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The Evolution and Future of Esophageal Tissue Engineering

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Brief Report

Esophageal illnesses such as atresia, tracheoesophageal fistula, esophagitis, and even cancer are on the rise globally. Traditional therapies, such as surgery, chemotherapy, or/and radiotherapy, etc., always encounter complications, resulting in a decline in patient quality of life and, in certain cases, a worse survival rate. Tissue engineered oesophagus, an unique biologic substitute with tissue architecture and biofunctions, has been touted as a potential future replacement. However, esophageal tissue engineering research is still in its early stages. The development of perfect scaffolds using optimal materials and fabrication processes has received a lot of attention. In vivo tests and clinic trials are moving forward.

Traditional treatments such as surgery, radiotherapy, or/and chemotherapy, as well as surgically replacing the stomach, colon, small intestine, and other organs, did not significantly increase the survival rate. Furthermore, autologous/allogeneic replacement of the oesophagus from the human body is extremely unusual. A tissue-engineered substitute with integrated structure and function is regarded to be a promising and effective treatment option for esophageal disease, as it eliminates the need to collect replacement tissues from the patient's own body or from another human body. The oesophagus is a muscular canal that runs from the throat to the stomach and transports food and water from the mouth to the stomach. The mucosa, submucosa, muscularis externa, and adventitia are four layers of tissue made up of three types of cells: stratified squamous epithelial cells, fibroblasts, and smooth/skeletal muscle cells. The lumen epithelium (E) is made up of stratified squamous epithelial cells that act as a barrier or protective layer against mechanical stresses caused by food bolus.

The muscle component of the oesophagus is responsible for motor function longitudinally and circumferentially via peristalsis. The upper third is striated skeletal muscle, the middle third is a blend of skeletal and smooth muscle, and the lower third is pure smooth muscle. The muscle is arranged in a bilaminar pattern. The endocircular and exolongitudinal myofibrils are packed bilaminarly to propel swallowing food and water into the stomach through sequential contraction of the circular muscles by occluding the esophageal lumen, and longitudinal muscles by shortening the duct and enlarging the lumen, or increasing the fibril density of the circular muscle, which improves the circular muscle's contracting.

Tissue engineering, as proposed by Langer and Vacanti, is an interdisciplinary field that uses engineering and life science ideas to the production of biological substitutes that restore, maintain, or improve tissue function. Tissue engineering study revolves around scaffolds, cells, and their combinations. In scaffold construction, material is a necessary substratum. Resorbable substances, decellularized matrices, acellular patches, and composites made from natural and/or manufactured polymers are some of the materials that have been produced as scaffold matrices to form esophageal tissue. A range of tissue-derived extracellular matrix (ECM) products, such as decellularized urinary bladder submucosa, gastric acellular matrix, aortal acellular matrix, acellular dermal grafts, and decellularized oesophagus, have all been studied extensively for use as oesophagus replacements.

In animal models and even human trials, some have been evaluated for esophageal damage recovery. Alternatively, synthetic and/or natural materials, as well as their composites, have gotten a lot of interest in tissue engineering and regenerative medicine research. Poly glycolic acid (PGA) and silicone with collagen covering were used to make tubular scaffolds; According to literature, small intestinal submucosa (SIS) has been used to substitute tubular organs such as the oesophagus and large-diameter vascular grafts. Nonetheless, when the materials or scaffolds are implanted into humans, complications or postoperative difficulties such as inflammation, leakage, stenosis, and extrusion are still present.

Extracellular matrix (ECM)-based iologic scaffolds have been employed to aid in the repair or remodelling of a variety of tissues, including the oesophagus. The ECM produced from the precise tissue to be treated, that is, site-specific or homologous ECM, is the theoretically perfect scaffold for tissue healing. In the esophageal location, the preference or potential benefit of using site-specific ECM is unknown. The goal of this work was to compare the in vitro cellular response and the in vivo host response to homologous esophageal ECM (eECM) to non-homologous ECMs produced from the small intestinal submucosa and the urinary bladder. Migration, proliferation, and three-dimensional (3D) organoid creation assays were used to assess the in vitro response of esophageal stem cells.

The in vitro response of esophageal stem cells was characterized by migration, proliferation, and three-dimensional (3D) organoid formation assays. The in vivo remodeling response was evaluated in a rat model of esophageal mucosal resection. Results of the study showed that the eECM retains favorable tissue-specific characteristics that enhance the migration of esophageal stem cells and supports the formation of 3D organoids to a greater extent than heterologous ECMs. Implantation of eECM facilitates the remodeling of esophageal mucosa following mucosal resection, but no distinct advantage versus heterologous ECM could be identified.

Migration, proliferation, and three-dimensional (3D) organoid creation assays were used to assess the in vitro response of esophageal stem cells. In a rat model of esophageal mucosal excision, the in vivo remodelling response was assessed. The study found that the eECM retains tissue-specific features that promote esophageal stem cell migration and facilitate the creation of 3D organoids to a greater extent than heterologous ECMs. Although the use of eECM improves the rebuilding of the esophageal mucosa following mucosal resection, there was no clear advantage over heterologous ECM.

Fabrication of a 3D scaffold for tissue engineering in the oesophagus

Biodegradable 3D scaffolds act as extracellular matrix (ECM) substitutes in designed tissues and organs. As a result, the scaffold's chemistry and macro and/or microscale architecture must aid in the maintenance of cell functions such as cell matrix adherence, cell-cell

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adhesion, cell migration, proliferation, differentiation, and so on. The 3D scaffold, on the other hand, should provide spatial cues for cell infiltration, allowing cells to integrate with the underpinning substrate. People are constantly looking for new ways to make spatial scaffolds. Foaming, porogen leaching, electrospinning or other fibre processing, phase separation, 3D microprinting, and other technologies have all been developed to create 3D porous scaffolds. Electrospinning technology and the thermally induced phase separation (TIPS) approach, in particular, have been intensively researched for forming 3D scaffolds in esophageal tissue engineering.

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