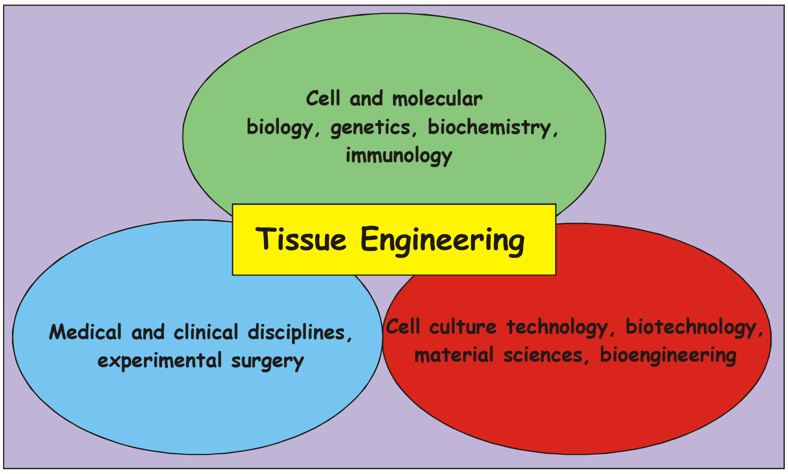
Tissue Engineering

Tissue engineering belongs to the major field of medical biotechnology which covers the following four techniques:

1. proteins and vaccines for diagnostics and prophylaxes
2. antibodies and recombinant proteins for therapy
3. ***tissue engineering***
4. gene therapy

Tissue engineering is a rapidly growing interdisciplinary research field which applies the principles of engineering and life sciences.



Picture 1: Disciplines involved in *tissue engineering*

The aim of this research field is the development of biological substitutes that restore, maintain or improve tissue functions.

An official definition was given at a conference of the National Science Foundation in 1988:

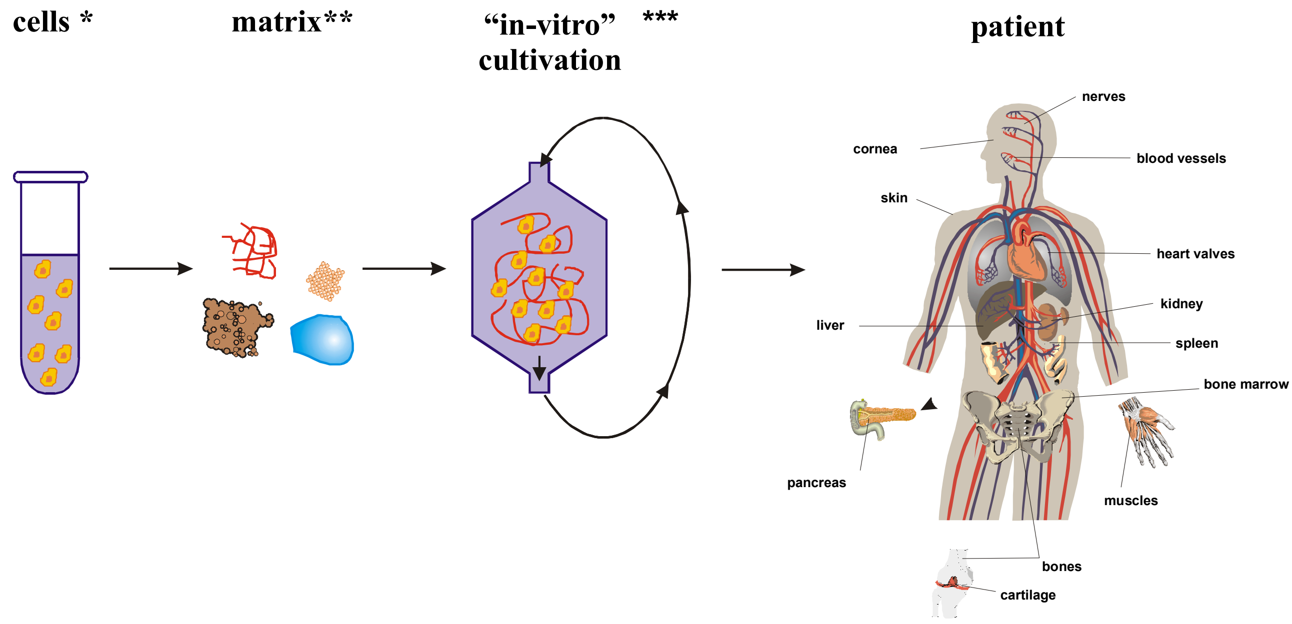
„...the application of principles and methods of engineering and life sciences toward fundamental understanding of structure-function relationship in normal and pathological mammalian tissues and the development of biological substitutes to restore, remain or improve tissue function.“

Over the past 10 years encouraging results have been achieved. Today *tissue engineered* skin is already used, e.g., for therapy of severely burned patients, or stem cells can be taken from a patient suffering of leukemia and are extracorporally cultivated. After chemotherapy these autologous cells can be reimplanted avoiding rejection reaction of the body. Scientists are attempting to engineer almost every human tissue or organ because the demand of *tissue engineered* cells and organs is still growing due to the fact of organ shortage for transplantation.

The creation of three-dimensional tissue constructs which can mimic all functions and metabolic activities like organs (e.g. liver or pancreas) is still a crucial challenge. The first *tissue engineered* heart valves have been implanted to a patient and show promising results in function and mechanical stability. The strongly interdisciplinary approach *in tissue engineering* is best characterized in the following fictitious conversation:

I imagine a conversation between a new graduate student and his/her mentor at a major research institution as follows:
Graduate student: „Give me a great tissue engineering thesis project that will win you the Nobel Prize and make sure that I get a great job when I leave your laboratory."
Mentor 1 (biologist): „Go study published papers in the library on exactly how embryos fabricate tissues, write down all key events, and use these as rules of the road to tissue engineer the regeneration of organs or complex tissues in adult organism."
Mentor 2 (material scientist): „Go study published papers in the library on the material properties of adult tissues, write down all key parameters and characterize specifications, and use them as rules of the road for designing tissue substitutes whose material properties exactly match those of the adult tissue."
Mentor 3 (engineer): „Go study published papers in the library on the mechanical properties of tissues, and use these properties as rules of the road to design a mathematical (finite element) model to predict how the tissue will change with age and change in various modalities."
Mentor 4 (surgeon): „Go study published papers in the library on the new molecules and/or cell types that we can surgically implant into tissue defects to regenerate tissues (that won't heal naturally) or that will accelerate the healing process."
Mentor 5 (molecular biologist): „Go study published papers in the library on all of the sequencing information that you can obtain from the Human Genome Project and elsewhere on the promotor control elements that are involved in forming and/or repairing different tissues, and use these to design vectors to transform primitive cells into cells which will fabricate the tissues we're interested in."
A voice from above: „Combine all of the above and call it tissue engineering."
(Arnold I. Caplan; Tissue engineering designs for the future: new logics, old molecules, *Tissue engineering Vol 6 No 1(2000), 1-8*.).

The principle of tissue engineering can be demonstrated in the following way: first cells have to be isolated and put into in culture system or bioreactor. After addition of medium (with nutrients, growth factors) the cells are seeded to a matrix and are extracorporally cultivated. After cultivation the resulting tissue is reimplanted into the patient see scheme in picture 2.



***	tissue or stem cells (autologous or allogen)**

****	natural, synthetic or xenogenic (membranes, hydrogel, capsules)**

*****	static, stirred or dynamic flow conditions**

Picture 2: Scheme of the principle of *tissue engineering*

Tissue engineering can be performed using one of the three approaches:

1. in-vitro cultivation of autologous cells on organic, synthetic or natural matrices
2. in-vitro cultivation of autologous cells on xenogenic matrices
3. tissue generation from embryonic stem cells

Depending on the tissue of interest, one of the following different general strategies is applied for the use of the *tissue engineered* cells:

- close system – extracorporal device
- open system – biodegradable polymer scaffold
- direct cell injection

The focus of the work carried out in the *tissue engineering* group covers the creation of suitable matrices and their targeted functionalisation as well as the development and optimisation of culture condition and bioreactors. Also the control of the 3 D formation of tissue constructs from different human cell cultures and the correct differentiation is being observed. The techniques applied are: biomatrix design and functionalisation, bioreactor design and optimisation, cell/tissue culture, flow cytometry, microarrays, HPLC, capillary and gel-electrophoresis, 2D-fluorescence spectrometry, in-situ-microscopy, ELISA, MALDI-MS, PCR.