

# Scenario E – Monitoring the Gene Expression of Cancer

## Background:

One of the first uses of GeneChip microarrays was to monitor the genes active in cancerous tumors. These GeneChips were perfect for the job because they allow the researcher to monitor the activity of multiple genes at a time. Since most cancers are due to mutations in multiple genes, this technology is a perfect fit.

Your group is a research group assigned to look at the activity of specific genes during the progression of cancer cells from normal cell to a cell dividing out of control. Understanding which genes are responsible could lead to multiple therapies and treatments in the future. The cancer you are studying is a type of lung cancer known as small cell lung cancer (SCLC). Currently, this cancer has only an 8-12% five year survival rate once diagnosed; therefore, knowledge of this cancer is crucial. The cancer has four basic stages to it. The following is the basic description for each stage:

Stage 1 – Localized (cancer is small or growing into the airways)

Stage 2 – Early Spreading (cancer has grown larger and has spread to lymph nodes closest to lungs)

Stage 3 – Multiple Spreading (cancer has now spread to nodes furthest from the lung on other side of chest)

Stage 4 – Other Body Parts (cancer has spread to another lobe of the lung and to another part of the body such as liver or bones)

Your group decides to use a Human Genome microarray that looks at the expression of approximately 21,000 human genes. You isolate mRNA from each patient's normal, non-cancerous cells. Then, you isolate mRNA from tumor cells from patients as they progress from stage 1 to 4 and apply each to the array and scan for results.

The main idea is to look at which genes change their expression as the cells change from a normal, non-cancerous cell through the cancer stages. Those genes that become active as the cell changes might be a target for drugs to suppress the gene. On the other hand, those that turn off as the cell progresses might be ones that could be a target to turn on the expression.

To simplify the readouts, you decide to focus on an area of 10 genes that your research shows to be implicated in small cell lung cancer development. You take 8 total mRNA samples from each patient throughout the study at seven stages – Early Stage 1 (ES1), Middle Stage 1 (MS1), Early Stage 2 (ES2), Middle Stage 2 (MS2), Early Stage 3 (ES3), Middle Stage 3 (MS3), and Stage 4 (S4) as well as a sample from a normal, non-

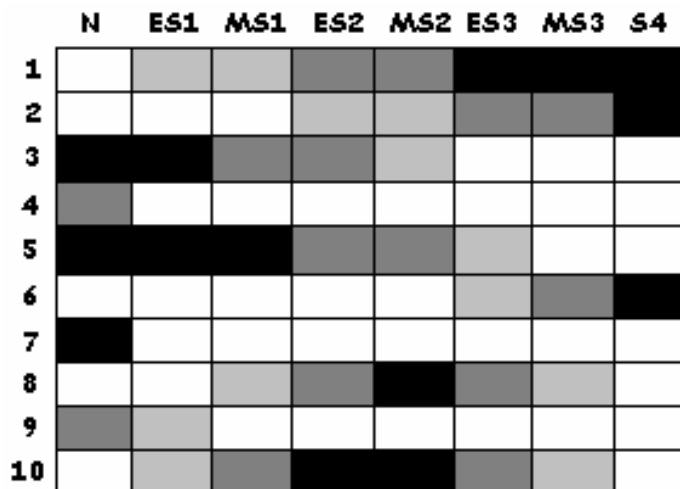
cancerous cell (N). Here list below is of the ten genes. Each one is given a specific number:

<u>Gene #</u>	<u>Gene Symbol</u>	<u>Gene#</u>	<u>Gene Symbol</u>
1	SCLC1	6	TP53
2	SCLC2	7	KRAS2
3	EGFR	8	BRAF
4	NULL	9	RB1
5	MGP	10	IGHG3

**Results:**

After collecting samples from each patient as they progress through lung cancer, you noticed that, except for few abnormalities, all of the patients had the same results. This means that their gene expression patterns are all very similar. The resulting microarray output is the common expression pattern that over 90% of the patients in the study showed. Even those that didn't have this exact pattern had mostly similar results with only a few genes acting differently.

The features numbered from 1 to 10 are the genes and those going from "N" to "S4" are the different stages. The features have three possible colors in them. The white feature means the gene is non-active, completely shut off. The light grey means the gene is expressed at a low level while the dark grey indicates the gene is expressed at a higher level. Finally, the black feature means the gene is extremely active at that stage.



**Directions:**

Your job is to analyze the results above and determine what is happening. Here are a few questions to think about when you analyze them. How did the genes change in activity as the cell progressed from normal cell to stage four cancer cells? How does the normal cell compare to the cancerous ones? If you were a drug company, which genes would you target to try to turn on or off? Why?