1. How can the expression microarray contribute to cancer research and the improvement of cancer treatment? (8 points)

Cancer is a complex disease and often involves many genes and molecular pathways. Expression microarrays allow researchers and clinicians to survey global changes in transcriptomes without bias towards particular pathways.

In cancer research, microarrays can be used to determine the molecular signatures of different types of cells and cells at different stages of differentiation. This information can be helpful in identifying the cell-of-origin in different cancers and addressing the existence of cancer stem cells. Microarrays can also be used to shed light on genetic changes in a tumor as it goes from being non-invasive to metastatic, or from treatment-sensitive to treatment-refractory. Information gleaned from these studies can identify molecular pathways of interest that may make a cancer susceptible when modulated with chemotherapy. The microarrays studies may also result in discovery of new tumor suppressors, oncogenes, and other genes that promote cancer or have a protective effect against it. They may lead to the discovery of new molecular markers that can be used to detect cancer cells.

In cancer treatment, microarrays may help clinicians determine the prognosis of a patient and which treatment plan to recommend. Clinicians currently rely on patient characteristics (e.g. age, risk factors, etc.) and tumor pathology in identifying and staging cancers. However, tumors that have the same pathological appearance may have different molecular properties. By knowing the transcriptomes of cancers, clinicians may be able to better predict the clinical course of a cancer and the additional information can help guide treatment. Molecular signatures of different cell types can be useful for identifying recurrent tumors and for distinguishing between primary and secondary tumors.

2. Which research question do you wish to ask and get the answer for through comparative expression microarray analysis? (2 points)

What molecular changes does a cancer cell undergo when it becomes refractory to treatment with Avastin? Biopsies can be taken from patients before they begin treatment, and after their cancers have become resistant to treatment. Genes that are up- or down-regulated between the two time points can be determined with expression microarrays, and may be the target of additional therapy.
1) How can the expression microarray contribute to cancer research and the improvement of cancer treatment? (8 pts)

Histological and clinical evaluation of a tumor can only tell us so much about a tumor and how its cells might behave in the future (risk of metastasis), and conservative assessments often cause many individuals to undergo and suffer from the side effects of unnecessary chemotherapy. Evaluating the gene expression of tumors provides more information about the potential cells of origin of the tumor, and also about the risk of metastasis of the tumor, given which genes are up- or down-regulated in its cells. In addition to tumor behavior, supervised analyses can be performed using patient survival data to determine a “signature” of gene expression that is strongly associated with either good or poor prognosis. Measuring the expression of these signature genes in the tumor cells of future patients can thereby allow clinicians to accurately determine the prognosis of the patient, ideally irrespective of disease progression. For example, if a primary tumor expresses an aggressive signature associated with poor prognosis, appropriately aggressive treatment steps can be taken early. Or, on the other hand, if a tumor expresses a gene signature associated with good prognosis and little risk of metastasis, it may be appropriate and safe for the clinician to decide the patient does not need to undergo chemotherapy or other difficult treatments.

Another way that expression microarrays may be able to contribute to cancer research and treatment is by identifying new target genes or molecular pathways that contribute to the pathogenesis of cancerous cells. So far, many genes identified this way are nothing new – cell cycle, growth, motility-associated genes – but it is possible that there are still targets to be discovered. At the very least, expression array analyses may allow scientists to evaluate the effectiveness of a treatment in development by measuring any changes in the expression of targeted genes after treatment exposure. An ideal treatment may be able to drive the cells of an initially “poor prognosis” tumor to express a “good prognosis” signature.

2) Which research question do you wish to ask and get the answer for through comparative expression microarray analysis? (2 points)

I am very interested in the etiology of autism, a disorder that has a large genetic component. However, the genes that contribute to the development of autism spectrum disorders appear to be highly heterogeneous, much like the presentation of the disorder itself. So, I would like to narrow the focus and compare autistic individuals with specific comorbidities to healthy controls, and to a random selection of autistic individuals. For example, I would like to determine the gene expression pattern associated with the comorbidity of autism and seizures, autism and food allergies, or autism and gastrointestinal dysregulation. Many autism studies focus only on gene expression in the brain, when in fact, this disorder may be highly systemic for some percentage of cases. By evaluating the gene expression associated with each of these systemic, yet frequently comorbid, conditions, it may be possible to identify additional candidate genes or molecular pathways that contribute to the development of autism.