Module 10 Assignment

585.751 Immunoenginnering

1. (50 points) PEG is extensively used in designing nanoparticles and larger biomaterials to prevent immune cell recognition. Answer the following questions about PEG:

    a. (20 points) What is the mechanism by which PEG reduces immune recognition of and response to a nanoparticle or implanted biomaterial?

PEGylation is the process that involves conjugating hydrophilic polyethylene glycol (PEG) polymer chains to a molecule, such as a drug, therapeutic protein, or the surface of nanoparticles and biomaterials. It produces changes such as conformation, electrostatic binding, hydrophobicity etc. PEG chains are hydrophilic, which contribute to create a "water cloud" around the conjugated material. The PEG layer sterically hinders nanoparticles from interacting with other particles and proteins in the blood. By preventing opsonization and reducing protein adsorption to the nanoparticles, macrophages do not bind and recognize the nanoparticles, and they evade immune recognition and engulfment by the MPS.

    b. (15 points) What are the advantages and disadvantages of PEGylation?

PEGylation increases the circulation time of the nanoparticles or therapeutics agents in the blood and avoid them to be quickly cleared from the blood. By masking the therapeutic agent or nanoparticle from the immune system, PEGylation decrease the likelihood of an immune response against the nanoparticle, potentially reducing adverse events. The hydrophilic nature of PEG can improve the solubility of hydrophobic drugs, facilitating their absorption. PEGylation, also allows the nanoparticles to circulate and extravasate to the tumors or target tissues.

There are a variety of disadvantages to PEGylation:

- **Limited efficacy**: 50% of injected dose end up in the liver and spleen after 48h.
- **Liver or Spleen Accumulation**: a significant portion of PEGylated substances may end up in the liver of spleen, which can lead to off-target effects.
- **Can reduce uptake by target cells**: PEG prevents protein bindings.
- **May induce immune response**: people develop anti-PEG antibodies, anti-PEG IgM, which leads to accelerated blood clearance (ABC) upon subsequent injections. After second injection, association of anti-PEG IgM with the PEG particles may allow the immune cells to bind to the particles and clear them but also can lead to IgM mediated complement activation immune response.

    c. (15 points) Describe one alternative approach to PEGylation in engineering materials with "stealth" properties.

Shape modulation: Engineered material shape can be modulated to control MPS recognition and uptake. In vitro, it has been shown that particle shape affects macrophage uptake, and in vivo their distribution within the body with the ellipsoid particles being dispersed throughout the animal. Spherical particles compared to elongated ellipsoidal or cylindrical particles are more rapidly phagocytosed by macrophages and cleared by the MPS organs. Ellipsoidal or cylindrical particles, have a different biodistribution pattern compared to spherical particles, leading to longer circulation in the bloodstream.

, whereas, whether the particle approaches with the long pointed end or on the flat elongated side, will determined how quickly it's phagocytosed: compared to the other type, particles approaching with the long pointed end will be internalized more rapidly.

2. (50 points) The immune system plays a key role in tissue engineering and regenerative medicine that is still being elucidated. List 3 ways in which the immune system has been shown to be involved in tissue regeneration (either from the lecture videos or your own research). Additionally, describe one way in which a biomaterial for tissue engineering can be designed to modulate the immune system in order to improve regeneration.