

3.1 Definition and Requirements for Scaffolds Used in Tissue Engineering:

A scaffold is an artificial three-dimensional frame structure that serves as a mimic of extracellular matrix for cellular adhesion, migration, proliferation, and tissue regeneration in three dimensions.

An ideal scaffold for tissue engineering should possess the following characteristics:

1. It is highly biocompatible and does not elicit an immunological or clinically detectable foreign body reaction.
2. It is three-dimensional and capable of regenerating tissue and organs in their normal physiological shape.
3. It is highly porous with an interconnected pore network available for cell growth and nutrient and metabolic waste transport.
4. It has a suitable surface chemistry allowing for cell attachment, migration, proliferation, and differentiation.
5. It has controllable degradation and resorption rates that match the rate of tissue growth in vitro, ex vivo, and in vivo for biodegradable or resorbable materials.
6. It possesses the appropriate mechanical properties which match those of the normal tissue and organs.
7. It has a bioactive surface to encourage faster regeneration of the tissue.

3.2 Principles of Scaffold Design:

All tissue and organs in the body are three-dimensional structures. In order to repair and regenerate lost or damaged tissue and organs, three-dimensional scaffolds must be designed, fabricated, and utilized to regenerate the tissue similar in both anatomical structure and function to the original tissue or organ to be replaced or repaired. Therefore, certain principles of scaffold design must be established to ensure proper tissue regeneration.

1- Tensegrity Concept:

Ingber proposed an important principle in scaffold design based on the tensegrity concept. The tensegrity concept sounds new, but it is not a brand new concept because it has been used for centuries in the area of civil engineering. The core of this concept is that mechanical forces are evenly distributed on all regions of the entire scaffold. Therefore, stable structures that can bear forces uniformly, such as triangles, pentagons or hexagons, are preferred structures in a scaffold.

2- Nutrient and Metabolic Concept:

Any living thing needs to consume nutrients and release waste products in order to survive. To keep tissue-engineered grafts alive, the diffusion of nutrients and metabolic products into and out of the three-dimensional scaffold is a key parameter to maintain. Highly porous and interconnected structures have been employed to facilitate the transport of materials through the scaffolds. However, these measures are not sufficient for the regeneration of large tissue and organs, such as the regeneration of liver. Unfortunately, there is not a good answer for this problem yet.

3- Neovascularized Network Concept:

The neovascularized network concept is an advancement of the nutrient and metabolic concept. In order to ultimately solve the nutrient and metabolic problems of engineered tissues, well-organized and uniformly distributed blood vessel networks are required. However, the technology to construct sufficient blood vessel networks outside the body has not been established yet. So far, one vital obstacle in the creation of tissue-engineered whole organs is the inability to provide proper vascularization to the newly created tissue or organ. This problem is especially serious in the development of a tissue-engineered liver.

The longest possible distance from a cell to blood vessels necessary to keep the cells alive in most healthy tissue is less than 1 mm. Therefore, when designing a tissue or organ, the time frame of blood vessel development must be well thought-out. With knowledge of neovascularization obtained from developmental biology and cancer studies well established, this problem may finally be solved. Currently, most scientists are trying to incorporate angio-genic factors into scaffold design in order to encourage the formation of blood vessel networks in the grafts.