Reviewer’s report

Title: Can MiR-503 be used as a marker in diabetic patients with ischemic stroke?

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Reviewer: Stefan Bilz

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General comments:

The authors report on the expression of mir-503 in diabetic and non-diabetic patients with ischemic stroke, patients with diabetes and healthy controls. The main findings is that mir-503 expression in peripheral blood leucocytes is increased in patients with an acute ischemic stroke with diabetes when compared to controls without diabetes and in patients with diabetes and no acute disease when compared to healthy controls. In those suffering a stroke mir-503 expression decreases to levels of healthy controls in both groups. In both groups with no acute disease mir-503 expression remains stable but clearly increased in diabetic patients.

The rationale of the analysis is the previous finding that several miRNAs have been implicated in the pathophysiology of both diabetes complications and ischemic stroke. Specifically, mir-503 expression has been shown to be increased in the endothelial cells of diabetic mice and in the muscle tissue of amputated legs of diabetic patients with lower limb ischemia.

The results of this human in vivo study are interesting and extend those of previous research to suggest that the expression of mir-503 could serve as a diagnostic or prognostic biomarker in patients with diabetes and acute stroke.

Specific comments:

1. The small number of participants has to be discussed as a major limitation of the study.

2. Due to the small number of subjects in each group it is strongly advised that non-parametric statistical tests are employed unless a normal distribution of the data of interest has been proven.

3. Diabetes per se seems to be a major modifier of mir-503 expression. Fasting blood glucose is the only measure of glycemic control provided and positively correlated with mir-503 expression. The authors should indicate further measures of glycemic control, especially HbA1c.

4. Experimental work indicates that mir-503 expression is increased in endothelial cells under diabetic conditions. In this study, mir-503 expression is increased in peripheral blood leucocytes. Please comment.
5. Due to the obviously prominent role of endothelial cells in the regulation of mir-503 expression it should be indicated whether there is an association between microvascular complications (e.g. microalbuminuria, retinopathy) and mir-503 expression.

6. The authors report a positive correlation of plasma cholesterol concentrations with mir-503 expression. Please provide a rationale/discuss this observation.

7. It is concluded that antagonizing mir-503 may be a therapeutic option in patients with ischemic stroke. From the data presented, this statement seems very premature and should not be part of the conclusions.

8. In patients with diabetes mir-503 expression decreases to control levels 3 months after stroke. Since glycemic control is a major regulator, HbA1c and fasting blood glucose 3 months after the stroke should be presented.

9. The discussion is quite lengthy and not easy to read. The manuscript should be edited by a native English speaking person.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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I am able to assess the statistics

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