Multidrug Resistance in Normal and Cancerous Mussel Blood Cells

Gillian Jones¹,², Bryan Cole², Jim Moore², and Gary Cherr²
¹ Mercyhurst College, Erie, Pennsylvania ² Bodega Marine Laboratory, University of California, Davis

Introduction
- Drug transporter proteins (DTP) remove a diverse range of chemicals from cells and are responsible for Multidrug Resistance (MDR) – the first line of defense against toxins.
- MDR is the #1 cause of failure of chemotherapeutic drugs to kill cancer cells as these cells upregulate DTPs.
- There are 3 main classes of DTP – we investigated 2 in mussel hemocytes (blood cells): MRP and PGP.
- Invertebrates are not known to normally develop cancer. However, the bay mussel, Mytilus trossulus, develops a terminal cancer (neoplasia) of the hemocytes.
- To date, no studies exist regarding DTP activity in M. trossulus cancer cells.

Research Questions
1) Do normal hemocytes in the bay mussel express DTPs? If so, which are present?
2) Do neoplastic hemocytes exhibit different DTPs?
3) How do the levels of drug transport activity in normal hemocytes compare with those in cancer cells?

Methods
- Hemocytes drawn from adductor mussel
- Cells plated and treated with DTP inhibitors and a fluorescent DTP substrate
- Incubated at 15 °C for 1 hour
- Cells imaged with epifluorescence scope using MetaMorph Image Analysis program
- Quantitative pixel analyses of images

Results: Normal Hemocytes Exhibit MRP-1 Activity but not PGP Activity
- Fluorescence levels in MRP inhibited cells were consistently higher in normal cells, therefore hemocytes of uninfected animals express high MRP activity

Results: DTP Activity in Cancer Cells Varies Among Individual Mussels
- Fluorescence levels in PGP- and MRP-inhibited cells are higher, therefore this individual exhibits both PGP and MRP activities

Relevance
- Because mussel cancer cells showed varying levels of DTP activity, including PGP increases similar to human cancer cells, comparisons can be made to human cancer research
- Variability in DTP activities may be due to the stage of cancer cell development among individuals

Further Research
- By using flow cytometry, characterization of cancer cells at various stages of development would better characterize DTP expression in these novel invertebrate cancer cells

Acknowledgments
A special thanks to the Cherr lab, Susan Williams, Max Castorani, the entire 2010 REU cohort, and everyone else who made this project possible. This research was supported by a grant from the National Science Foundation to SL Williams and ED Sanford (DBI- 0753226).