BME 626 Engineering Nanomedical Systems
October 23, 2014

Lecture 13: Designing nanomedical systems (NMS) for in-vivo use

13.1 Bringing in-vivo considerations into NMS design
- 13.1.1 the in-vitro to ex-vivo to in-vivo paradigm
  - 13.1.1.1 In-vitro - importance of choosing suitable cell lines
  - 13.1.1.2 adding the complexity of in-vivo background while keeping the simplicity of in-vitro
  - 13.1.1.3 all the complexity of ex-vivo plus the "active" components of a real animal
- 13.1.2 In-vivo systems are open, "active" systems with multiple layers of complexity
  - 13.1.2.1 In-vitro and ex-vivo are mostly "closed" systems, but not absolutely
  - 13.1.2.2 What is an "open" system?
  - 13.1.2.3 Attempts to isolate open systems
- 13.1.3 Layers of complexity of in-vivo systems
  - 13.1.3.1 Human cells in nude mice – a mixture of in-vitro and in-vivo
  - 13.1.3.2 "Model" small animal systems
  - 13.1.3.3 better model larger animal systems

13.2 Circulation time and biodistribution
- 13.2.1 factors affecting circulation time
  - 13.2.1.1 size/shape
  - 13.2.1.2 "stealth layer" coating
  - 13.2.1.3 zeta potential in-vivo in varying environments
  - 13.2.1.4 filtration and excretion
  - 13.2.1.5 dose/targeting
- 13.2.2. where do the NMS go in-vivo?
  - 13.2.2.1 checking the obvious organs (liver, spleen, kidney, blood…)
  - 13.2.2.2 finding NMS in tissues and organs
    - 13.2.2.2.1 in-vivo
    - 13.2.2.2.2 within dissected tissue sections
    - 13.2.2.2.3 in blood (ex-vivo versus in-vivo flow cytometry)
    - 13.2.2.2.4. what is excreted?
- 13.2.3 Circulation time and dose optimization
  - 13.2.3.1 measure drug concentration over time
  - 13.2.3.2 is there an optimal drug dose?

13.4 In-vivo targeting and mistargeting
- 13.4.1 mode of administration (intravenous, oral, intra-tumor…)
- 13.4.2 how can we assess targeting in-vivo? (MRI, fluorescence, …)
- 13.4.3 a rare-cell targeting problem
- 13.4.4 consequences of mistargeting
- 13.4.5 balancing dosing, therapeutic efficacy, and consequences of mistargeting

13.5 Evaluating therapeutic efficacy in-vivo
- 13.5.1 advantages of non-invasive measurements
- 13.5.2 measures of tumor load/shrinkage (tumor size, weight,..)

13.5.3 other measures of disease effects
13.5.3.1 direct measurement of restoration of lost or compromised functions
13.5.3.2 indirect measures of disease effects (e.g. behavior, weight gain/loss, .)
13.5.4 Some examples of in-vivo work with NMS

13.6 Summary
13.6.1 Choosing an appropriate animal model and getting it approved takes time!
13.6.2 Animal experiments are expensive and time-consuming
13.6.3 Performing in-vivo measurements of drug delivery and therapeutic efficacy are more challenging and expensive than in-vitro or ex-vivo work!
13.6.4 But ultimately you must show that the NMS works in-vivo

References

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