UNIVERSITY OF OSTRAVA
FACULTY OF MEDICINE

Faculty of Medicine University of Ostrava

MONOCLONAL GAMMOPATHY AND HAEMATOLOGICAL MALIGNANCIES

CONTENT

MONOCLONAL GAMMOPATHY AND HAEMATOLOGICAL MALIGNANCIES

The name of one of the main scientific directions hides several unknown expressions for an unprofessional reader. Monoclonal gammopathy is the state that reflects an immune cells disorder in the case when cancer-causing processes are starting there. The research at the Faculty of Medicine is helping to the improvement of the diagnostics and to the increase of the cancer treatment effectiveness, especially the haematological cancers. In addition, many findings discovered during the research are applicable in general as well. It is, therefore, more than evident that for the practice and for the patients, the field of this research is very important and useful.

#osu #research #science #bcrg
#gammopathy #bloodcancer #healing
#laboratory #tumor #hematooncology

MONOCLONAL GAMMOPATHY AND HAEMATOLOGICAL MALIGNANCIES

Functional genomics and bioinformatics with the development of personalized medicine tools

To understand what we are talking about, a bit of theory and of facts is needed. The team of the Faculty of Medicine, Blood Cancer Research Group (www.bcrg.cz), dealing with the monoclonal gammopathies, tries to identify and understand the genetic changes in the haematological malignancies and put the obtained knowledge subsequently into practice. The clinical part is closely interwoven with the University Hospital Ostrava. In addition, the laboratory is also in close contact with other universities and research centres in the Czech Republic and abroad.

The research has several levels. The basic preclinical research works with the hypotheses that are tested at the cell culture level. The further part of the research involves the new pieces of knowledge verification on the patients' tumor cells. The archiving and samples sharing is provided by Biobank that is collecting samples from patients and volunteers. "*On real patients' samples, we test what we learned from verifying hypotheses on cell cultures. We also need animal experimental models, and for this purpose, the construction of an animal facility will be completed at the Faculty of Medicine of the University of Ostrava next year, and the equipment will be purchased mainly from our projects. Meanwhile, we use the animal facility of the allied workplace in Gliwice. Subsequently, the verification of knowledge must be carried out in clinical studies, but this is not our task. The research has three priority pillars described below. Our team focuses on the preclinical part, which makes maximum use of patients tissues,*" prof. MUDr. Roman Hájek, CSc., the guarantor of monoclonal gammopathy, explains. If everything goes well, the process may result in a successful therapy method.

The branch of cell immunotherapy is worthy of a lot of attention. "*Cell therapy is now a super-modern field that is being dealt with by two or three workplaces in the Czech Republic, not more*," prof. Hájek clarifies. "*In the next decade, cell therapy will become an important part of tumors treatment. It is our ambition to build, in cooperation with the commercial sector and with the Moravian-Silesian Region, a biomedical cluster that would be an attractive job opportunity for scientists not only from Europe*."

The research activity thus helps to create a platform for personalized treatment that maximizes the effect on a specific patient. Just at that point, a patient living in Ostrava can come into contact with the real research results. "*In our team, we use knowledge of the basic research and develop the methods that could be used in clinical practice in the relatively near future*," RNDr. Michal Šimíček, PhD., the head of translational research in the field of haematological tumors at the University of Ostrava, elucidates. He is also a holder of the Neuron Award in Medicine in the category for young promising scientists for the research on the processes causing malignancies and their medicament resistance. He received the award in November 2019 and so he became the second scientist from the University of Ostrava receiving this prestigious award granted to the best Czech scientists

Monoclonal gammopathy is still quite new direction at the University of Ostrava and the team is composed mainly of young scientists. Even in very mature teams, the positive results are found out only once per two or three years, so it's not easy to explore something completely new. There is a lot of work and verification behind it all. A unique interdisciplinary Cell CooLab Ostrava research and development centre for cell therapy in hematology and oncology is also being founded to accelerate drug development. The university researchers can develop their skills there, using practically oriented experiences of the employees from the companies operating in the field of biotechnology and medical diagnostics

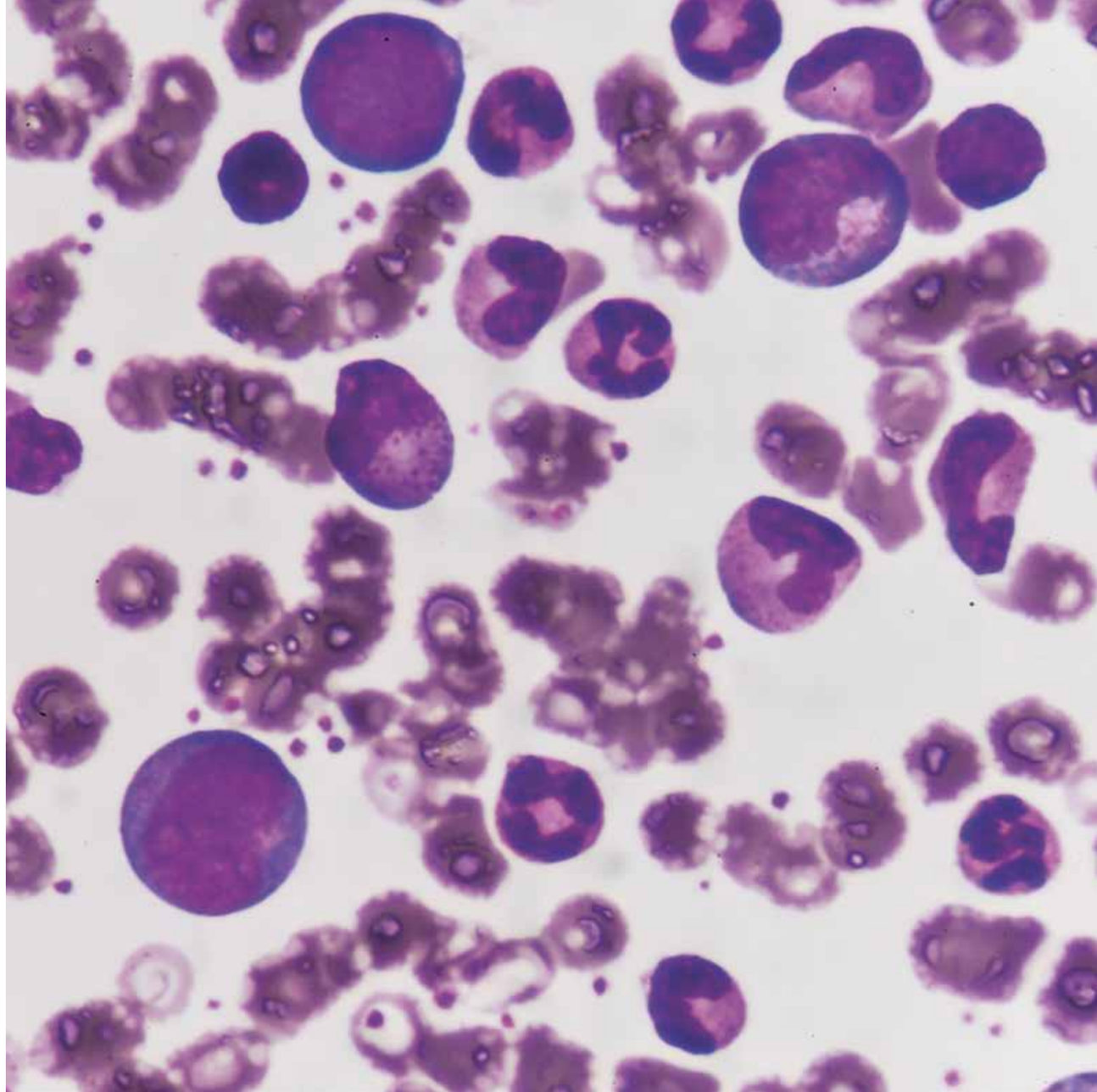
BLOOD CANCER RESEARCH GROUP (BCRG)

Blood Cancer Research Group is a joint activity of the Faculty of Medicine of the University of Ostrava and of the University Hospital Ostrava. The research workplace is located at the local haematology-oncology clinic, where prof. Hájek founded it. The team leader is RNDr. Michal Šimíček, PhD., who has returned from his prestigious Cambridge site to his native region with the prospect of great potential to build a successful scientific team. The international team communicates in English and is composed of young but very experienced people, mostly doctoral students, from Spain, Italy, Russia, India, the Balkan states and other countries. The selection of the new members is done through online search engines and specialized web servers. It is so because there are only very few doctoral students, and therefore potential employees, in the Czech Republic. That is the reason why most BCRG team members come from abroad, but this, from the point of view of the international team knowledge and experiences diversity, is good in the end.

Follow Blood Cancer Research Group activities and progress on Facebook @BCRG. Ostrava (www.facebook.com/BCRG.Ostrava/?ref=page_internal).

CAN A CANCER BE PREVENTED?

Not only the Blood Cancer Research Group scientists would appreciate this, but there is no positive answer to this question yet. The occurrence of mutations is largely a coincidence. As we grow and develop, also our cells continue to grow, the number of genes always doubles and the cell splits. And it is this DNA duplication process that leads to the generation of errors causing mutations. Fortunately, our cells have mechanisms that are capable of mutations repairing. Every day in our body, millions of mutations arise, but the body can repair them. If not, cancer would be a daily routine, which fortunately is not. But since the system is not perfect, it happens that in a cell, a mutation occurs, that survives and develops. Mutations and disorders in DNA and the subsequent cancer development are also influenced by the environment and lifestyle: an active and healthy lifestyle together with a clean environment are certainly the best prevention. Nevertheless, the goal of the research team is not to prevent cancer, but to have the ability to identify the patient groups for the appropriate specific treatment that will be highly effective with minimal or ideally no side effects.



RESEARCH AREAS

STUDY OF ABERRANT CELL MUTATION SPECTRUM IN MONOCLONAL GAMMOPATHIES

The basic research includes the study of the cancer cell mutations diversity. It is a case of genetic research during which scientists try to understand the reasons why the disease arises. Nowadays, for a large number of cancer diseases the symptoms are known, the doctors are able to diagnose the disease, but they are unable to identify the cause. And that‘s why the scientists are trying to find out what leads to the development of a specific disease. The cancer is, in principle, a genetic disease arising from disorders in the genetic material.

How does such research work in reality? From the tumor cells of patients with blood cancer, the genetic material DNA or RNA is isolated and the sequence of individual nucleotide bases is read. These can then be compared with the healthy donors to determine the presence of changes, mutations or disorders that may cause them, or may be related to the disease development, or to the resistance to the treatment used. Then, a connection between the gene mutation and the drug is looked for. As a result, the patients can be categorized into groups by genetic code and then treated by the medicaments that really help them. This is called personalized medicine, which is tailored for the specific patient.

IDENTIFICATION OF THERAPEUTIC TARGETS FOR THE TREATMENT OF BLOOD TUMORS USING MODERN METHODS OF MOLECULAR BIOLOGY AND GENETIC ENGINEERING

The second area of research is directly based on the first area. We can imagine the genetic information DNA as a guide to how a cell should function. In that guide, there is information about how much proteins should be produced and how they should look in the given cell. This research phase seeks to understand how the specific proteins act together in the cell, and how they lead to the cell acquiring the characteristics of a tumor cell, migrating and colonizing another tissue.

The mutations themselves may not lead to cancer, some of them are silent and never manifest themselves. However, the formation of the secondary sites - metastases - is fatal. To enable the cancer to metastasize, the cells must acquire the ability to migrate from the primary site. This happens when some proteins are present in another quantity than expected and they acquire different characteristics than they have in the healthy cells. If the research team understands the particular protein interaction process, it can target the treatment more precisely. In the collaboration with other workplaces, they might then create a substance that would disable proteins binding to each other, or that would disable further reactions, so that the cell loses the ability to migrate.

The identification of specific processes of proteins takes up to some years, production of the subsequent description and verification unfortunately takes further years, often even fifteen to twenty years. The longest part is drug development and testing. Only one of several thousands of medicaments will eventually reach the patient. At the beginning of this very time-consuming process, it is nevertheless the basic research which describes the unknown happening in the cell.

RESEARCH ON THE POTENTIAL OF THE TREATMENT PROCEDURES USING CELL-THERAPY FOR THE TREATMENT OF HAEMATOLOGICAL MALIGNANCIES

The first two areas could be included in the basic research sector. The area of cell therapy, on the contrary, has a more applicable potential that can be utilized in clinical practice. The cellular therapies consist of the scientists being able to modulate a patient‘s cells so that their own immune system is able to kill the tumor. Great, right? The patient‘s white blood cells are taken and then in the laboratory, using genetic engineering methods, altered to target them at the tumor. The tumor has on its surface the molecules that healthy cells do not have. The basic research identifies them and the laboratory team is then able to input the information allowing the recognition, localization and consequently the destruction of the tumor cells into the immune cells.

This is a very promising direction, which has become more and more used in recent years but is extremely expensive. It works with human cells, everything takes place under extreme conditions, and technology and material are expensive. The treatment of one patient costs tens of millions of Czech crowns in this way, which is unrealistic in practice. Therefore, the nearest endeavor of the team is to come up, over the next few years, with a product or method leading to a dramatic reduction of the costs. If the team succeeds to develop their own method without the need of using services of commercial companies, then a routine treatment based on this method could be used also in Ostrava.

IMPORTANT PUBLICATIONS

- Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomised, phase 3, open-label, multicentre study. Lancet Oncol (2016).

  Dimopoulos MA, Moreau P, Palumbo A, Joshua D, Pour L, Hajek R, Facon T, Ludwig H, Oriol A, Goldschmidt H, Rosinol L, Straub J, Suvorov A, Araujo C, Rimashevskaya E, Pika T, Gaidano G, Weisel K, Goranova-Marinova V, Schwarer HH, Minuk L, Masszi T, Karamanesht I, Offidani M, Hungria V, Spencer A, Orlowski RZ, Gillenwater HH, Mohamed N, Feng S, Chng WJ.

The publication compares the combinations of medicinal products for patients with relapsed multiple tumors arising from the bone marrow cells, or tumors not reacting to the usual treatment. So, the new possibilities for the patients' therapy with this incurable tumor disease are opened. The work is the result of the international cooperation of excellent workers, and its results have a significant clinical impact on the multiple myeloma treatment.

- Transcriptional profiling of circulating tumor cells in multiple myeloma: a new model to understand disease dissemination. Leukemia Journal (2019).

  Garcés, J.J., Simicek M., Vicari M., Brozova L., Burgos L., Bezdekova R., Alignani D., Calasanz M.J., Growkova K., Goicoechea I., Agirre X., Pour L., Prosper F., Rios R., Martinez-Lopez J., Millacoy P., Palomera L., Del Orbe R., Perez-Montaña A., Garate S., Blanco L., Lasa M., Maiso P., Flores-Montero J., Sanoja-Flores L., Chyra Z., Vdovin A. , Sevcikova T., Jelinek T., Botta C., El Omri H., Keats J., Orfao A., Hajek R., San-Miguel J.F., Paiva B.

The publication deals with the description of the changes in bone marrow tumor cells that are able to travel to the bloodstream and settle other places in the body. By combining the research of the BCRG team and of colleagues in Spain, a comprehensive study has arisen which has helped to identify the major genetic factors in the tumor and in its nearest surroundings that allow cancer cells to leave the bone marrow environment and to circulate in the bloodstream.

- The publications in Molecular Cell
- The publications in EMBO Journal

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