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Examination paper for
Mol3015 Nanomedicine II - Therapy

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Date Signature

Please adhere to the indicated lengths of answers, font is considered, illustrations do not count. Good luck!

Biomaterials are evolving into hypermodern approaches for advanced therapy in many clinical settings.

1a: What do we mean by biomaterials? (1/2 page, 5pts)

Bioactive/bioinert materials/substances designed for use in treatment and diagnostics, developed through material science, biology, chemistry, immunology to come in contact with biology and perform a function.

1b: What basic and general requirements must we demand from a biomaterial for it to be clinically useable? (1/2 page, 5pts)

Biocompatible (non-toxic, non-toxic degradation products, non-inflammatory, non-carcinogenic, nonteratogenic, non-mutagenic, blood-compatible), sterilizable, manufacturable, correct physicochemical properties (elasticity, strength, toughness, surface properties, topography, degradability), appropriate functional timeline

1c: How is the nanoscale important for the interaction between a bulk biomaterial and cells? (1 pages, 10pts)

Molecular organization of the cell and therefore the mode of interaction is in the nanoscale, what the cell "sees" is subcellular, the cell does not see large surface, only the surface it is in direct contact with. The cell can see functional groups, charge or hydrophobicity, topography, 2D or 3D environment, biomolecules, sugars, proteins, lipids, which interact with surface molecules with high or low specificity. The surface molecules are connected to the cell interior and the organization of these transmembrane proteins conveys a message to the cell on how it is supposed to react. Therefore it is the nanoscale organization in the materiel in the interface with the cell and that directly influence cell behavior, activation/differentaiation, decision making, compatibility and all the rest. By gaining control over the nanoscale mechanical features (topography, fibrosity, patterned islands) and the biomolecular organization will make the whole difference in how cells respond to biomaterials.

1d: Briefly describe one top-down and one bottom-up method for creating biopatterned surfaces (1 page, 10pts).

Top down: from large to small, removing material Many answers possible, including lithography, etching, electronbeam etching (FIB), atomic layer deposition, UV-light destruction, protective layers and much more

Bottom up is from small to large, (photo)chemical conjugation, AFM/dip pen, self-assembly, stamping etc

Detailed explanations on the chosen approach needed

Biocompatibility and nanotoxicology. The vast possibilities in creating novel biomaterials also lead to questions related to safety and biocompatibility.

2a: What is the sequence of immunological events that lead to foreign body giant cell formation in response to an implanted biomaterial? (2pages, 10pts)

Briefly: implant, contact with body fluids, deposition of proteins/formation of corona (albumin other), deposition of immunoactive substances (complement, antibody, soluble scavengers, clotting factors), recruitment of nearby tissueresident cells, inflammation, additional recruitment, increased inflammation, fibrosis, macrophage cell fusion, possibly chonic inflammation. This is driven by ROS and proinflammatory cytokines.

2b: How can one improve a surface to become less bio-**in**compatible (i.e. more biocompatible) (1page, 10pts)

Several ways, these are suggestions based on understanding of 2a

The initiating response is corona formation: prevent corona (by PEG or other functionalized surface (avoid –OH), wettability, charge, hydrophilicity, multifunctional surfaces, promote binding of "silent" proteins.

prevent cellular activation by deposited material: shape, size, spacing and curvature of topographical features, functionally patterned surfaces

active inhibition: inhibit complement activation (charge, interspaced inhibitors), inactivate immune cells, surface chemistry/topography to actively inhibit immune cell activation.

Drug delivery systems (DDS) emerge as promising tools for treating difficult diseases.

3a: What are the advantages and disadvantages with nanoscale drug delivery systems? (1page, 5pts)

Protection of drug, combinatorial drugs, protein/peptide drug, targeting, depot effect, monitoring, multifunctional, external activation, crossing barriers, tolerating different pH, intracellular targeting, exploiting biological differences, theranostics, transferability (one DDS for many drugs, diseases with minor changes)

3b: Briefly describe one drug delivery process each for a nanocarrier system based on 1) passive

targeting, for 2) active targeting and for 3) stimuli-responsive drug delivery. (2pages 20pts)

Passive=EPR

Active= molecular targeting (cancer, endothelium, transferrin, folate ++) or physiological targeting (pH, O2 etc)

Stimuliresponsive (physiological stimuli, pH etc) but it should be understood external energy sources (electromagnetism, heat, light, ultrasound, mechanical, trigger molecules)

Explanations expected, also on the mechanism for the chosen DDS.