Reviewer’s report

Title: Impact of Gastroesophageal Reflux on MicroRNA Expression, Location and Function

Version: 1 Date: 4 December 2012

Reviewer: Christopher S Davis

Reviewer’s report:

This study by Smith et al supports that miRNA expression is altered in esophageal mucosa in those with ulcerative esophagitis, which is the precursor to Barrett’s esophagus. These findings follow their earlier work which found similar differences among those who had already developed Barrett’s esophagus. Though the sample sizes are relatively small, the findings are supported by in vitro data. There are minor critiques to be addressed.

Minor Essential Revisions

1. It would have been best to compare miRNA levels among controls, those with ulcerative esophagitis, and those with Barrett’s esophagus within the same experiment. This approach would reduce inter-study variation that may (or may not) be present in your current investigation. For example, you previously reported that the expression of miR-21, miR-143, miR-145, miR-194, and miR-215 were significantly upregulated in columnar tissues. To support your argument, one would expect these same miRNAs to be upregulated in ulcerative esophagitis. Although this is true for miR-143, miR-145, this is not true for miR-21, miR-194, and miR-215. Likewise you previously reported higher expression of miR-203 and miR-205 in normal squamous epithelium, but in your present study miR-205 is significantly higher with reflux while there is no difference for miR-203. Can you please comment on this?

2. Why were Spearman’s correlations done online when your statistical program (GraphPad) does this? Similarly, were tests of normality performed on these data to guide the statistical approach? What were these?

3. You do not comment on possible therapeutic implications of your study. Are there any? If so what are these? Even an abstract extrapolation would increase the impact of your work. Similarly, what specific future studies should be conducted in order to further medical knowledge in this field. Your statement in the conclusion that “proving this will require further studies” is quite vague.

Discretionary Revisions

1. Did the biopsies have multiple freeze-thaw cycles? This could potentially alter your results. Please comment.

2. I would suggest changing “reflux damaged” to “reflux-damaged” throughout the
manuscript.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I have no declaration.