Response to "Is High Prorenin Level Related to Relative Aldosterone Excess?"

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To the Editor: We would like to thank Dr. Satoh and colleagues for their interest in our recent study titled "Plasma Levels of Prorenin and Renin in Black and Whites: Their Relative Abundance and Associations with Plasma Aldosterone Concentration."[1] We reported that blacks and whites had similar plasma prorenin levels, but that in blacks the plasma renin concentration (PRC) was markedly lower, and prorenin was negatively associated with plasma aldosterone concentration (PAC). In their Letter to the Editor, Dr. Satoh suggested we should further examine the association between prorenin and aldosterone to plasma renin activity ratio (aldosterone/renin ratio, or ARR), for indication that prorenin might have played a role in the relative excess of aldosterone, especially in blacks, who are thought to be more susceptible to a salt-sensitive form of hypertension. We appreciate this suggestion and agree that this is a logical and potentially important question that should be addressed in a follow-up analysis.

We reexamined the data as requested. The relationships between prorenin and ARR are presented in Figure 1. Contrary to the letter's hypothesis, we found prorenin to be negatively associated with ARR in blacks ($\beta = -0.341$; $P = 0.039$), and not associated with ARR in whites ($\beta = 0.180$; $P = 0.301$). Of note, these results essentially mirrored our previous reports on the prorenin-PAC relationships in the two race groups. Careful examination of Figure 1c and Figure 1d of the original report revealed that at any given level of PRC, prorenin was negatively associated with PAC in blacks, and positively associated with PAC in whites. The new analysis reaffirmed this observation.

We agree with Dr. Satoh and colleagues that ARR is a useful gauge for salt sensitivity, characterized by inappropriate aldosterone production and unattenuated sodium reabsorption in the presence of volume overload. Previous reports have demonstrated that ARR is higher in hypertensive blacks than in hypertensive whites.[2] Our data, showing that ARR levels were marginally higher in young and normotensive blacks (Table 2 of the original paper), suggest that this difference may already be present before hypertension occurs. The new analysis, however, yielded no clear evidence for a prorenin role in aldosterone production, neither in blacks nor whites. In fact, the negative prorenin-ARR association in blacks argues against the hypothesis that prorenin promotes aldosterone production, at least in young and healthy blacks. As we have commented in the original article, this does not exclude the possibility that in some circumstances aldosterone production may become more autonomous to kidney-derived renin; when upregulated (pro)renin receptor (PRR) expression leads to a prorenin-dependent generation of angiotensin II, it is conceivable that aldosterone excess may occur with increased prorenin levels. Although the plausibility of such a hypothesis is supported by the observations that aldosterone elevation is associated with the PRR overexpression in transgenic rats and PRR gene polymorphisms in white males,[3,4] the validity of the hypothesis in salt-sensitive blacks remains to be investigated.

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Initially submitted October 28, 2012; accepted for publication October 29, 2012.

doi:10.1093/ajh/hps059

ACKNOWLEDGMENTS

This work was supported by the National Heart, Lung, and Blood Institute grant RO1 HL095086 and a Veterans Health Administration Merit Review grant.

DISCLOSURE

The authors declared no conflict of interest.

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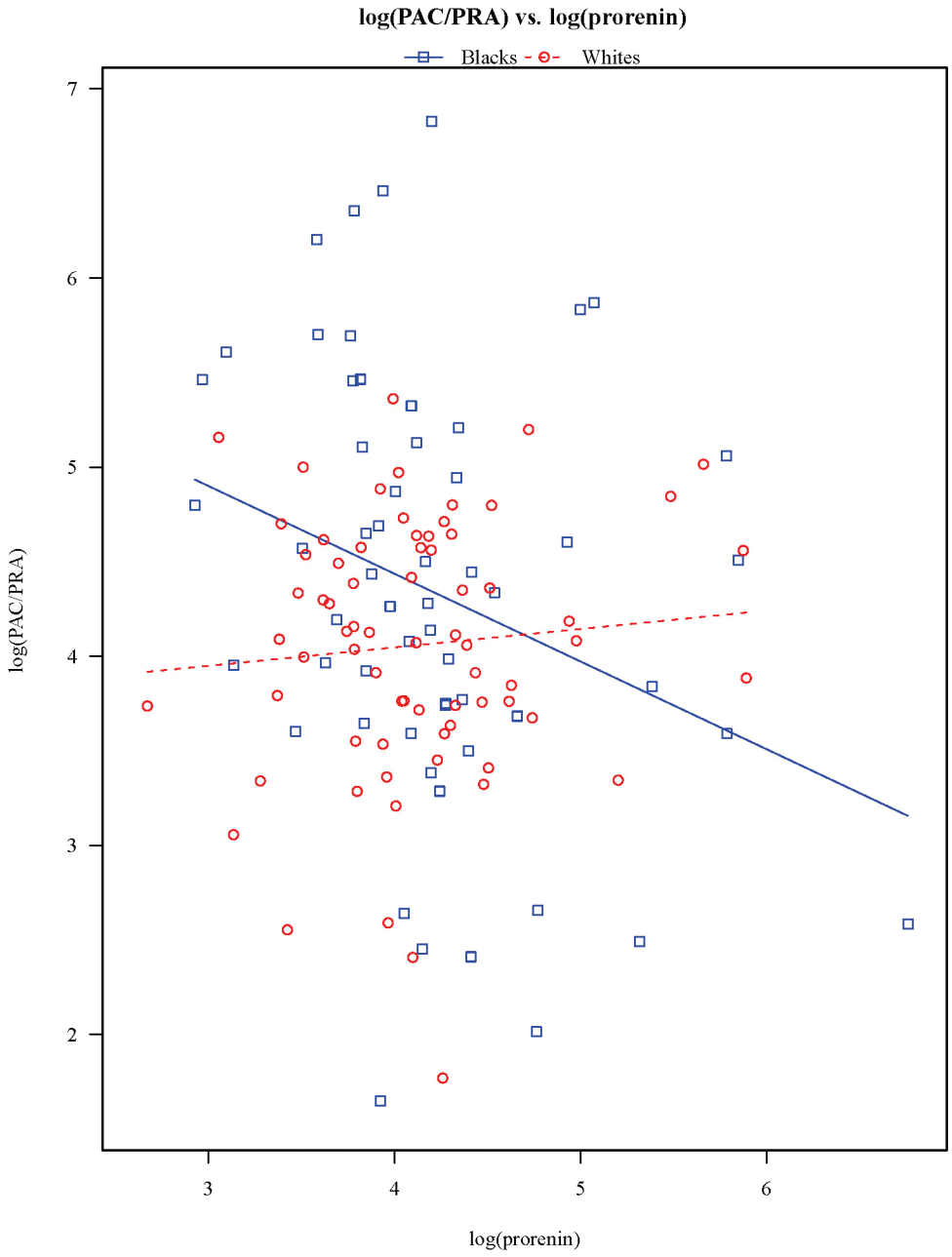

Figure 1. Relationship between plasma prorenin concentration and plasma aldosterone to renin activity ratio in blacks and whites. Abbreviations: PAC, plasma aldosterone concentration; PRA, plasma renin activity.