

Problem Set 5

Issued: 04/04/06

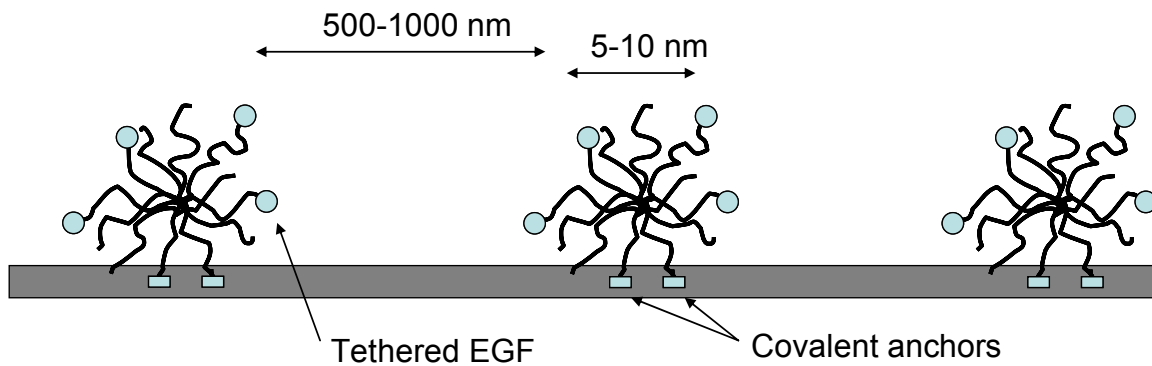
Due: 04/13/06

100 points total

20.462J/3.962J**Spring 2006**

1. (50 points) Compare and contrast a natural extracellular matrix based on collagen fibers with a synthetic matrix formed by a covalent PEG-based hydrogel containing –APGL- peptide linkages sensitive to the enzyme collagenase—answer in brief paragraphs:
 - a. Structurally, do these gels present the same barrier to cell movement/migration?
 - b. Which type of gel would you predict to be more rapidly degraded *in vivo*? Why?
 - c. *In vivo*, cells in either of these matrices will also be surrounded by other cells and ECM components. In what ways would you expect these matrices to differ in the way they mediate the interactions of cells with their surroundings?

1. (50 points) One of the first studies of immobilized growth factor signaling utilized poly(ethylene oxide) (PEO) star polymers as anchors for the presentation of epidermal growth factor (EGF) on a solid surface (see schematic below). EGF receptor-expressing cells seeded on such a surface can bind the surface-bound EGF and receive stimulation to grow or migrate. EGFR is a receptor tyrosine kinase that begins signaling by homodimerization- two EGF receptors bound to their ligand dimerize and phosphorylate one another to initiate the biochemical signaling chain. The covalent linkages linking EGF to the star polymer and the star polymer to the surface are stable and not enzyme-sensitive. Let's analyze differences between signaling cells receive from a star-PEO-EGF surface compared to signaling received if the cells are simply incubated with soluble EGF:
- Identify two ways in which the physical chemistry of the EGF-EGF receptor signaling will be affected by presentation by star PEO relative to soluble EGF, and discuss how these differences could **augment** signal transduction from the star-PEO surface.
 - Identify and explain one potential mechanism by which star-PEO presentation of EGF could **reduce** EGF signaling relative to soluble EGF.



2.