



Lunch & Learn: Science, Statistics, and Getting it Right
ASIP 2018 Annual Meeting at Experimental Biology

Vignette 4

While investigating miRNA expression in the blood of mouse models of breast cancer, you identify the ratio of miR-101/miR-25 as being highly associated with development of metastatic disease. You hypothesize that the ratio of these markers in human blood may be prognostic for patients with breast cancer.

Your institution has an archive of blood samples taken from patients prior to lumpectomy for breast cancer. You are able to obtain 15 samples from patients who did not have disease recurrence within 5 years after lumpectomy, and 15 samples from patients whose disease recurred within 5 years after lumpectomy. You develop real-time RT-PCR based assays compatible with the archived blood samples that are capable of assessing miR-101 and miR-25. You successfully assess all 30 samples and calculate miR-101/miR-25 (miR ratio) for the samples as shown in the Table below. You run into your mentor on the way out the door for the day and arrange to go over the results the next morning.

That night, you research predictors of recurrence in breast cancer, and discover that a number of pathological parameters at the time of lumpectomy, such as tumor grade and size of tumor, are associated with the risk of recurrence. Likewise several other blood based biomarkers have been assessed for their ability to predict recurrence, including cancer antigen 15-3 (CA 15-3), which you know was run on the blood samples you assessed.

No Recurrence		Recurrence	
miR ratio	CA 15-3 (ng/mL)	miR ratio	CA 15-3
0.34	45	0.96	34
0.28	30	0.75	45
0.35	48	0.94	1000
0.15	55	0.47	49
0.65	29	0.77	700
0.23	75	0.81	63
0.21	96	0.98	38
0.76	4	0.82	2000
0.05	26	0.86	34
0.17	90	0.51	81
0.12	75	0.40	92
0.55	64	0.89	58
0.26	71	0.26	300
0.77	10	0.52	73
0.41	38	0.66	21

- 1) What statistical tests can you use to determine whether the miR ratio is associated with the risk of recurrence in your data set?
- 2) Your mentor can access a cohort of 200 samples and wants to know what is the best miR ratio value (cut off) to decide whether a sample is positive or negative. How can you assess the diagnostic performance across the range of potential miR ratio values (0-100)?
- 3) What tests can you use to determine whether the miR ratio is a “better” biomarker for recurrence than (CA 15-3)?
- 4) Is it important to consider the pathological parameters in your evaluation of the potential clinical performance of the miR ratio? If you were to design a large validation study, how would you try to account for the clinical parameters, and how can you determine whether the miR ratio may have clinical utility?