A long, costly journey lies ahead before use on patients

The information, released by his research team at the beginning of July, that he had succeeded in discovering a possible new means of the biological treatment of so-called squamous-cell carcinoma of the head and neck, and that he had even had it patented, attracted a massive amount of attention from not only the media, but also the general public. However, in an interview for iForum, the Head of the Anatomical Institute of the CU 1st Faculty of Medicine , Professor Karel Smetana, urged restraint and noted a long, costly journey still lay ahead between laboratory research and eventual use of the treatment on patients. Whether they start this journey will depend on whether a suitable partner could be found in the private sector.

What started you on the path leading to patents for the biological treatment of malignant carcinomas of the head and neck?

Since the Second World War our institute has been engaged in embryology, and I, too, started out as an embryologist. A key factor in the genesis of an embryo is communication between a variety of different cells. We noticed that something similar, that is, crucial intercellular communication, also takes place in pathological conditions, for example between malignant cells and tumorous stroma cells – the stroma is the tissue that supports the activity and growth of tumorous cells –, so we decided to look into this question. We are looking for the molecules through which tumorous cells speak to stroma cells, and then trying to block them with the aid of e.g. blocking substances.

How do those substances work?

Blocking substances connect to the active part of the molecule, used in conversations between cells. The substance blocks off this spot, and the molecule ceases to act as a carrier of information. For this, however, we are using substances that are not usable in clinical medicine. Substances that are to be administered to humans must ideally be humanised, i.e. they should consist of a mixture of animal and human blocking substances. The development of such substances is, however, quite costly; there are pharmaceutical firms that possess this technology to a very high level – we hope that they might be interested in our research.

The second option is to develop special, small molecules, capable of connecting to either the active spot of an information molecule so that the molecule ceases activity, or to a specific receptor for that molecule, thus stopping the exchange of information.

We started cooperation with Professor Jean-Marie Lehn, the Nobel laureate for supramolecular chemistry, and have now published a joint article *(Professor Jean-Marie Lehn is a member of the Scientific Board of the CU First Faculty of Medicine and also gave a lecture at the CU Faculty of Science in June of this year – ed.)*. We hope that this collaboration can help us find some commercial entities that may be interested in our results.

In the course of your research we found that the growth of a carcinoma is significantly influenced by non-tumorous cells in its vicinity, and primarily by so-called fibroblasts, that is, cells within connective tissue. What led you to research these cells?

It was, in a way, just by chance. About ten years ago one of our colleagues, who started his career in our laboratory and now works in Singapore, was given the task of isolating and cultivating tumour cells. It didn't quite work out, but he did end up with a large quantity of fibroblasts. We felt that we had to use this in some way. We knew from our embryological studies that the exchange of information between surrounding fibroblasts and epithelial cells plays a major role in the creation of skin derivatives such as hair, nail and, in the case of the oral mucous membrane, teeth. It was therefore, an offshoot of what we were doing already, and one that proved very fruitful.

So sometimes even relative failure can lead to good results. Do scientists in your field require a lot of patience in their research?

Yes. Nowadays it's something of a problem, because most of us live off grants and projects are usually very short in duration, up to three years, or five, if they work out. Once you've started something, you may not see success within the first five years. Thank god that grants exist in the first place; on the other hand, it's a shame that they are relatively short-term, because it means that we're missing out on a lot of interesting results. All everyone wants nowadays are quick results and quick publication, which isn't entirely right. But, that's all we have.

How have you been able to finance the project?

We were part of the faculty's research plan. Now we are part of Charles University Research Development Scheme (known under the Czech acronym PRVOUK) no. 27 and the project run by the Biotechnological and Biomedical Centre (BIOCEV), as well as receiving grants from the Czech Grant Agency and the Internal Grant Agency of the Czech Ministry of Health. We are also part of the European project consortium Glycopharm, which is interested in the use of glycobiological knowledge in diagnosis and the development of new therapeutics; this is one of our laboratory's other areas of interest. At this point in time we are therefore financially very well-covered; however, the grants will soon end and we are looking for new ones. If it doesn't work out, then I don't know what'll happen.

Before your discoveries can be used in the treatment of patients, blocking substances must be developed and clinically tested. When do you expect this to happen?

I'm concerned that it won't even start, as it's an extremely costly process and it will be very difficult to find someone to finance it. We can't take our project any further with grant money, even though the amounts we receive are quite good. We are currently very actively searching for a commercial partner, but so far without success.

What would the treatment itself look like?

If it ever did take place, about which I am not entirely confident, because when you do research you find that there are thousands of similar patents all over the world, and only one of them catches on per ten years. But if it nevertheless did, then it would be like any other biological treatment. Following surgery or any other type of therapy, the patient would receive intravenously a cocktail of blocking substances or small molecules that would block the exchange of information between the stroma and tumorous cells. From our experiments we know that, when tumorous cells don't have information, after a period of time they lose their ability to reproduce and start dying off. However, it's very difficult to say how this would work in a macro-organism.

Apparently you are currently investigating options for applying this form of treatment to malignant melanomas …

We collaborate with both the Department of Otorhinolaryngology and Head and Neck Surgery and the Department of Dermatology of the CU 1st Faculty of Medicine, with whom we share postgraduate students, who research the possibilities for using this discovery in the treatment of malignant melanomas. However, we are finding that, in this case, application is much more complicated than is the case with squamous-cell carcinomas. There is still a major question-mark over whether it will be at all possible. We hope that it will, because the interaction of tumour cells with stroma cells is a very common phenomenon that affects virtually all types of malignant tumour. It is possible that some principles could have a very general application and be usable in the fight against other types of melanoma.

Teams of scientists from the Anatomical Institute, the Department of Otorhinolaryngology and Head and Neck Surgery, the Department of Oral, Jaw and Facial Surgery of the Neck of the CU 1st Faculty of Medicine and the Institute of Molecular Genetics of the Czech Academy of Sciences gained patents for a new means of biological treatment of malignant squamous-cell carcinomas of the head and neck.

In recognition of his research in the field, the Head of the Anatomical Institute of the CU 1st Faculty of Medicine, Professor MUDr. Karel Smetana, DrSc., received the 2010 Minister of Education, Youth and Sports' Award. Apart from intercellular interactions, his research interests also include tissue engineering, glycobiology and the biology of stem cells. In 2002 he received the national Czech Head award.

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