DOMINICAN UNIVERSITY of CALIFORNIA 1890

Mission

Dominican University of California transforms lives. We are an independent, learner-centered, international university of Catholic heritage, which interweaves Dominican values, the liberal arts and sciences, and the skills and knowledge necessary to live and work in an interdependent world.

Department of Natural Science and Mathematics
Chemistry and Biology Research Methodology I
CHEM/BIO 2990.5 – 1 Unit

Location: Science Building Rm 107

I. Scientific Article Confirming Your Knowledge:
Molinski et al., **2009** *Nature Reviews Drug Discovery.*
Drug development from marine natural products.

20 pts, Due week 2

1. In terms of drug leads, why was/is the search for marine derived compounds justified?

2. Besides drug leads, what 2 other areas of biomedical research have marine natural products played an important role in terms of discovery?

3a. What was the name of the first marine natural product that served as a lead compound to create derivatives that were used clinically to treat cancer?

3b. What type of marine organism did they come from and where was it collected?

4. What 2 developing factors may be responsible for a renaissance in the discovery of drugs from sea?

5. List the first 2 marine natural products to be approved by the US Food and Drug administration (FDA)

Compound name:	Source organism:	therapeutic for	Year Approved
1)_____	_____	_____	_____
2)_____	_____	_____	_____

6. What has been a major impediment (problem) for the development of drugs from marine sources?

7. What was the biological mechanism of action (reason for it's anti-cancer activity) for ET-743 (trabectidin ®)?

8. In a rat incisional model of post operative pain, ***approximately*** how many times more potent in terms of the effective dose @ 50% (ED_{50}), is ziconotide (Prialt ®, ED_{50} = 49 pM) vs Morphine (ED_{50} = 2 nM)? (1pt)

Recall gen chem I ☺: mM = micromolar
uM = micromolar
nM = nanomolar
pM = picomolar

9. What were the two types of source methods for providing ET-743 (trabectidin ®) for clinical trials in cancer?

10. How much collection of the sea hare source organism *Dolabella auricularia* (Figure 2d) was required to provide the 1st milligram (mg) to determine it's structure? Note: 1 mg is about the size of 4 grains of sand.

11. How was the structure of bryostatin solved?

12. What is a major reason for suggesting pursuing natural products for new drugs in the modern age vs combinatorial chemical libraries (i.e. random molecules synthesized by a machine, not made by nature to affect a specific biological target)?