

生醫工程與材料設計

1. The Problem of the Missing Organs

Drugs typically replace or correct a missing function at the molecular scale; by contrast, regeneration templates replace the missing function at the scale of tissue or organ.

An organ may be lost to injury or may fail in disease: The usual response of the organism is repair, which amounts to contraction and synthesis of scar tissue. Tissues and organs in the adult mammal typically do not regenerate. There are any exceptions, such as epithelial tissue of the skin, gastrointestinal tract, genitals, and cornea, all of which regenerate spontaneously; the liver also shows ability to synthesize substantial organ mass, though without recovery of the original organ shape. There are reports that bone and the elastic ligaments regenerate.

These exceptions underscore the fact that the loss of an organ by the adult mammal almost invariably is an irreversible process, since the resulting scar tissue largely or totally lacks the structure and function of the missing organ. The most obvious examples involves losses due to injury, such as the loss of a large area of skin following a burn accident or the loss of substantial nerve mass following an automobile accident. However, irreversible loss of function can also occur following disease, although over a lengthy time: Examples are the inflammatory process, and inability of liver tissue to synthesize enzymes due to its progressive replacement by the fibrotic tissue (cirrosis).

2. Approaches for Missing Organs

Five approaches have been used to solve the problem of the missing organ.

(1) Autografting

In autografting, a mass of similar or identical tissue from the patient is surgically removed and used to treat the area of loss. The approach can be considered to be spectacularly successful until one considers the long-term cost incurred by the patient. An example is the use of sheet autograft to treat extensive areas of full-thickness skin loss; although the patient incorporates the autograft fully with excellent recovery of function, the “donor” site used to harvest the autograft remains scarred. When the autograft is not available, as is common in cases of burns extending over more than 30% of body surface area, the autograft is meshed in order to make it extensible enough to cover the large wound areas. However, the meshed autograft provides cover only where the graft tissue provides direct cover; where there is no cover, scar forms, and the result is one of low cosmetic value.

(2) Transplantation (Allograft or Xenograft)

The donor sites is typically harvested from a donor, cadaver or animals, and the recipient has to cope with the problems of rejection and the risk of

transmission of viruses from those donors.

(3) Synthesized Tissues

Another approach has been based on effort to synthesize tissues in vitro using autologous cells from the patient; this approach has yielded so far a cultured epidermis (a tissue which regenerates spontaneously provided there is a dermal substrate underneath) about 2-3 weeks after the time when the patient was injured. In vitro synthesis of the dermis, a tissue which does not regenerate, has not been accomplished so far.

(4) Engineered Biomaterials

Perhaps the most successful approach from the commercial standpoint has been the one in which engineered biomaterials are used; these materials are typically required by their designers to remain intact themselves without interfering with the patient's physiological functions during the entire lifetime; overwhelming, this requirement is observed in its breach.

(5) Analog of the Extracellular Matrix (ECM)

A fifth approach is based on the discovery that an analog of ECM induces partial regeneration of the dermis, rather than of scar, in full-thickness skin wound in adult mammals where it is well known that no regeneration occurs spontaneously. This fifth approach of solving the problem of organ loss and in situ regeneration.

3. Conclusion

Efforts to induce regeneration have been successful with only a handful of ECM analogs. Evidence of regeneration is sought after the ECM analog has been implanted in situ, i.e., at the lesion marking the site of the missing organ. When morphogenesis is clearly evident, based on tests of recovery both of the original tissue structure and function, the matrix which has induced these physiological or nearly physiological tissue is named a regeneration template.

Textbook:

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