

**Biomaterials - Tissue Interactions**

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**Quiz #3**

**1 (50%). Design of a study to replace scar with skin.**

You are working under a very tight budget due to your company's efforts to survive the recession. You are asked to develop a device for regenerating skin in patients who have scars in their skin of size about 10X10 cm<sup>2</sup>. Each scar will be removed surgically and your new device will be grafted on the freshly generated skin wound. If your device works, skin will be regenerated at the site of the former scar.

**A (10%).** Select an animal species with which you will conduct model studies of your candidate device(s). The animal species you select should have approximately the same scar-forming ability as the human. As a measure of scar-forming ability you can take the fractional percent of initial area of an experimental skin wound that forms scar asymptotically following injury ( $A_{\infty}$ ). Since the human forms large scars, the asymptotic scar-forming ability of humans (on the back) is about 45%. The animal species you select should have an asymptotic scar-forming ability of at least 25%.

**B (10%).** Describe the wound model that you will generate in order to test the ability of your device to replace scar. Explain briefly why you are selecting this wound model.

**C (20%).** Consider the following 6 protocols that have been suggested for inducing skin regeneration in your animal model at lowest cost. For each candidate protocol provide a prediction of its efficacy and explain your answer briefly.

- a. Keratinocytes (KC) + dermis regeneration template (DRT) [in vitro]. It is proposed that new skin will hypothetically be formed in vitro using these two reactants, followed by grafting on this hypothetical skin onto the model wound. DRT is formed by coprecipitating collagen and a glycosaminoglycan in acetic acid solution, followed by freeze drying to form a scaffold with average pore size of 100  $\mu\text{m}$  and is crosslinked to give a degradation half-life in vivo of about 14 days.
- b. KC in cell culture medium will be pipetted onto the wound [in vivo].
- c. KC + FB will be pipetted into the wound, each cell type to be pipetted in its own cell culture medium [in vivo].
- d. TGFb1 solution will be pipetted on to the skin wound, followed by grafting the wound with KC + DRT [in vivo].
- e. KC + dermis regeneration template (DRT) [in vivo]. KC will be seeded into DRT before grafting onto the model skin wound.
- f. Fibroblasts (FB) + KC + DRT [in vivo]. FB and KC will both be seeded into DRT, before grafting onto the model skin wound.

**D (10%).** Your budget is tight and you can select one (only one) test that you will use to assay the efficacy of your chosen device(s) to meet your objective of replacing scar with a

physiological dermis. (Safety will not be studied at this time.). Describe this test briefly in terms of the data that it provides which distinguish between scar and dermis. (Do not discuss the basic physics of the laser scattering process.)

## **2. (50%). Biomaterials for total knee replacement**

You have been hired by a medical device company that is in the business of commercializing biomaterials to be used for total knee replacement procedures (Fig. 1). The femoral component of knee prostheses (Fig. 1a) is generally fabricated from cobalt-chromium alloy, and the tibial component can be made from cobalt-chromium alloy or titanium alloy. The condyles of the femoral component articulate with an ultra high molecular weight polyethylene tibial insert. The femoral component of the prosthesis cannot be made from titanium alloy because of the poor wear resistance of titanium.

A (25%). Figs. 1c show a radiograph obtained from a patient 1 year after implantation of a prosthesis (with both components made from cobalt chromium alloy) from a competing company. The femoral and tibial components were fixed with polymethyl methacrylate (PMMA; “bone cement”). The orthopaedic surgeon and radiologist have agreed that there are certain regions of abnormal bone loss under the femoral (X) and tibial (Y) components.

1. (5%) The CEO of your company thought that this bone loss was somehow caused by fragmentation of the cement. What mechanism of bone loss would you offer in support of such a theory related to breakdown of the cement?
2. (5%) Careful examination of the tissue obtained from the sites of bone loss after the implant was removed (even using electron microscopy) revealed no particles at the locations of the bone loss. Is that negative finding proof that particles were not the cause of the bone loss?
3. (5%) What alternative explanation (*i.e.*, other than due to particles) would you offer for the loss of bone at X and Y in Fig. 1c?
4. (10%) How would you propose to alter the design of the prosthesis to address your explanation in (3) for the femoral and tibial components?

B (15%). Instead of using PMMA for fixation of the femoral component, your company has developed a calcium phosphate mineral (hydroxyapatite, HA) coating to enable bone to bond directly to the prosthesis.

1. (5%) One of the engineers at the company has suggested that prior to packaging the HA-coated prosthesis it be incubated in a simulated body fluid. This will add to the expense of the prosthesis. Can you provide a supporting rationale for such a treatment?
2. (10%) Clinical trials of the HA-coated prosthesis have provided evidence that large portions of the plasma-sprayed HA coating detach from the metal. Removal of a few prostheses from which the coating detached has yielded surrounding tissue that contains large numbers of myofibroblasts and lubricin coatings on the tissue folds. Your CEO has proposed that the commercialization of the HA-coated devices continue. What case would you make in support of continuing or discontinuing the commercialization?

C (10%) The company is considering various products to treat the large bone defects in X and Y of Fig. 1c when the prosthesis needs to be removed and another implanted.

1. The CEO has been told that she could use the same HA particles that are employed in the plasma-spray coating process (to produce the HA coatings) as a bone graft substitute product to fill the defects. She was told that the particles (which for this application would be about 1 mm in diameter) are commended by their high strength and density. What recommendation would you make to the CEO?
2. Another approach that has been recommended for the treatment of the defects in X and Y is to inject a suspension of autologous marrow-derived mesenchymal stem cells into the defects. What rationale would you offer for first incorporating the cells into a mass of suitable particles, and the subsequent implantation of the cell-seeded particles?

Image removed due to copyright restrictions.  
Diagram of knee joint implant (artificial knee joint).

Image removed due to copyright restrictions.  
Before and after drawings of total knee replacement procedure (by A.D.A.M.)  
See <http://www.nlm.nih.gov/medlineplus/ency/imagepages/9494.htm>

Fig. 1 a) Typical total knee replacement prosthesis.  
b) Sketch showing the location of the prosthesis in the knee joint. c) Radiograph of a side view (lateral) of a total knee prosthesis that was fixed with polymethyl methacrylate (“bone cement”), 1 year post-implantation.

Image removed due to copyright restrictions. Side-view radiograph of a total knee prosthesis, with labels 'X' and 'Y' pointing to two darker patches in the remaining bone near the implants.

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20.441J / 2.79J / 3.96J / HST.522J Biomaterials-Tissue Interactions  
Fall 2009

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