Healing bone defects using regenerative medicine

June 19 2014

Regenerating bones based on a mixture of tissue engineering approaches is coming of age.

Bone is one of the most frequently transplanted tissues. And the demand is rising. Transplants treat large defects like those caused by trauma, complicated fractures, tumour resection or osteoporosis. Conventionally, a piece of bone is transferred from one body site to another of the same patient. But this has the disadvantage of causing a defect in an otherwise healthy part of the body. And using bone obtained from a donor also has side effects, such as immunogenic reactions. New methods are thus needed to meet the growing demand.

Now, the EU-funded project VascuBone, due to be completed in December 2014, may offer an alternative solution based on engineering bone grafts to regenerate defects. The project is developing a toolbox for bone regeneration that combines various methods and materials of tissue engineering. "We would like to include everything in our toolbox that is necessary to put together the ideal therapy for a patient", says project coordinator Heike Walles, professor of tissue engineering and regenerative medicine at the University Hospital of Würzburg and also head of the oncology group at the Fraunhofer Institute IGB in Würzburg, Germany. The tools developed and optimised in the project may help to overcome existing shortcomings.

Walles previously developed a three-dimensional scaffold derived from a piece of pig bowel that contains structures supporting the development

of blood vessels. Different types of adult stem cells, for example, so-called mesenchymal cells derived from bone marrow, are supposed to grow on such scaffolds to form the bone substitute. "These cells are even present in old people," Walles tells youris.com. While the cells' potential decreases with age, "they are still there and are able to regenerate", she explains. "But they have to be enriched, which is increasingly difficult with increasing age," she continues.

In the current project, researchers therefore analysed how age influences the stem cells' properties. They identified markers that indicate whether the cells are suited for therapeutic use. They also looked at other types of cells, so-called endothelial cells. These may be necessary for treating very large bone defects. "We analysed which cell type is ideal for therapeutic purposes, such as microvascular endothelial cells or endothelial progenitor cells, a stem cell type that can be found in the blood", Walles tells youris.com. After successfully testing the first engineered bone grafts in animal models, "the first clinical trials are going to start this year", Walles tells youris.com. After the clinical trials, she hopes, that these therapies can be offered to patients.

One expert appreciates the need for such tools. "It's a very nice idea to put together different tools and combine different types of cells", says Richard Oreffo, professor of musculoskeletal science at the University of Southampton, UK. "There is a significant need for bone regeneration, given our aging population," he tells youris.com. He believes engineering bone substitutes with the help of adult stem cells and translating the approaches to clinical settings is not far out of reach. "It is just fantastically complicated", he says. "But we have a number of scaffolds in clinical use. We are developing strategies to harness cells. Thus we now have a step-wise approach to reach the clinic in the not too distant future," he adds.

Another expert also welcomes the toolbox approach. "It offers a

combination of matrix, cells, bioreactors and automated systems, which can be used to grow tissue under controlled conditions," says Cornelia Kasper, professor for biopharmaceutical technology at the University of Natural Resources and Life Sciences in Vienna, Austria. Researchers "look for biological alternatives to screws, nails and titanium plates", particularly for treating defects larger than three centimetres," she tells youris.com. Providing scaffolds with vessel structures for regenerating large bone defects is "something special and unique", she says.

Kaspar believes using stem cells from the patient's own fat tissue or bone marrow and from the umbilical cord offer a huge potential for bone regeneration and has various advantages. "Particularly, mesenchymal stem cells are easily accessible", she tells youris.com. There are no ethical concerns attached to using such cells and there are no immunogenic side effects. What is more, these cells exist in everyone. "Even slim or old patients have fat tissue," she adds.

She also hopes that such engineering based solutions will be more widely approved and available for patients within the next five to ten years. In her view, it is up to politics and the regulation authorities "to create the prerequisites for a comprehensive patient care". But the cooperation between life scientists, engineers and medical scientists "still remains a real challenge", she concludes.

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