

Nuclear Receptors, Drug Metabolism, Prodrugs

1. Imagine that you are a doctor for an early-menopausal female patient who has been diagnosed with estrogen receptor positive breast cancer. The patient was first treated in the summer of 2007 with tamoxifen and showed a marked improvement for a few months. However, the patient was strongly bothered by the loss of libido, and upon suggestion of her friends, started to use natural genistein (picture on the right) and cocaine as a libido boosters. She is now mildly addicted to cocaine and appears unwilling to give it up, however, the cancerous growth in her breast is progressing despite the regular treatments with tamoxifen. The patient strongly objects to the surgery and insists that she'd rather enjoy her last months of life aided by cocaine and amorous friends.



- Discuss the metabolism and mechanism of action of tamoxifen in suppressing the growth of estrogen receptor positive breast cancers (2 pts)
- Cocaine in small quantities is often associated with enhanced libido via direct CNS effects. However, the patient feels that her libido responds to cocaine more than the libidos of her somewhat older, post-menopausal women. Is there a rational explanation? (1 pt)
- Would you recommend that she stop taking natural genistein? Explain your reasoning and back it up with specific evidence from scientific literature. (2 pts)
- Given that she is unwilling to get off cocaine, how would you modify her breast cancer treatment to save her life? You can give a general discussion of ideas, or provide a justification for the use of a specific alternative drug. (2 pts)

2. Photodynamic therapy relies on a technologically advanced combination of a drug delivery and prodrug approaches. The approach has been tried by many companies over the last decades, including Miravant Medical Technologies in Santa Barbara. Referring to photodynamic therapy, Steven Kriegsman, investment adviser who specializes in undervalued technology stocks said in an interview with CEOCFInterviews in February 2001 (<http://www.ceocfinterviews.com/AR01-2.htm>):

"Miravant Medical Technologies (NASDAQ: MRVT) is also currently very undervalued. Their stock has come down from about \$30 to only \$8. This company has probably the best technology in the world to treat age related macular degeneration. We expect their product to reach the market next year and it could be the leading product in the world."

Discuss some reasons why photodynamic therapy in general has failed to live up its promise as a clever combination of prodrug approach with innovative targeting.

(3 pts)

