Bioinspired Tissue Engineering Approaches for the Formation of Complex Tissues

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A significant challenge in the field of tissue engineering is the simultaneous formation of multiple types of tissues and their functional assembly into complex tissues or organ systems. For example, musculoskeletal motion is facilitated by synchronized interactions between multiple tissue types and the seamless integration of bone with soft tissues such as tendons, ligaments or cartilage. In the body, many of these soft tissues connect to bone through a multi-region fibrocartilaginous interface, which serves to minimize the formation of stress concentrations while enabling load transfer between soft and hard tissues.

Given its functional significance, re-establishment of tissue-to-tissue interfaces is thus critical for promoting integrative tissue repair as well as the formation of multi-tissue systems. Focusing on the challenge of engineering complex tissues and enabling biological fixation, bioinspired approaches to regenerating common orthopaedic tissue-to-tissue interfaces (ligament-to-bone, tendon-to-bone, or cartilage-to-bone), and the strategic biomimicry implemented in stratified scaffold design for multi-tissue regeneration will be highlighted.

This biomimetic approach is often rooted in an in-depth understanding of the structure-function relationship at the tissue-to-tissue interface, and changes at this critical junction during prenatal and post-natal development, which has yielded physiologically relevant scaffold design parameters for interface tissue engineering. In addition, elucidation of the mechanism of interface regeneration has revealed the role of heterotypic cellular interactions in directing the formation, repair and maintenance of the tissue-to-tissue interface. Based on these understandings, current interface tissue engineering efforts have largely been guided by the working hypothesis that this junction may be regenerated by controlled co-culture or tri-culture of interface-relevant cell populations on a stratified scaffold pre-designed with a biomimetic gradient of structural and functional properties.

It is anticipated that the successful regeneration of tissue-to-tissue interfaces through this bioinspired approach will promote integrative and functional tissue repair, as well as enabling the clinical translation of tissue engineering technologies from bench to bedside. Moreover, it will be instrumental for the development of complex tissue systems with biomimetic complexity and functionality.