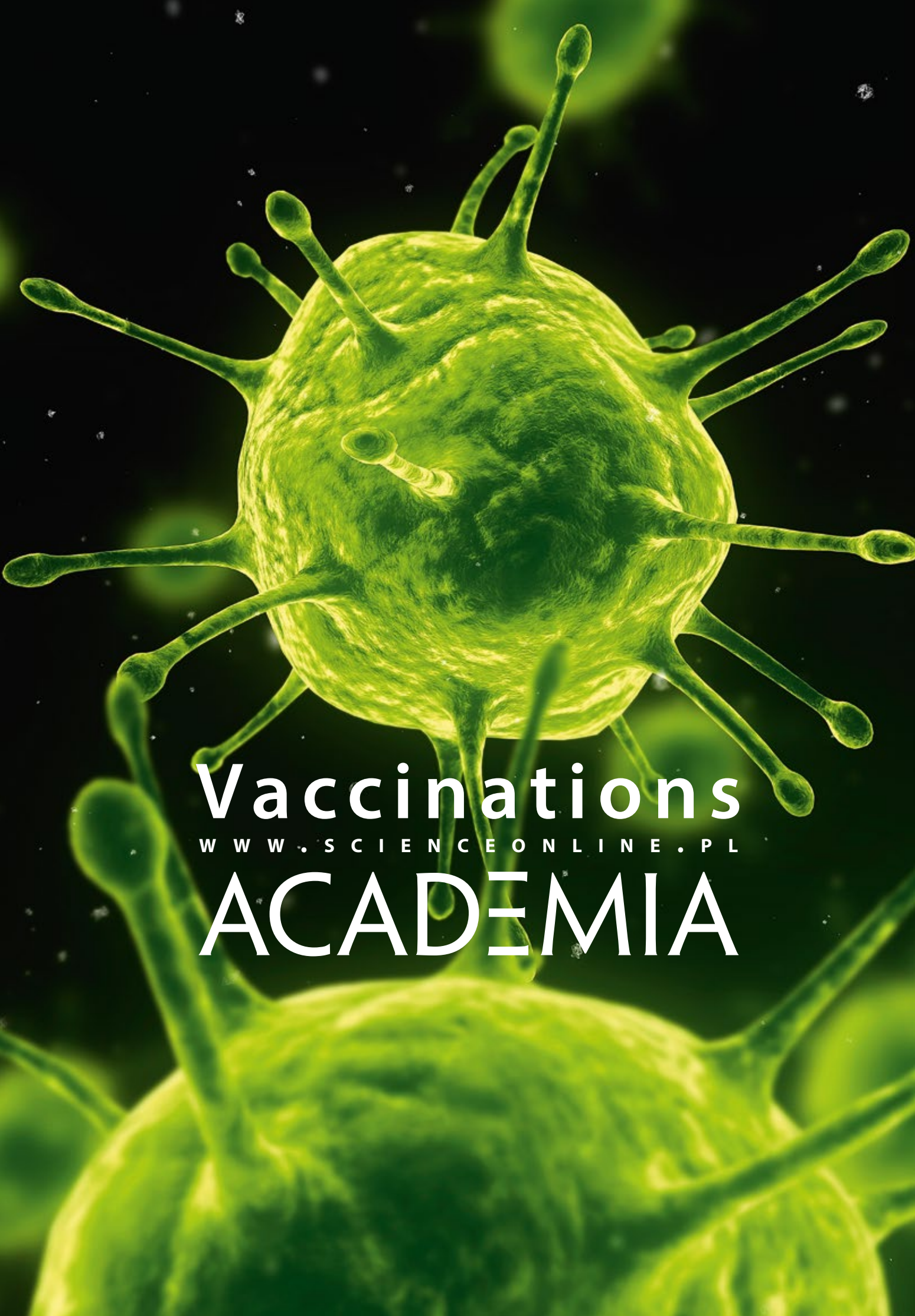
I guess so, but I don't necessarily see obtaining a grant as success. Of course we need this money to build a team, etc., but this is not the goal, just a means to an end. For me, the goal would be to use this grant for something sensible, if we had to measure it. We should really care not about receiving a grant, but about the contribution it makes. So I see the grant as a chance to invest in the team and to create or discover something. Then again, it is difficult to ascertain whether these discoveries are important and accurate. Only time and the findings of others will tell. When making an apparent discovery, scientists run the risk of having their findings turn out to be accidental, of misinterpreting something, or of reporting something that actually only works in specific conditions. It is difficult to say whether something is actually a success or not, it's so unquantifiable and fuzzy. I would be extremely satisfied, and call it a success, if another research team obtains the same results as we have reported in our research.

Would you be more satisfied with yourself and your team's work, if you saw that your work has a real impact on people's lives?

I think so, although I am aware that our results are only a small contribution and as of yet no one has found any practical use for them. Recently, some therapeutic strategies have become introduced in which cells are taken from patients and equipped with special receptors that recognize a specific CD19 antigen that occurs in leukemia and in lymphomas. There was one scientist studying this antigen twenty-thirty years ago, but with a huge problem obtaining funds for it. There are hundreds of antigens on lymphocytes and the regulation of this particular one was of little interest to the scientific world. Until last year, when two new drugs were registered that recognize this particular antigen. Now this scientist has become famous because his initial research from years ago, on how the amount of this antigen is regulated, has become the basis for treatment.

Your research, at the time you are doing it, may seem locked away in a niche and you never know if someday your findings will be useful to someone. They may never be useful, but I don't see that as failure. We are in the process of constantly discovering new things. It's more important that we go through the process thoroughly and with awareness, and not think too much about whether the findings will one day be useful in practice.

INTERVIEW BY **JUSTYNA ORŁOWSKA**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