REGIONE DEL VENETO
ULSS3 SERENISSIMA

AVVISO PUBBLICO, PER TITOLI E PROVA COLLOQUIO, PER L'ASSEGNAZIONE DI DUE BORSE DI STUDIO, RISERVATE A LAUREATI IN FARMACIA, PRESSO L'UOC FARMACIA OSPEDALIERA DEI PRESIDI OSPEDALIERI DI MESTRE E VENEZIA, CIASCUNA DELLA DURATA DI 12 MESI E PER 35 ORE SETTIMANALI.

PUBBLICAZIONE CRITERI DI VALUTAZIONE DELLA COMMISSIONE ESAMINATRICE E DELLE TRACCE DELLA PROVA ORALE

In ottemperanza a quanto disposto dall'art. 19 del D.Lgs 14 marzo 2013, n. 33 e s.m.i., vengono elencati i criteri di valutazione e le tracce della prova orale, estratti dai Verbali della Commissione Esaminatrice n. 1 e n. 2 del 21 giugno 2022:

- *Omissis* -

CRITERI DI VALUTAZIONE

- *Omissis* -

La Commissione ritiene di valutare gli aggiornamenti professionali (corsi, congressi, conferenze) effettuati dopo la Laurea e di argomento attinente esclusivamente alla materia prevista dal Bando.

- *Omissis* -

La Commissione stabilisce, sulla base del relativo bando, che la prova orale deve riguardare argomenti relativi alla "Farmacologia e modalità di erogazione dei farmaci" e, nell'ambito del colloquio, sarà altresì accertata la conoscenza della lingua inglese attraverso la lettura e la traduzione di testi.

- *Omissis* -

F.to il Segretario della Commissione

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ARTICLE OPEN

Hyaluronan is a natural and effective immunological adjuvant for protein-based vaccines

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One of the main goals of vaccine research is the development of adjuvants that can enhance immune responses and are both safe and biocompatible. We explored the application of the natural polymer hyaluronan (HA) as a promising immunological adjuvant for protein-based vaccines. Chemical conjugation of HA to antigens strongly increased their immunogenicity, reduced booster requirements, and allowed antigen dose sparing. HA-based bioconjugates stimulated robust and long-lasting humoral responses without the addition of other immunostimulatory compounds and proved highly efficient when compared to other adjuvants. Due to its intrinsic biocompatibility, HA allowed the exploitation of different injection routes and did not induce inflammation at the inoculation site. This polymer promoted rapid translocation of the antigen to draining lymph nodes, thus facilitating encounters with antigen-presenting cells. Overall, HA can be regarded as an effective and biocompatible adjuvant to be exploited for the design of a wide variety of vaccines.

Keywords: Hyaluronan; natural polymer; immunological adjuvant; HA-bioconjugate vaccines

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INTRODUCTION

Hyaluronan (HA) is an anionic, linear, nonsulfated glycosaminoglycan that is composed of repeating units of D-glucuronic acid and N-acetyl-D-glucosamine linked through alternating β-1,3 and β-1,4 glycosidic bonds. HA is ubiquitously present in the human body as the primary component of the extracellular matrix.[1] In addition, its remarkable inherent physicochemical properties, such as mucoadhesiveness, biodegradability, biocompatibility, and lack of toxicity, make this natural polymer appealing for several medical applications.[2] Among these applications, HA has been successfully exploited as a carrier for proteins, peptides, cytokines, nucleotide therapeutics, and anticancer drugs, ensuring their targeted and long-acting delivery and water solubility.[3–5] HA is present in tissues in a wide range of molecular weights (MWs), each endowed with different biological functions.[6] Indeed, while native high MW (> 10^3 kDa) HA promotes tissue integrity and has immunosuppressive functions, low MW (LMW, < 10^3 kDa) fragments produced during various physiological and pathological processes are characterized by immunostimulatory, proinflammatory, and strong angiogenic properties.[7] The biological behavior and turnover of HA are based on interactions with specific receptors, some of which mediate polymer endocytosis (HA receptor for endocytosis);[8] others, its cellular uptake and degradation (CD44), signal transduction (receptor for hyaluronate-mediated motility),[9] and regulation of homeostasis and catabolism (lymphatic vessel endothelial hyaluronan receptor-1, LYVE-1).[10] Of note, HA also plays critical roles in both innate and adaptive immune responses by direct interactions not only with the abovementioned receptors,[11] but also with Toll-like receptors (TLRs).[12] In the latter interactions, HA fragments act as endogenous damage-associated molecular pattern molecules (DAMPs), which are recognized by TLR2 and TLR4 receptors expressed by a wide range of immune cells, including dendritic cells (DCs), monocytes, natural killer cells, and neutrophils. In addition, TLR2 functions as a costimulatory molecule in all activated T cells, including memory T-cell subsets.[13,14]

Although some authors have described HA as a TLR agonist able to induce sterile inflammation by activating DCs and stimulating the production of cytokines,[15,16] the potential of HA as an effective immunostimulatory and immunomodulatory agent for medical applications has been poorly investigated.[16] Notably, TLR agonists are emerging as a new outstanding class of vaccine adjuvants since they offer a unique possibility of orchestrating adaptive immune responses by finely regulating the crosstalk between innate and adaptive immunity. In particular, this kind of vaccine adjuvant has been reported to induce the activation and maturation of DCs, increase cross presentation and cross priming, and stimulate memory responses.[17] Additionally, different TLR ligands can be exploited to engage different receptors and hence to finely tune the type of Th immune responses elicited against a

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