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## Skin from a Laboratory



Polish scientists have developed an innovative method for culturing human skin to enable fast and effective treatment of hard-healing wounds caused by burns or resulting from diabetes.

With the method, sheets of a patient's skin cells would be transferred from a special matrix directly to the wound.

Researchers from the Polish Academy of Sciences' Center of Polymer and Carbon Materials in the southern city of Gliwice are studying polymers sensitive to temperature changes. Such materials can provide an excellent substrate for cell cultures, the scientists say.

"We are working to develop sheets of skin cells that doctors could easily move to a wound," says Prof. Andrzej Dworak, coordinator of the project. "The substitute skin prepared in this way, cultured in vitro on innovative, polymer substrates and applied to a properly prepared wound could decidedly speed up the healing process."

The process starts with the preparation of a substrate that is coated with a polymer attractive to skin cells. Once they multiply on the sheet matrix in a process that also involves the use of an extracellular matrix, it is enough to lower the temperature of the culture for the sheet to be easily separated from the substrate. According to the researchers, this method strongly reduces the number of damaged cells, which was a problem with previous methods for the mechanical or enzymatic separation of cells from the substrate. With these older methods, a large part of the cells were crushed in the process of scraping them off with a knife. The continuity of the sheet was disrupted, and no more than 60-odd percent of the culture could be saved. Enzymatic separation also caused losses because an enzyme is capable of destroying a cell.

"In our innovative method, we do not treat the cultured sheet with anything harmful. Simply the change in the temperature causes it to come off from the matrix on its own," says Dworak.

Collaboration between chemists and biologists and doctors is essential in this interdisciplinary research project. Doctors specializing in the treatment of burns made the rest of the team aware of the importance of joint work on skin substitutes that could help seriously ill people.

"Burns and chronic wounds are a major medical and social problem," says Dworak. "Every few minutes across Europe doctors amputate a foot due to non-healing diabetic wounds. In the case of burns, the treatment procedure is based on transforming this type of wound into a surgical wound as soon as possible—with a view to conducting surgery to remove the burned, damaged cells. Later, it is necessary to address the problem of missing skin because without that recovery would not be possible. And this must be done quickly."

In medical practice various methods are used to treat burns, including dressings such as those from pig skin. However, these need to be removed after some time. Frequent replacement of dressings is painful and does not always produce the expected results. An optimal method is to transplant the patient's own skin, it's just that then, instead of one wound, there are two because the skin for the transplant needs to be taken from somewhere. That is why cell culture is a promising method.

"It is necessary to culture not a skin cell suspension but a skin sheet that can be placed on the wound," says Dworak. "To this end we decided to use the polymer materials we developed. Biochemists are checking if the cultured cells have not been harmed in any way. Multiplying them is quite a complicated process because they may be subject to undesired mutations. We currently have substrates on which growing cells do not mutate. They do not lose the connections between one another, either. We know that the sheet created from them can be separated. Here, however, we have technical difficulties to overcome. Now we will upgrade this method to make it reproducible and verifiable, which will make it possible to put it into practice." Even though

the project is well advanced, practical applications are still a distant prospect. Risks still exist. Further tests are needed and the researchers still need to go through some formal procedures. This is because any materials that come into contact with a living organism must be put into medical practice under special supervision. Despite these obstacles, Dworak says he is optimistic. He expects that developing substitute skin will make it possible to treat extensive burns and hard-to-heal chronic wounds more quickly, efficiently and comfortably. In addition, the new method will be competitive, he says, because it is better than those previously used.

The scientists are working on a technique that could be applied on a wider scale. Cell culture substrates obtained with the new method have been submitted for patenting. The team still has two years to determine the size of the potential market for the method—and to set the terms and conditions for a producer willing to buy a license and produce skin substitutes on an industrial scale.

Many researchers in centers around the world are conducting studies on cell cultures. Teams from Japan are leading the way in this field of research. The results of their work are known from patent publications and conference presentations.

The Polish project is a collaborative effort. Researchers from the Łódź University of Technology in central Poland are handling issues related to radiation, because radiation is a good method for preparing such substrates. Biologists and biochemists from the Medical University of Silesia in the southern city of Katowice are examining the cultured cells, and doctors from the Burn Treatment Center in Siemanowice Śląskie are culturing skin sheets and evaluating the usefulness of the new solutions.

The success of the project not only opens the way to the treatment of chronic wounds and burns, but the developed method can also be applied wherever there is a need for tissue engineering. In order not to squander the results of the research work so far and be able to think of putting the method to commercial use, it is necessary to press ahead with further research. The aim is to develop optimum methods for obtaining and standardizing thermosensitive substrates. More cell cultures are needed to secure the necessary approvals and certificates required for putting the product on the market.

The project—called "Thermosensitive biocompatible polymers as skin substitutes for the treatment of burns and wounds"—started in 2009 and its planned budget is around zl.4 million. The funds have been provided by the National Center for Research and Development.

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