Alginate Nanoparticles for Drug Delivery and Macrophage Reprogramming
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INTRODUCTION

Current cancer treatments are systemic and often cause many negative side effects, such as hair loss, anemia, and loss of appetite. The use of M1 activated macrophages, coupled with alginate nanoparticles, to deliver cancer-fighting drugs, could allow for more targeted cancer treatment and fewer undesirable side effects. Advantages of using nanoparticles include the ability to sterilize and purify the nanoparticles, and potential for modification with different functional groups. This is significant, as different polymers may induce different types of macrophage activation and have different drug release profiles.

PARTICLE SYNTHESIS AND MODIFICATION

Sodium Alginate
38 mL 0.12% low viscosity
Calci
2 nm 18 mM
Calcium Alginate Pegol
16 nm 0.37%
Alginate nanoparticles
Refrigerated overnight
Centrifuged 20,000rpm 45 minutes
Poly-L-arginine (PLR)
16 nm 0.37%
1 hour magnetic stirring
Freeze-dried
Suspended at 1% in PBS

Figure 3. Particle synthesis. Solutions were added dropwise.

MTT (MACROPHAGE VIABILITY)

Cell viability assays were performed on three groups of RAW 264.7 macrophages, non-activated, IL-4 (M2) activated, and LPS (M1) activated, after incubation with each of the modified nanoparticles.

Figure 4. Modifiers. The amine group of each monomer bonds with the carboxylic acid groups of the sodium alginate.

Macrophages are derived from monocytes in the blood, producing a spectrum of macrophage phenotypes. The M1 and M2 phenotypes exist at opposite ends of this spectrum.

M1 macrophages foster helper-T cell type 1 (Th1) responses, including immune response, tumor suppression and inflammation. M2 macrophages foster helper-T cell type 2 (Th2) responses, including parasite destruction, inflammation reduction, and angiogenesis (see Figure 1).

Alginate is a naturally-occurring polymer (Figure 2) found in species of brown algae (kelp). It has applications in cosmetics, foods, manufacturing industries, dentistry and a growing profile in medicine.

CONCLUSIONS AND FURTHER WORK

Combining the effects of macrophage reprogramming and controlled release, treating cancer with encapsulated chemotherapeutics which target macrophages is still a viable option. The modified alginate nanoparticles do not appear to have any direct adverse effects on Raw 264.7 cells. The loaded nanoparticles release their contents in a slow, steady fashion, which is ideal for efficiently delivering chemotherapeutics to cancer cells. Although further replicates are needed for drug release, it appears the different modifications result in different release profiles, and differences in the amount of drug released. Further work may include verification of viability assay results, replication of drug diffusion trials, and various assays to determine the effects the functional groups have on macrophage polarization.

REFERENCES


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