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Naturally derived and synthetic scaffolds for skeletal muscle reconstruction☆

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ABSTRACT

Skeletal muscle tissue has an inherent capacity for regeneration following injury. However, severe trauma, such as volumetric muscle loss, overwhelms these natural muscle repair mechanisms prompting the search for a tissue engineering/regenerative medicine approach to promote functional skeletal muscle restoration. A desirable approach involves a bioscaffold that simultaneously acts as an inductive microenvironment and as a cell/drug delivery vehicle to encourage muscle ingrowth. Both biologically active, naturally derived materials (such as extracellular matrix) and carefully engineered synthetic polymers have been developed to provide such a muscle regenerative environment. Next generation naturally derived/synthetic "hybrid materials" would combine the advantageous properties of these materials to create an optimal platform for cell/drug delivery and possess inherent bioactive properties. Advances in scaffolds using muscle tissue engineering are reviewed herein.

Contents

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1. Introduction

Select tissues within adult mammals (e.g., skeletal muscle, liver, among others) possess the regenerative potential to repair injured tissue. However, most postnatal mammalian tissues, such as cardiac muscle and central nervous system tissues, respond to injury by a well-defined process of inflammation and eventual downstream scar tissue formation. While skeletal muscle tissue possesses a robust innate regenerative ability, this response is incapable of regenerating severe injuries in which large volumes of muscle tissue are lost or damaged, a condition referred to as volumetric muscle loss (VML) [1,2]. Currently, limited therapeutic options for VML exist, thus tissue engineering/regenerative medicine (TE/RM) strategies for this condition have received increasing attention in recent years.

The discipline of TE/RM attempts to provide functional tissue repair for challenging medical problems such as VML. TE/RM strategies to replace/regenerate injured tissues and organs typically involve cell based approaches, bioactive molecules, biologic or synthetic scaffold materials, or combinations thereof (Fig. 1). The majority of preclinical research efforts and clinical investigations aimed at augmenting the innate response to skeletal muscle injury have been cell-centric (i.e., cell transplantation). Unfortunately, these approaches have shown limited clinical success due to factors including low cell viability and regulatory issues, among others [3–6]. Alternatively, bioscaffold materials, harvested from naturally occurring sources (e.g., extracellular matrix [ECM]) or created by artificial means using synthetic materials (e.g., PLGA), have been used as a guide or inductive template to facilitate skeletal muscle repair [2,7–12]. Hybrid devices, in which some or all of these strategies are combined, have also been attempted [13–16]. These next generation hybrid materials can be designed to deliver these bioactive molecules (e.g., small molecules, pharmaceuticals) and/or cells in a spatiotemporal manner. The use of scaffold materials to facilitate skeletal muscle reconstruction in TE/RM applications will be discussed herein.

2. Scaffold materials for skeletal muscle regeneration

2.1. Naturally occurring materials

The ECM was once considered as a material that provides structural support, shape, and strength for tissues and organs. It is now widely appreciated that the ECM, in addition to its structural and mechanical properties, is an information highway for signals and molecules that augment many aspects of cell behavior. A variety of naturally occurring scaffold materials composed of ECM have been used to support skeletal muscle reconstruction/regeneration [2,7–12]. These ECM scaffold materials are derived from various species, a variety of tissues and organs,

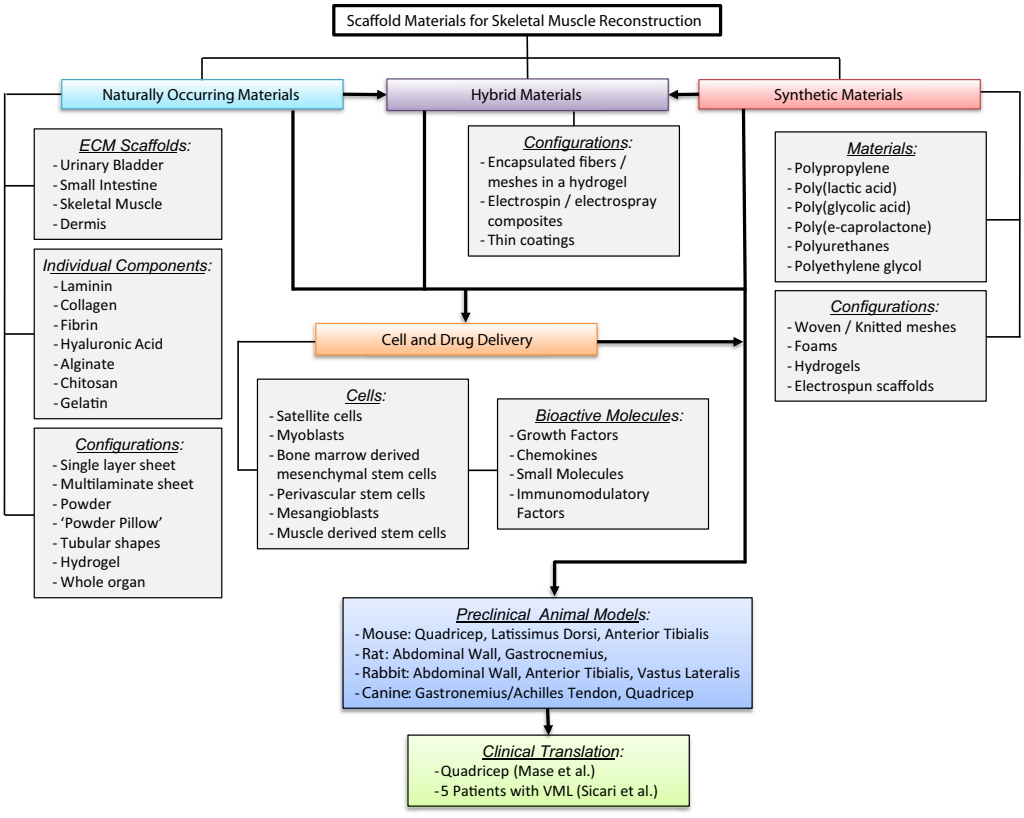

Fig. 1. Schematic overview of scaffold materials used for skeletal muscle reconstruction in tissue engineering/regenerative medicine applications. Several overarching strategies have emerged, including the use of naturally occurring, synthetic, and/or hybrid materials. These materials have been characterized in numerous preclinical animal models and successfully translated to clinical use.
Adapted from [17–19].