Commentary

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# Low-Intensity Pulsed Ultrasound and Hydrogels in Regenerative Medicine

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## Description

In the field of regenerative medicine, acoustic manipulation, or disruption of biological soft matter, has shown potential as a clinical treatment for a variety of conditions, from neuro-modulation to bone fracture repair. Ultrasound remains a potential modality for applying mechanical stimulation capable of initiating a series of molecular signals in uninjured cells. In particular, low-intensity pulsed ultrasound, has been linked to bioeffects that include changing gene expression and cell morphology, as well as activating particular cellular pathways. The degree of these effects can be adjusted by adjusting Low Intensity Pulsed Ultrasound (LIPUS) parameters like intensity, frequency and exposure duration. Numerous studies clearly describe the modulation of specific ultrasonic parameters as a technique to guide the differentiation of a particular group of stem cells towards adult and fully differentiated cell types, even though the molecular mechanisms behind ultrasound remain to be fully understood. In this article, we describe the ways that ultrasound is being used in regenerative medicine, along with the *in vitro* and *in vivo* research that has demonstrated the platform's boundless clinical potential. We summarize the most recent attempts to use this technology to support tissue engineering methodologies for tissue healing or disease modeling and we highlight the most recent advancements targeted at examining the physical and biological mechanisms of action of ultrasound. Finally, we describe tissue-specific uses of ultrasound stimuli and provide insights into the design of novel structures and treatment approaches. In general, our goal is to establish a stronger knowledge of the mechanisms behind LIPUS-based therapy, which will help the area of regenerative medicine develop safer and more efficient methods for tissue regeneration.

### Basic characteristics in term

Hydrogels are three-dimensional structures with exceptional physicochemical and biological properties that operate as Extracellular Matrix (ECM) substitutes. Their permeability to wound healing and their moisture content make them analogous to the natural extracellular matrix, which is why they are becoming more and more important in regenerative medicine. Advances in tissue engineering have led to the creation of flexible hydrogels that imitate the dynamic properties of the Extracellular Matrix (ECM). Hydrogels with improved functional and structural properties derived from biopolymers have been created using a variety of techniques for use in Tissue Engineering and Regenerative Medicine (TERM). An extensive summary of hydrogel's applications in tissue engineering, drug delivery and wound healing is given in this article. We list the various kinds of hydrogels according to their basic characteristics, applications in TERM and crosslinking, both chemical and physical. Within five years, this review article presented the latest research on hydrogels for tissue engineering and regenerative medicine. The discussion of recent advancements in hydrogels based on biopolymers for advanced tissue engineering and regenerative medicine has highlighted the major obstacles and potential opportunities in this field. Leukemia, gastrointestinal cancer and other malignant disorders are closely associated with the development and progression of uncontrolled activation of c-Kit. Even if there are many inhibitors on the market, it is still required to design and find highly selective inhibitors that target c-Kit kinase, particularly the gain of function mutation (like c-Kit D816V), because of the inhibitors' limited selectivity and undesirable side effects.

### Molecular dynamics simulation

Our recent study's results showed that, in addition to the random coil that was frequently observed in the crystal structure, the residues near the  the activation loop might also fold into short α-helices. We were able to increase the conformation pool of the activation loop and create many structural models of the c-Kit kinase intermediate between the inactive and active states. Upon assessing the thermal stability of the metastable state through molecular dynamics simulation, a particular structural model demonstrated increased α-helix stability while maintaining the activation loop. Given that the wild-type and D816V mutant KIT kinase shared comparable metastable states throughout the kinase activation process, we conjectured that the discovered intermediate could potentially reveal inhibitors from the chemical database that target D816V mutations. In addition to suggesting a novel structural model for the identification of selective c-Kit D816V inhibitors, the results of our current study also identified a number of potential inhibitors among the kinase inhibitors currently on the market. These findings may provide new insights into the development of novel therapeutic strategies for malignant diseases driven by c-Kit mutations. In order to find new c-Kit inhibitors, a virtual screening method based on metastable states, It was used in the current work and was effectively applied to other kinase inhibitors.