Letter to the Editor to GENE

When figures and data contradict text: miR346 is apparently reduced in breast cancer tissue, contrary to claims by a paper's author.

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Abstract:

A recent article in *Gene* highlighted potential function of miR-346 in human breast cancer (Yang et al., 2017). We request an explanation or correction of the report. In its current state, the text will certainly create confusion in the field and lead to incorrect assumptions. The authors made several critical errors. The abstract stated "we found that the expression of miR-346 was higher in breast cancer tissues than in their paired corresponding non-cancerous tissues" and the main text and legend for Fig. 1A stated "miR-346 expression was significantly higher in breast cancer tissues than in their paired corresponding non-cancerous tissues (Fig. 1A, Yang et al., 2017)" and "miR-346 was upregulated in breast cancer tissues and cell lines. (A)", respectively. It was also stated that "SRCIN1 expression levels were significantly down-regulated in breast cancer compared to the adjacent normal tissues (Fig. 5B, Yang et al., 2017)". The problem with these statements is that they contradict the actual data presented in the paper! This misrepresentation of the effects of miR-346 in breast cancer could prove harmful by sidetracking future research. Further, clinical trials may be incorrectly directed towards lowering miR-346 without a complete and fair assessment of the internal contradictions in the data. Inaccurately-presented data impede progress of biomedical research, deplete scientific resources and compromise public trust.

Key words:

miR-346, microRNA, cancer, gene regulation, misleading results

An article in recent issue of *Gene* highlighted potential function of a microRNA, specifically miR-346 in human breast cancer (Yang et al., 2017). This letter is to request an explanation or correction of the report. In its current state, the text will certainly create confusion in the field and lead to incorrect assumptions. The article is therefore in need of retraction or, at the very least, an erratum that revises the conclusions presented in the abstract, as it appears in indices such as Medline/PubMed and is presumably read and accepted by several scientists who may not access the full text.

The authors made several critical errors. Specifically, the abstract stated "we found that the expression of miR-346 was higher in breast cancer tissues than in their paired corresponding non-cancerous tissues" and the main text and legend for their Fig. 1A stated "miR-346 expression was significantly higher in breast cancer tissues than in their paired corresponding non-cancerous tissues (Fig. 1A)" and "miR-346 was upregulated in breast cancer tissues and cell lines. (A)", respectively. It was also stated that "SRCIN1 expression levels were significantly down-regulated in breast cancer compared to the adjacent normal tissues (Fig. 5B)".

The problem with these statements is that they contradict the actual data presented in the paper! Regarding the first statement, Fig. 1A of Yang et al. shows a mean relative expression normalized by U6, δCt of ~14.5 for normal tissue, while the mean value for the tumor tissue is ~13.5. The presented data therefore indicate that miR-346 levels in the "Tumor" tissue are lower than "Normal" controls. The upper error bar for "Tumor" is higher than the error bar for "Normal", but that is not taken as the appropriate measure of the sample group. By contrast, the selected cell lines, HBL-100 (normal), MCF-7 (Tumor) and MCF-7/Doc (docetaxel-resistant) appear to follow

the reported trend with large and roust increases in cancer lines. These contradictory findings need to be explained with greater rigor.

The second major claim referring to the authentic tumor tissue is that relative levels of SRCIN1 mRNA are lower in breast cancer tissues than in non-cancerous samples. The presented data (Fig 5B of Yang et al) actually show a higher mean value of SRCIN1 mRNA (~14 relative units) over normal control breast tissue (~11.5). Once again the cell line studies show that the presumably normal HBL-100 expresses over twice as much SRCIN-1 as the MCF-7 cancer lines (Fig. 5C of Yang et al).

Multiple experiments were reported in the paper using "[h]uman breast cancer cell line MCF-7 and human breast epithelial cell line HBL-100" as proxies for breast cancer and normal breast tissue. This is not necessarily problematic, but it is well known that cell lines are not perfect mimics of actual tissues or disorders. Thus, the authors wisely included data derived from actual breast cancer clinical samples and non-cancerous breast tissue samples. The majority of the paper concentrates on cell culture manipulation, and these data appear to be correctly presented. The problems arise when examining specific claims made by the authors regarding actual breast cancer tissue vs. normal breast tissue.

Medical research is based on prior work, and inaccurately-presented results can only impede progress. Unreliable findings in biomedical research create useless "cures" and drain precious resources (Munafò, 2017). It is astonishing that two such glaring errors or mispresentations could have undetected by peer review. We do not dispute that the data is correctly described for cell

culture experiments, but the actual cancerous tissue results appear to directly contradict the claims in the article. As such, this misrepresentation of the effects of miR346 in breast cancer could prove harmful by sidetracking future research, at the very least. Also, clinical trials may be incorrectly directed towards lowering miR-346 without a complete and fair assessment of the internal contradictions in the data. The danger is exacerbated by emphasis of the in vivo conclusions in the abstract, which contradict the findings presented in the figures.

In short, the tumor tissue results suggest that reduced miR-346 may associate with pathology, in direct contradiction to the claims made by the authors. We again strongly suggest that the paper and abstract be revised so text will fit the data.

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Yang, F., Luo, L.J., Zhang, L., Wang, D.D., Yang, S.J., Ding, L., Li, J., Chen, D., Ma, R., Wu, J.Z. and Tang, J.H., 2017. MiR-346 promotes the biological function of breast cancer cells by targeting SRCIN1 and reduces chemosensitivity to docetaxel. Gene 600, 21-28.

Legends to Figures (adapted from Yang, et al., 2017)

Fig 1. 1A (reproduced from Yang et al., 2017). "(A) The relative expression of miR-346 in breast cancer tissues compared with their paired corresponding non-cancerous tissues was detected by qRT-PCR."

Fig. 5B-C (reproduced from Yang et al., 2017). "(B) The relative expression of SRCIN1 mRNA in breast cancer tissues compared with their paired corresponding non-cancerous tissues was detected by qRT-PCR. (C) The relative expression of SRCIN1 mRNA in breast cancer cells was detected by qRT-PCR."

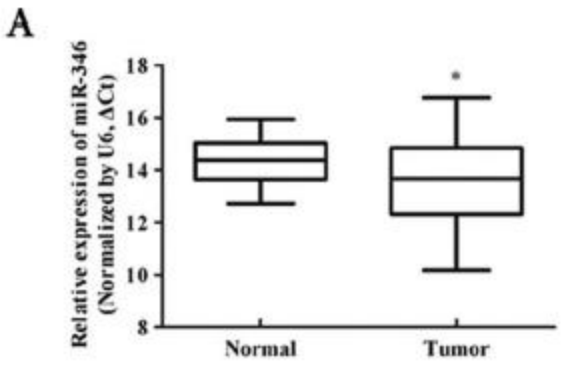

Figure 1

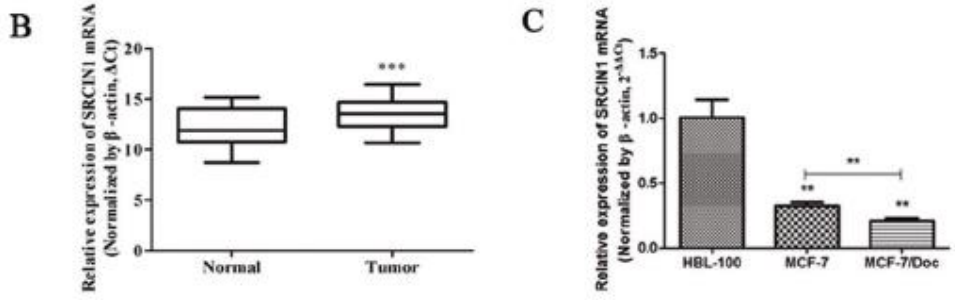

Figure 5