



SDI Review Form 1.6

Journal Name:	<u>Journal of Advances in Medical and Pharmaceutical Sciences</u>
Manuscript Number:	Ms_JAMPS_22134
Title of the Manuscript:	MicroRNA Memory I: the positive correlation between synergistic effects of microRNAs in cancer and a novel quantum scoring system
Type of the Article	Original Research Article

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	1. Since the title is "MicroRNA Memory I: the positive correlation between synergistic effects of microRNAs in cancer and a novel quantum scoring system", it would be helpful if "microRNA memory" is well defined in the introduction, instead of jumping out at the end of the discussion. 2. It is interesting that the author(s) compared several target prediction web programs of miRNA, and found some short comings of the individual algorithms. The author(s), then, suggested that there might be synergistic interaction between/among diverse miRNAs that would affect the outcomes of prediction. The nucleotide sequences of miRNAs were converted into respective binary codes for their static nexus, dynamic nexus and context + score analyses. Nonetheless, TargetScan was used without comprehensive description of selection (or adding a comparison table of all the prediction web programs). In fact, some of miRNA interactions have been summarized by Morozova, et al., in RNA 2012; 18: 1635–55. 3. It is arguable that only Guanine (G) has a positive electrical charge. From structures of the four nucleobases (nitrogenous bases), Adenine, Guanine, and Cytosine, but Thymine, have a $-N^+H_2$ sidechain (a representative of positive electrical charge); that is, A, G, and C, but T, are positively charged. 4. It is therefore worth noting that the author(s) use DNS, and SNS to compare several target prediction of cancers. However, like milk fat synthesis, many	1. I added simply explanation about microRNA memory at the end of introduction to clarify its concept. (Line 85~). 2. I added a table that supports information of existing prediction tools (algorithms, filtering options, etc.). (Line 56~, all table number were +1 shifted). Thanks for introducing attractive report. I referred to it to support our claim and added it into references. (Line 71~, all reference numbers more than 22 were +1 shifted) 3. In our report, electro static potential by the fragment molecular orbit methods (FMO) is distinct from electrical charge. FMO was calculated by winMOPAC software (Fujitsu, corp. Tokyo) in reference [24]. According to the previous report, electrical potential in nucleobases were measured by referring to FMO rather than polarity, so only guanine have a positive potential. To explain it, a subsection titled "2.2 conversion of sequences" was inserted into the MATERIAL



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	miRNA pairs in category of gliomas and carcinomas did not show specific value of synergistic effect. It would be helpful to describe the difference among various categories, if the category of milk fat synthesis were used as “negative control”. In that case, the value of context + score in “milk fat synthesis” would be above the prediction values of RAS, CDK and Rho. Mutations in Ras have been a focus in carcinogenesis, and possibly, therapeutic target(s). Nevertheless, there is no information of these oncogenes in Table 2. They were not mentioned in other Tables either. Addition of those data could be more supportive for clarifying the concept in this manuscript.	AND METHODS section (line 96~), and an erratum in line 189 was fixed (charge -> potential). 4. I think it's a great idea. However, because of very limited sample size, we concluded it is a bit risky to set one case as negative control. We just use a phrase “~in cancer” in title since almost all of the papers we referred in this study were related to cancer. Although RAS, CDK and Rho were frequently shown in reference papers, they are not target of miRNA sets used on our study.
<u>Minor</u> REVISION comments	1. The scope and depth of this manuscript are quite reasonable. However, English requires extensive polishing. 2. In general, this is a good manuscript. However, some rationale should be added, and some attention in details should be focused on, when the excellence is anticipated.	1. I tried my best. (I'm sorry if there are some terrible expressions.) 2. Some rationale was added according to Compulsory REVISION comments.
<u>Optional/General</u> comments		