fMLF-Based Supramolecular Hydrogels Prolong Inflammation Response (Case 1152)

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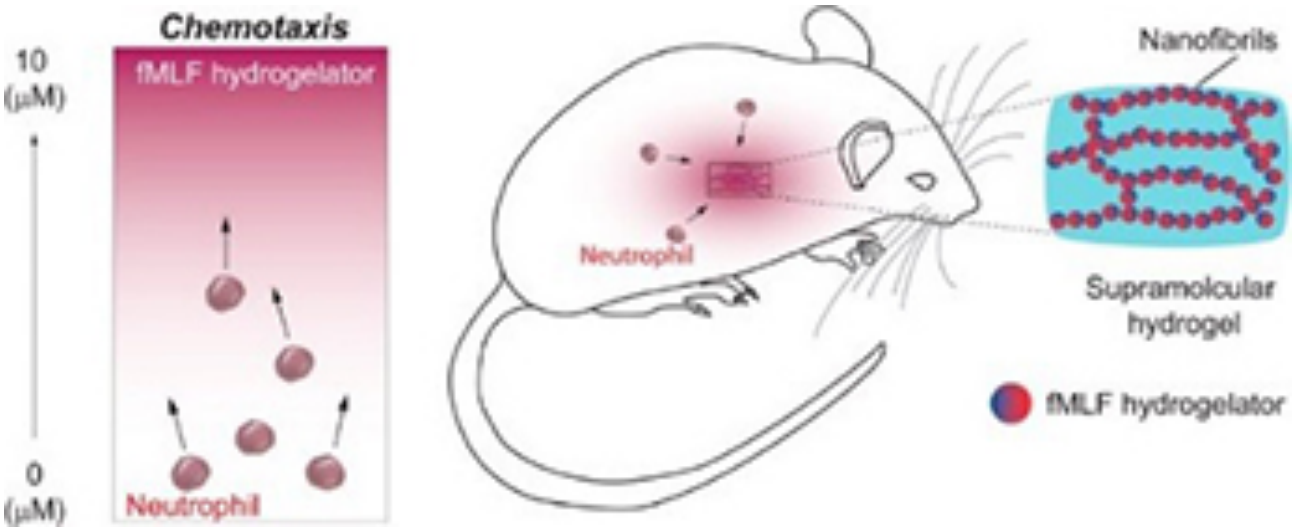
Technology description

fMLF-Based Supramolecular Hydrogels Prolong Inflammation Response:

Hydrogels of chemoattractants preserve neutrophil activity for immunomodulation



Background:

Neutrophils play a key role in combatting infection in the human body. Efficient local accumulation of neutrophils depends on gradients of N-formyl peptides, such as N-formyl-L-methionyl-L-leucyl-L-phenylalanine (fMLF), to signal neutrophils to the site of infection or disease. As a chemoattractant, fMLF has been used in aqueous or heterogeneous solutions for inducing acute inflammation to slow tumor growth or treat bacterial infections. However, current fMLF delivery methods have relatively weak and transient effects and suffer from burst release and low capacity payload.

The innovative approach developed to obviate these limitations incorporates fMLF into D-peptides to create self-assembling hydrogels of multifunctional chemoattractants that maintain their potent chemotactic activity towards neutrophils. As self-delivery-drugs, the fMLF-hydrogels hold promise as cancer therapies, treatment for microbial infections, and vaccine adjuvants. The modular aspects of these scaffolds can be further implemented towards neutrophil chemotaxis inhibition, rather than promotion, for chronic inflammation and pain treatments.

Summary

· D-peptides conjugated to immunogenic N-formyl peptides (i.e., fMLF) self-assemble into hydrogel
· The fMLF-hydrogels induce sustained release of chemoattractants, leading to neutrophil accumulation at the site of administration
· Administering fMLF-hydrogels at tumor site promotes innate immune response & inhibits growth
· The fMLF-hydrogels shrink tumor size when injected intratumorally every 48 hours
· Effective to treat bacterial infection, reduce sepsis, and promote resolution of septic condition
· Replacing fMLF with formyl peptide receptor (FPR) antagonists inhibits neutrophil activation for treating undesirable inflammation and pain

Publication

"De Novo Chemoattractants Form Supramolecular Hydrogels for Immunomodulating Neutrophils In Vivo."Bioconjugate Chem., **2014** , 25 (12), pp 2116–2122. DOI: 10.1021/bc5004923

Advantages

· Immunomodulating hydrogels are structurally tunable scaffolds to treat diseases and infections
· fMLF-hydrogels of D-peptides are proteolytically stable, prolonging the sought therapeutic effects
· Self-delivery method allows high capacity payload, eliminate burst release, and sustain treatment
· The hydrogels may be tailored to apply to prosthetic devices or organs to remove biofilms
· Low administration frequency of fMLF- or FPR-hydrogels reduce cost and patient discomfort

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