Lecture 14: Challenges of proper drug dosing with nanodelivery systems

I. Overview of drug dosing problem
   A. Problems of scaling up doses from animal systems
   B. Basing dosing on size, area, weight of recipient
   C. Vast differences between adults in terms of genetics, metabolism
   D. Dosing in children – children are NOT smaller adults!
   E. Pharmacokinetics – drug distribution, metabolism, excretion, breakdown
   F. Conventional dosing assumes drug goes everywhere in the body
   G. Targeted therapies – a model for future nanomedical systems?

II. From the animal dosing to human clinical trials
   A. Importance of picking an appropriate animal model system
   B. Does drug dosing really scale?
   C. The human guinea pig in clinical trials and beyond

III. Some drug dosing methods
   A. Attempts to scale up on basis of area
   B. Attempts to scale up on weight/volume
   C. Attempts to use control engineering principles

IV. Genetic responses to drug dosing
   A. All humans are not genomically equivalent!
   B. Predicting on basis of family tree responses
   C. SNPs, chips, and beyond…predicting individual drug response
   D. After the $ 1000 individual genome scan… more closely tailored individual therapies

V. Dosing in the era of directed therapies – a future model for nanomedical systems?
   A. How directed therapies change the dosing equation
   B. Current generation directed antibody therapies dosing
   C. Some typical side effects of directed therapies
   D. Nanomedical systems are the next generation of directed therapies

VI. Most directed therapies are nonlinear processes
   A. Current and pending FDA approved directed therapies
   B. Some examples of how a few directed therapies work
      1. Complement directed cytotoxicity
      2. ADCC-mediated adaptive immunity switch
      3. Antibody-directed enzyme producing therapy

VII. Other ways of controlling dose locally
   A. Magnetic field release of drugs
   B. Light-triggered release of drugs

References:

Adams, G.P., Weiner, L.M. Monoclonal Antibody Therapy of Cancer. Nature Biotechnology 23(9): 1147- 1157 (2005)

Bailey, J.M., Haddad, W.M. Paradiigms, Benefits,and Challenges: Drug Dosing Control in Clinical Pharmacology. IEEE Control Systems 35-51, April 2005

McCoy, C.P., Rooney, C., Edwards, C.R., Jones, D.S., Gorman, S.P. Light-Triggered Molecule-Scale Drug Dosing Devices. J. AM. CHEM. SOC. 2007, 129, 9572-9573

Miller, A.A Body Surface Area in Dosing Anticancer Agents: Scratch the Surface! Journal of the National Cancer Institute, Vol. 94, No. 24, December 18, 2002

Nigel Baber & Deborah Pritchard Dose estimation for children. *Br J Clin Pharmacol* 56 , 489–493 2003