

### **Homework Nano-scale Engineering #2, Due Date: March 4, 2014**

Study the reference paper on “nanoparticle therapeutics: an emerging treatment modality for cancer” by Davis et al., Nature Reviews, Vol. 7, Sept. 2008, pp. 771-782. In particular, pay attention to its Table 2 “comparison of pharmacokinetics (human) of small-molecule drugs with nanoparticle therapeutics.” Answer the following three questions:

- 1) The doxorubicin-carrying nanoparticles SP1049C, NK911 and Doxil are compared with doxorubicin in the table. Based on the table, choose one you like the most. Why?

Answer: Doxil is chosen. It carries Doxorubicin (DOX) using PEG–liposome nanoparticles and achieves  $t_{1/2} = 84$  hours, which is much longer than DOX’s 0.8 hour. In addition, its clearance is only 0.02 ml/min•kg, which is much smaller than DOX’s 14.4 ml/min•kg. The longer circulation times of the nanoparticles compared with the free drug alone can improve tumour uptake. Of course, the potential side effects resulting from the very long circulation times should be studied.

- 2) For Abraxane, there is a comment: “status in vivo unknown.” Why is such a status unknown?

Answer: There is a possibility that Abraxane’s nanoparticles dissolve when infused into the patient. If it is indeed the case, the clinical benefit from Abraxane is not related to use of nanoparticle. Instead, it could result from the removal of toxic Cremophor El from the formulation.

- 3) IT-101 has mechanisms to control the release of the drug. What are typical methodologies to control the release of the drug?

Answer: A typical methodology is based on cleavage of a chemical bond between the particle and the drug by hydrolysis. Another methodology is based on cleavage of a chemical bond between the particle and the drug by enzymes, which are located within and outside cells or located only within cells. The lysozymes and esterases are examples of the enzymes located within and outside cells. The cathepsin B. is an example of the enzymes located only within cells.