Reviewer’s report

Title: Sry Delivery to the Adrenal Medulla Increases Blood Pressure and Adrenal Medullary Tyrosine Hydroxylase of Normotensive WKY Rats

Version: 1 Date: 26 December 2006

Reviewer: Maria Vieira-Coelho

Reviewer’s report:

General
This paper reports an in vivo effect of Sry (a transcription factor on the Y chromosome) on blood pressure and tyrosine hydroxylase activity (TH) in the adrenal medulla. Exogenous Sry or control vector were deliver to the adrenal medulla of WKY rats by injection/electroporation. This study is in the line of a series of interesting studies published by the same group of investigators concerning Y chromosome in spontaneously hypertensive rats (SHR) and the development of hypertension. In fact the same group has reported that the Sry gene, previously unknown as a regulator of TH, gene expression, can increase TH transcription. The methods used in this study are appropriate and in general well described, only a small change in TH activity is proposed. The results are new, relevant an important in this field supported by well controlled data. The title and abstract are adequate and writing acceptable. However some major revisions considering data interpretation are need.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. In the present study the author hypothesized: Sry increases TH activity in specific tissue recognized to play a role in cardiovascular function, thereby leading to an increase in BP. This hypothesis/question is pertinent but should be more defined, since the method used to address this issue was the administration of exogenous Sry gene to the adrenal medulla of a WKY and see if there was any change in TH activity in the adrenal medulla, catecholamine levels and blood pressure. So the "specific tissue" was in fact adrenal medulla and no other tissue was studied. However it should be noted that its not direct that an increase in TH in the adrenal medulla increases blood pressure values, in fact spontaneously hypertensive rats have been reported to have lower adrenal TH activity (Moura E, 2005) despite higher peripheral sympathetic activity. So the hypothesis proposed by the authors should be clear and directly related to the present study.
2. The discussion should be improved since some conclusions are not quite precise, as an example and similar to the hypothesis above described, the authors related the increase in blood pressure rise directly with the increase in TH activity in the adrenal medulla and NE plasma levels. However, plasma NE is predominantly derived from sympathetic nerve endings in which it acts as a neurotransmitter. In contrast, epinephrine (E) is synthesized in the adrenal medulla and despite higher TH activity in the adrenal medulla, no changes in this catecholamine plasma levels were observed in the study. Another topic that should be introduced in the discussion is neuroendocrine events, given that the two adrenal systems, the cortisol- and androgen- producing cortex and the catecholamine (E and NE)-producing medulla, are related ontogenetically, anatomically, and functionally, the effect of Sry in the cortex of the adrenal gland should be rule out. In fact, the same authors have reported that the SHR Y chromosome may accelerate the start of puberty and a cascade of molecular and neuroendocrine events that raise blood pressure, so the experience of this group could enrich the discussion of this paper.
3. TH activity should be considered a single method and it should be noted that although Hooper et and Kumai et al used this method, in fact the original paper is by Nagatsu T in 1979 (Journal of Chromatography 163 (3), 247-252. The way that TH is expressed in the results should also be clear, like : L-Dopa formed per min and mg of tissue or protein...

In respect to TH activity reported in figure 2, results from control animals should be given, specially considering the values founded for vector control in the present study, about 25000 fmol/min/mg and in the study by Kumai et al (Hypertension 1995; 26: 208-212 the values for activity of TH in the adrenals of control WKY rats were 1000 nmol/g tissue/h (about 16666,67 fmol/min/mg). This is relevant when considering the difference between vector control and sry (250000 to 350000).
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1. All references must be numbered consecutively, in square brackets.
2. In the PDF available some units are not well formatted, e.g., µM appears uM.
3. Results on figure 4 could be given in the text (results).
4. Page 9 in legends to figures figure 2 and figure 3 are not correct (2 is 3..)
5. Titles with conclusive phrases should be removed from figures

Discretionary Revisions (which the author can choose to ignore)
Blood pressure values were evaluated only for 3 weeks after treatment, however a time course would be very interesting to see and it’s not difficult to perform this measurement...

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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 declare that I have no competing interests