Response to Letter Regarding Article, “Human C-Reactive Protein Does Not Promote Atherosclerosis in Transgenic Rabbits”

We appreciate the comments by Nakajima and Saito on our recent article published in Circulation.

The major question they raised was why human C-reactive protein (CRP) transgenic rabbits failed to exhibit other metabolic disorders, because emerging data support that CRP levels are elevated in patients with metabolic syndrome. It is well documented that elevated plasma CRP levels are associated with many pathological states such as cardiovascular diseases and metabolic syndrome; however, these associations do not necessarily mean that high levels of CRP can cause these diseases. Indeed, population genetics studies have failed to link CRP single-nucleotide polymorphisms to the increased risk of cardiovascular diseases, although CRP single-nucleotide polymorphisms are associated with marked increases in CRP levels. Also, there is no evidence to date to show that elevation of plasma CRP alone can lead to metabolic syndrome both clinically and experimentally. It is apparent that further experiments with appropriate large-animal models are required to investigate CRP functions in metabolic syndrome. Because metabolic syndrome is composed of several metabolic disorders (e.g., hypertension, dyslipidemia, and hyperglycemia), which are mediated by multiple genes and many environmental factors, it is unlikely that overexpression of a single CRP gene in animals can lead to all these abnormalities. In fact, we have recently transgenically expressed human CRP in hypertensive animals and found that in the setting of hypertension, CRP does exert certain detrimental effects on both lipid and glucose metabolism (unpublished data). Taken together, CRP functions in both physiology and pathophysiology remain to be further elucidated with genetically modified large animals, as we reported in the study.

Disclosures

None.

References

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Tomonari Koike, Ying Yu, Jifeng Zhang, Jianglin Fan, Yukio Ozaki, Shuji Kitajima, Kazutoshi Nishijima, Masatoshi Morimoto, Teruo Watanabe, Sucharit Bhakdi, Yujiro Asada and Y. Eugene Chen

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