



Using Microarrays to Study Leukemia

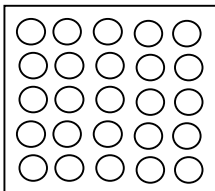
Diagnosis of ALL vs AML using microarrays

There is a good high school level activity online that includes use of microarrays to diagnose ALL vs AML. It is found as part of the packet entitled “DNA Chips: A Genetics Lab in the Palm of your Hand”

How this type of microarray works

The Gene Chip

In this lab, the microarray used is a commercial gene chip. Each spot on the slide (or microarray) is a single stranded DNA sequence from a different human gene. Scientists originally used a gene chip that contained 6,187 genes, one gene per spot. In the mini-microarray you view in this activity, they have selected 25 genes of interest and you will see results from only these 25 genes.

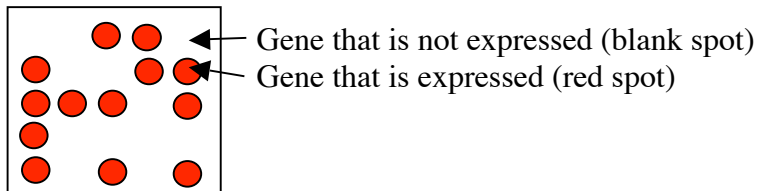


The Samples

The goal is to compare the gene expression (genes that are turned on) in white blood cells from ALL vs AML vs non-leukemia patients. Remember that when a gene is expressed, it is transcribed and an mRNA is made.

Messenger RNA is isolated from the white cells of a leukemia patient. The mRNA is used as a template to synthesize complementary single strand DNA (cDNA). The cDNA is made with a fluorescently labeled nucleotide. In this case, only one color radioactive label (red) is used. The resulting product is cDNA for each of the genes expressed in the white cells of the leukemia patient.

This cDNA probe is then allowed to anneal to the microarray, one person's cDNA per microarray. The labeled fluorescently labeled cDNA will bind to each of the human genes that are expressed in the white cells of that patient. A laser is then used to determine which genes had bound the labeled cDNA. If a given gene is expressed, the labeled cDNA corresponding to that gene will bind, and the spot where the gene is will light up red.



Scientists originally annealed the cDNA probes to microchips containing 6178 human genes. One patient's probe on one microchip. They then used a computer to compare the results for all 6178 genes between many ALL, many AML, and many non leukemia samples as well. They were able to identify sets of genes that are expressed only in ALL or only in AML.

For this activity a subset of 25 genes was selected. These genes are listed in the handout and are expressed in AML patients, in ALL patients or are control genes. Positive control genes should be expressed in all samples, and negative control genes should not be expressed in any sample.

The activity

A printable teachers guide and student activity can be found at http://science-education.nih.gov/newsnapshots/TOC_Chips/Chips_RITN/chips_ritn.html

The name of the package of activities is
"DNA Chips: A Genetics Lab in the Palm of Your Hand"
You can use this title to search for the activity if the URL has changed.

So what? Where do we go from here?

Above you saw the use of the microarray to diagnose ALL vs AML. We could already do this prior to the advent of microarrays. So what new information and abilities does the microarray allow?

- Diagnosis - We now know all the genes that are differentially expressed between the two types of leukemia allowing the development of additional (potentially improved) diagnostic tests.
- Tumor classification - We will be able to address whether different subtypes of cancers exist within AML and ALL.
- Treatments - The differing gene expression profiles can be used to design additional leukemia and patient-specific treatments.
- Basic Science - The differing gene expression profiles will give us insights into the cellular processes leading to and resulting from these leukemias.