Equality Pays

Professor Agnieszka Chacińska from the International Institute of Molecular and Cell Biology talks about her research on mitochondrial proteins and their association with neurodegenerative diseases and metabolic disorders

ACADEMIA: **You spent eight years working at the University of Freiburg, so you can compare how women scientists work in Poland and in the West. Are there differences?**

AGNIESZKA CHACIŃSKA: I worked at the University of Freiburg, in a fairly conservative region of Germany, between 2001–2009 and at that time there weren't many female professors. There were not enough day-care centers and preschools for children of working mothers. But the German federal government together with research organizations began to actively promote equal opportunities for both genders, and these initiatives have borne fruit. In other Western countries, such as the United Kingdom and the United States, these "childhood diseases" from back in the times when there was no gender equality, have now largely been cured. If we try to look at things objectively, it is obvious that no country can afford to waste human potential. Not giving women a chance to practice certain professions and be successful at them just because society has other ideas is harmful for ethical reasons and simply does not pay.

Are there certain gender-specific traits which make some people more suited for a career in research?

In every group it is individuals that matter, and it is they who decide when to expand the limits of scientific understanding. No matter if they are women or men. Everyone should have the same opportunities and have their success measured by the same yardstick in the eyes of society. Unfortunately, this is not always the case for women.

In your research work have you encountered gender discrimination?

There are many female professors in biomedical sciences. Doctoral students are not only surrounded by

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Prof. Agnieszka Chacińska, PhD, DSc, is a graduate of the Faculty of Biology at the University of Warsaw. In 2000 she completed her doctoral thesis in biochemistry at the PAS Institute of Biochemistry and Biophysics in Warsaw. She was a postdoctoral fellow and later a group leader at the University of Freiburg in Germany in 2001–2009. In 2008 she received her DSc (habilitation) degree at IBB PAS and her professorship title in 2014. Between 2009 and 2017 she worked at the International Institute of Molecular and Cell Biology in Warsaw, where she headed the Laboratory of Mitochondrial Biogenesis. Winner of prestigious grants of the WELCOME Foundation for Polish Science and the European Organization for Molecular Biology, as well as the 2016 FNP Nicolaus Copernicus Polish-German Award. Member of the Polish Academy of Sciences and European Organization for Molecular Biology since 2017. Currently, Director of the Center for New Technologies at the University of Warsaw.

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male supervisors. The scientific community does not consciously discriminate, though we can observe some prejudices. These are, however, much less significant in comparison to what is happening in Polish society as a whole.

Your research work focuses on mitochondrial proteins. What neurodegenerative diseases and metabolic disorders will we be able to take on if the basic research conducted on these proteins is successful?

It's hard to determine which neurodegenerative and metabolic diseases we will be able to tackle using the results of the research on mitochondrial proteins. What we know so far is that mitochondria are very important for the proper functioning of the cell, and their abnormal functioning is associated with practically all neurodegenerative and metabolic diseases. For clinicians, Alzheimer's and Parkinson's are completely different diseases. Biologists, however, see common elements, such as disturbed mitochondria and the homeostasis of cellular proteins or calcium ions. I'm a biologist, not a clinician, so I don't view diseases through their symptoms. I look at them from the molecular side and I realize that clinicians might not agree with my view. But generalizations are also needed to understand basic mechanisms. At the cellular level, many diseases exhibit similar biochemical and molecular symptoms. When it comes to neurodegenerative diseases we can't tell if it is possible to cure them. Once severe, well defined symptoms appear, it may be too late for treatment. These diseases develop over many years. And since they mostly affect older people, symptoms can easily be mistaken for age-related disorders. In younger people, neurodegenerative disease is linked to a genetic factor. We have no cure today for neurodegenerative diseases. We can only delay some stages of the disease at most. We need a better understanding of the processes preceding pathological states, so that we can better develop effective treatment or prevention strategies.

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Does amyloid protein buildup occur only in Alzheimer's disease, or is it characteristic of all neurodegenerative diseases?

Protein aggregates or deposits occur in most of the diseases. However, amyloid protein buildup is not the only symptom of disturbed protein homeostasis. The proteome, which is the set of proteins that are present in a cell, as a protein equivalent of the genome, is regulated by two major processes: protein synthesis and the removal of defective proteins. If this relationship is disturbed, it impairs the homeostasis of the proteins, throwing off the balance. This happens in all neurodegenerative diseases, so medical conditions that may look different on the outside, they have a common denominator. Unfortunately we detect them too late. What may be truly significant is what happens many years before the symptoms appear.

This is the reason why neuroscientists are working on developing tests to detect these diseases, especially Alzheimer's, as early as possible. Ideally, twenty years in advance. Recently a new test was developed in the UK.

Yes, this is what's happening at the moment. Scientists are looking for the right tests for gene expression levels and other early determinants of balance disorders. It is possible that changes in the mitochondria and/or proteome occur much earlier. Early detection is extremely important because it will enable prevention. If all neurodegenerative diseases have certain features in common at the molecular level, then perhaps prevention at this level will be the key. We all want to live life in good health so that we don't have to suffer.

Some scientists think that in the near future we will be battling not old-age diseases but rather aging itself, in order to prevent the development of these diseases. Is there a relationship between accelerated aging and disturbed protein homeostasis?

Certain symptoms of neurodegenerative disease appear in older people, such as memory problems. Aging is associated with the state of mitochondria, disturbed protein homeostasis, and with changes in metabolism. It is also known that a low-calorie but balanced diet supports longevity. If we could somehow activate the processes in the cells of our body and the brain that provide us with greater resistance to the triggers that can disturb their balance, so that they can handle them, I think that the degenerative processes of aging could be delayed. The work of clinicians and researchers in developing new drugs is key here, but it is also important to understand the processes that take place within the cells.

If mitochondrial proteins accumulate outside the mitochondria, is this a symptom of a disorder or something else?

We still don't know where the process begins. It may be that the mitochondria themselves are beginning to malfunction. This causes the energy capacity of the cells to decrease. This is because the mitochondria are the energy centers, the power stations of the cells. Reduced energy capacity means that the mitochondrial proteins have a harder time entering the mitochondria, because energy is needed for this process. They stay outside and cause an imbalance in protein homeostasis. Such a scenario is possible, but there are others. Perhaps the protein homeostasis problem effects mitochondrial proteins, which should either enter the mitochondria, or be degraded, but this does not happen due to impaired protein homeostasis. Depending on the case, the causes may vary. But in effect, it is a series of overlapping negative changes impacting each other. The focus of my group's research work is the "dialogue" between mitochondria and cellular protein homeostasis. We are among the pioneers in this type of research in the world. There are increasingly more scientific reports stating that this "dialogue" is important and that these two "speakers" influence each other. But only a few years ago this was not so obvious. There is a lot of interest in our work for this reason.

Does this work take place at the International Institute of Molecular and Cell Biology, or here at the Center for New Technologies at the University of Warsaw?

My group has just relocated to the Center. It's quite a big group.

And an international one.

Yes, it includes Dr. Ulrike Topf from Germany, and there are also three graduate students from India and a postdoctoral researcher, Dr. Minji Kim from South Korea.

Do you think that Polish science be more open to the world?

Yes, definitely. Working in an international environment opens the mind and introduces other perspectives. International contacts and discussions, as well as attending foreign conferences are all very important. I have always welcomed the opportunity to work with scientists from abroad, although it is not easily done in Poland as it involves more paperwork, including contacting Polish embassies. Another obstacle is the difficulty for our male scientists from countries such as India in finding accommodations. We had to seek help from a real estate agent. To sum it up, in science it is not only important to seek answers to questions, but also to stimulate intellectual exchange. The success of the world's top universities is due in part to their international staff. The lab in Freiburg where I worked was also an international institution, and its director was very supportive of women. In places where the emphasis is on high quality education, an ambitious and capable female scientist can be very successful. Unfortunately in Poland quality is not always of most importance. In addition, our lack of openness to novelty and otherness is short-sighted. And this is not wise.

Does getting a prestigious grant make it easier to be noticed in the international scientific community?

In the scientific community you will only be noticed if you make a discovery, not receive a grant. Grants are a tool. ERC grants have a special status and are considered very prestigious. We don't get too many ERC grants in Poland, but this is because we are not making discoveries on a large scale. Polish applications are too few and too weak, which is why there have only been a few recipients of ERC grants in Poland.

PAS has appointed an Office for Scientific Excellence, which helps prepare applicants for their final presentations in Brussels. Have you also applied for an ERC grant?

I am a member of the review committee of the European Research Council, but I have also been an applicant. I have not been able to receive a grant, but I will definitely apply for one again in the future. I will gladly utilize the services provided by PAS in this regard.

Have you ever reviewed an application from a Polish scientist?

I have never come across anyone from Poland in my panel, although it is one of the most popular biology panels, which includes cellular biology and development. As in all ERC panels, the competition is very tough and the applicants are all highly skilled scientists.

Which country submitted the most applications to your panel?

Most applicants were from Germany and Great Britain. Statistically, Israel is always very successful. It may be a small country but its scientists are very creative and effective. There are many cellular biology labs in Poland, but not only are there no ERC grant winners, there aren't even any applicants. I don't know why that is.

What would you like to see happen at the Center for New Technologies under your leadership?

Our goal is scientific excellence. Without it, there is no chance of receiving ERC grants.

INTERVIEW BY **ANNA KILIAN**