GraphSmarts: Cancer Biology

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Mutations and Cancer

Each person is made of trillions of cells. Over someone's lifetime, cells grow and divide as needed. When a cell is abnormal or becomes too old, it will typically die in a process called programmed cell death. Cancer is a disease characterized by uncontrolled cell growth, and often starts when something goes wrong in the process of programmed cell death. This results in cells continuing to grow and divide, making new, often abnormal cells. This sort of malfunctioning is often caused by changes, called mutations, in a cell's DNA sequence. Because DNA contains the instructions for making proteins, a mutation in DNA can lead to change in the function of a protein. Many proteins are involved in cell growth and cell death, and mutations in these proteins can allow cells to continue to grow and make new cells, even when they shouldn't.

By multiplying in an uncontrolled way, cancer cells can physically crowd out normal cells. The result of this crowding is that other bodily functions may be negatively impacted. Even worse, sometimes the cancer cells spread from the organ where they originated to other organs in the body. This is called metastasis. Metastasis makes it harder for doctors to treat the cancer because the cancerous cells are not all in one place.

KRAS and p53

Two proteins that are important for cell reproduction and death are called KRAS and p53.

The KRAS protein acts as an "on-off" switch that helps to regulate and control cell growth. When your body needs to make more cells, the KRAS protein switch is turned on and has high “activity”. When your body does not need to make more cells, the KRAS protein switch is turned off and the protein becomes inactive and therefore has no “activity”. A mutation in the *KRAS* gene can cause the KRAS protein to not switch on and off properly. Mutations in the *KRAS* gene are some of the most common mutations linked to cancer, with approximately 25% of tumors containing at least one KRAS mutation.

The p53 protein is involved in regulating cell division, apoptosis (programmed cell death), and DNA repair. A mutation that stops the p53 protein from working properly can prevent cells from dying when they should. Mutations in the *p53* gene are present in approximately 50% of cancerous tumors, making mutations one of the most common types that are linked to cancer.

Mutations and Pancreatic Cancer

You are excited to begin a summer research fellowship in a laboratory that studies how mutations contribute to development of pancreatic cancer. The pancreas is an organ involved in digestion of food and regulation of blood sugar, and cancers of the pancreas are among the most severe and deadly of all types of cancer. The project's main research question is:

> **What is the role of mutations in pancreatic cancer?**

As part of this project, the research team reasoned that cancer does not generally occur with normal cells. Rather, mutations in key genes like *KRAS* and *p53* lead to both cancerous cells and more severe forms of cancer, including pancreatic cancer.

Mutations in key genes, such as *KRAS* and p53, can increase the severity of pancreatic cancer by impacting additional mutations, metastasis, and patient survival. In other words, their hypothesis is:

> **Mutations in key genes, such as *KRAS* and *p53*, can increase the severity of pancreatic cancer by impacting additional mutations, metastasis, and patient survival.**

To investigate this hypothesis, three graduate students gathered clinical data on 20 patients from their cancer clinic (given ID numbers "Patient 1" through "Patient 20") who had pancreatic cancer. Among the data they gathered were:

Item Name	Item Description
Sex	Patients were categorized by biological sex (male or female).
Cancer Stage	Diagnosed cancers are classified as stage 1-4, with 1 being the mildest and 4 being the most severe.
Metastasis	Indicates whether the cancer cells spread from the pancreas to other parts of the body.
Survival time	The number of months the patient lived after being diagnosed with cancer.
KRAS mutation	Indicates whether the *KRAS* gene is mutated in cancerous cells.
P53 mutation	Indicates whether the *p53* gene is mutated in cancerous cells.
Number of additional mutations	Number of genetic mutations in cancer cells found, aside from those in *KRAS* and *p53*

The graduate students who helped collect data on this project developed predictions related to the research team's hypothesis.

Angel: **A mutation in the *p53* gene increases the number of additional mutations in the patient's cancer cells.**

Tracy: **Mutation of the *KRAS* gene decreases survival time.**

Riley: **A higher number of additional mutations makes it more likely a cancer will metastasize.**

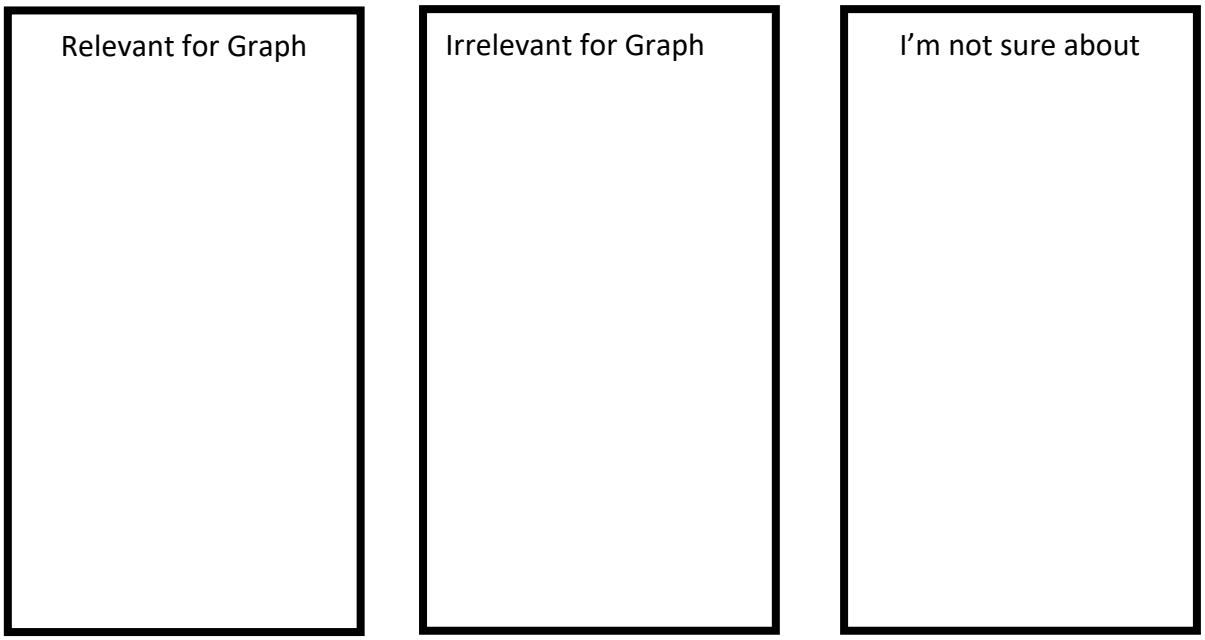
The raw clinical data are shown in the table below. In the upcoming pages, you will test each prediction in turn using the clinical data. (You will have access to these data later as well.)

Patient ID	Sex	Stage	Metastasi	Survival Time	KRAS Mutation	p53 mutation	Number of other mutations
1	M	Four	Y	7	Y	Y	33
2	F	Three	Y	74	N	Y	55
3	M	Three	N	19	Y	Y	74
4	F	Three	Y	31	Y	N	0
5	M	Four	Y	28	Y	Y	116
6	M	Three	Y	25	Y	N	21
7	M	Four	Y	12	Y	Y	34
8	F	Three	Y	22	Y	N	26
9	M	Four	Y	14	Y	Y	63
10	M	Three	Y	53	N	Y	73
11	F	Three	Y	33	Y	Y	536
12	F	Three	N	10	Y	Y	198
13	F	Three	N	11	Y	N	42
14	M	Three	N	15	Y	Y	25
15	M	Three	Y	37	Y	N	3
16	M	Three	Y	21	Y	Y	29
17	F	Three	Y	107	N	N	14
18	F	Two	N	43	Y	N	15
19	M	Three	Y	7	Y	Y	32
20	M	Two	N	38	Y	Y	53

Testing Angel's Prediction

Recall Angel's prediction: **A mutation in the *p53* gene increases the number of additional mutations in the patient's cancer cells.**

Q1. Which of the variables in the study are relevant to include in a graph to evaluate Angel's prediction?
(Write each variable from above in the appropriate box)



Make Your Graph

Please answer the following questions about the graph which you made to address Angel's prediction: **A mutation in the *p53* gene increases the number of additional mutations in the patient's cancer cells.**

Q2. Describe the pattern you see in the graph:

My graph shows that …

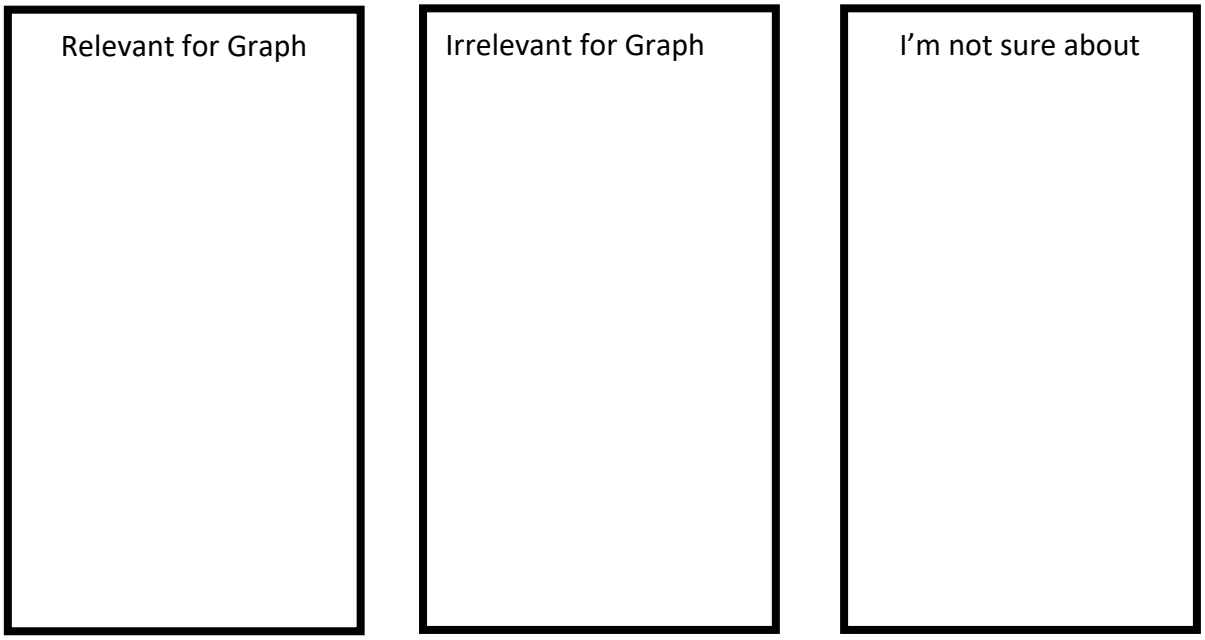
Q3. Do the data in your graph support or refute the prediction? Explain.

Q4. You chose to plot the data in a particular kind of graph (bar, line, scatter, etc.). What were your reasons for choose that graph type?

Testing Tracy's Prediction

Recall Tracy's prediction: **Mutation of the KRAS gene decreases survival time.**

Q1. Which of the variables in the study are relevant to include in a graph to evaluate Tracy's prediction?
(Write each variable from above in the appropriate box)



Make Your Graph

Please answer the following questions about the graph which you made to address Tracy's prediction: **Mutation of the KRAS gene decreases survival time.**

Q2. Describe the pattern you see in the graph:

My graph shows that …

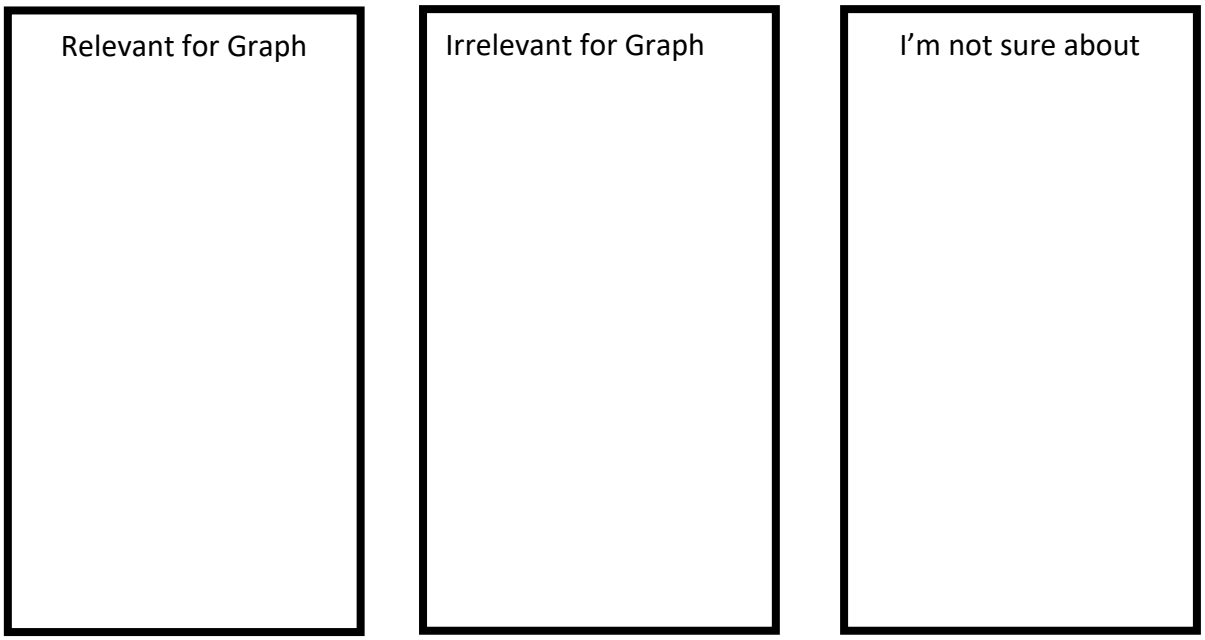
Q3. Do the data in your graph support or refute the prediction? Explain.

Q4. You chose to plot the data in a particular kind of graph (bar, line, scatter, etc.). What were your reasons for choose that graph type?

Testing Riley's Prediction

Recall Riley's prediction: **A higher number of additional mutations makes it more likely a cancer will metastasize.**

Q1. Which of the variables in the study are relevant to include in a graph to evaluate Riley's prediction?
(Write each variable from above in the appropriate box)



Make Your Graph

Please answer the following questions about the graph which you made to address Riley's prediction: **A higher number of additional mutations makes it more likely a cancer will metastasize.**

Q2. Describe the pattern you see in the graph:

My graph shows that …

Q3. Do the data in your graph support or refute the prediction? Explain.

Q4. You chose to plot the data in a particular kind of graph (bar, line, scatter, etc.). What were your reasons for choose that graph type?

Credits:

This is a pre-print and is not yet ready for public release. You may use in your class, but please do not distribute. If you have a colleague who would like a copy, please contact Stephanie Gardner (sgardene@purdue.edu) or Eli Meir (eli@simbio.com).

Faculty involved in designing this assessment scenario include
Melanie Lenahan
Melissa Rowland-Goldsmith
Susan Walsh

The research team included:
Stephanie Gardner
Joel Abraham
Ryan Baker
Eli Meir
Susan Maruca
Anupriya Karippadath
Kerry J Kim
Stefan Slater
Nouran Emad Amin
Amy Gallagher