BubR1 Insufficiency Results in Decreased Macrophage Proliferation and Attenuated Atherogenesis in Apolipoprotein E-Deficient Mice

In the article by Tanaka et al, “BubR1 Insufficiency Results in Decreased Macrophage Proliferation and Attenuated Atherogenesis in Apolipoprotein E-Deficient Mice,” which published online on September 24, 2016, and appeared in the September 2016 issue of the journal *J Am Heart Assoc.* 2016;5:e004081 doi: 10.1161/JAHA.116.004081, several errors occurred in Figures 1, 2, 3, and 4. On page 5, Figure 1A, the placement of ApoE<sup>−/−</sup> was incorrect and has now been corrected. On page 8, Figure 2A, the word “Descending” was incorrectly written as “Decend-ing.” In Figure 2B, the graph quantified with elastic van Gieson (EVG) stain was incorrectly identified as necrotic area and has now been corrected to aortic root lesion area. In Figure 2C, “N.S” was corrected to “N.S.,” and in Figure 2D, “MAC” was corrected to “Mac-3” (two points). On page 9, Figure 2E-F, the lines of the graphs were incorrect and have now been corrected. On page 11, Figure 3A, the lines of the graph were incorrect and have now been corrected. On page 12, Figure 3D, the placement of * was incorrect and has now been corrected. On page 13, the caption for Figure 4, the following sentence has now been included, “*P<0.05 Student t test. B, Migration capacity was not significantly different between ApoE<sup>−/−</sup> macrophages (black bar) and BubR1<sup>L-L</sup>-ApoE<sup>−/−</sup> macrophages (white bar; n=5 in each group) in chemotaxis assay.” The corrected figures are shown below.

The authors regret these errors.

The online version of the article has been updated and is available at http://jaha.ahajournals.org/content/5/9/e004081.full
Figure 1. Generation of BubR1°/°-ApoE°/° mice. A, BubR1 expression in the thymus of ApoE°/° and BubR1°/°-ApoE°/° mice. Data are presented as the mean±SE; *P<0.01 vs ApoE°/° mice, Student t test, n=5, 6 per group, respectively. BubR1 expression in the aorta of ApoE°/° and BubR1°/°-ApoE°/° mice, n=5 in each group. BubR1 expression in white blood cells of ApoE°/° and BubR1°/°-ApoE°/° mice, n=5 in each group. BubR1 expression in the heart of ApoE°/° and BubR1°/°-ApoE°/° mice, n=5 in each group. B and C, Western blotting for BubR1 protein in the testis. S1; ApoE°/° S7; BubR1°/°-ApoE°/°; n=3 in each group. *P<0.05, vs ApoE°/°, Student t test. ApoE°/° indicates apolipoprotein E-deficient; BubR1, Budding uninhibited by benzimidazole-related 1.
Figure 2. A, Photomicrograph evaluation of en face aortas, stained with Zudan III and quantitative analysis of atherosclerosis in the total aorta, aortic arch, and descending aorta after 12 weeks of a HCD. Data are presented as the mean±SE; *P<0.05 vs ApoE<sup>−/−</sup> mice, Student t test. n=7, 9 per group, respectively. B through F, Photomicrographs of atherosclerotic plaques in the aortic root stained with HE, EVG, MAC-3, PSR and α-SMA. Data are presented as the mean±SE; *P<0.05 vs ApoE<sup>−/−</sup> mice, Student t test (n=7 of BubR1<sup>L/L−/−</sup> ApoE<sup>−/−</sup> mice and n=9 of ApoE<sup>−/−</sup> mice). Scale bar, 200 μm. G and H, Immunofluorescence experiments identified PCNA<sup>+</sup>-Mac3<sup>+</sup> macrophages within the lesion area of the aortic root. PCNA<sup>+</sup>-Mac3<sup>+</sup> cells/Mac3<sup>+</sup> cells (%) in the aortic root of BubR1<sup>L/L−/−</sup> ApoE<sup>−/−</sup> mice was significantly reduced compared with those of ApoE<sup>−/−</sup> mice. Data are presented as the mean±SE; *P<0.05 vs ApoE<sup>−/−</sup> mice, Student t test. n=5, 6 per group. ApoE<sup>−/−</sup> indicates apolipoprotein E-deficient; BubR1, Budding uninhibited by benzimidazole-related 1; DAPI, diamidino-2-phenylindole; EVG, elastic van Gieson; HCD, high-cholesterol diet; HE, Hematoxylin-Eosin; PCNA, proliferating cell nuclear antigen; PSR, Picro-Sirius Red; SMA, smooth muscle actin.
**Figure 2.** continued.
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Figure 3. Effect of bone marrow transplantation on the atherosclerosis lesion area in ApoE<sup>−/−</sup> and BubR1<sup>L/L</sup>-ApoE<sup>−/−</sup> mice. A, Photomicrographs of the en face evaluation of ApoE<sup>−/−</sup> → ApoE<sup>−/−</sup>, BubR1<sup>L/L</sup>-ApoE<sup>−/−</sup> → ApoE<sup>−/−</sup>, ApoE<sup>−/−</sup> → ApoE<sup>−/−</sup>, ApoE<sup>−/−</sup> → ApoE<sup>−/−</sup>, ApoE<sup>−/−</sup> → BubR1<sup>L/L</sup>-ApoE<sup>−/−</sup> → ApoE<sup>−/−</sup> mouse aortas stained with Zudan III, and quantitative analysis of atherosclerosis of the total aorta after 12 weeks of a HCD. Data are presented as the mean±SE; *P<0.05, Student t test; n=6 in each group. B, Atherosclerosis lesion area of mice in the aortic root lesion, stained with EVG. Data are presented as the mean±SE; *P<0.05, Student t test; n=6 in each group. C, Necrotic core lesion area of mice in the aortic root lesion stained with HE. Data are presented as the mean±SE; *P<0.05, Student t test; n=6 in each group. D, Mac3-positive absolute cell count in the aortic root lesion area of mice. Data are presented as the mean±SE; *P<0.05, Student t test; n=6 in each group. ApoE<sup>−/−</sup> indicates apolipoprotein E-deficient; BubR1, Budding uninhibited by benzimidazole-related 1; EVG, elastic van Gieson; HCD, high-cholesterol diet; HE, Hematoxylin-Eosin.
Figure 3. continued
**Figure 4.** In vitro macrophage assay. A, Cell proliferation was slower in *BubR1<sup>L/L</sup>-ApoE<sup>−/−</sup>* peritoneal macrophages (white bar) than in *ApoE<sup>−/−</sup>* macrophages (black bar; n=6 in each group); *P*<0.05, Student t test. Cell proliferation was slower in *BubR1<sup>L/L</sup>-ApoE<sup>−/−</sup>* macrophage-derived bone marrow cells (white bar) than in *ApoE<sup>−/−</sup>* macrophages (black bar; n=5 in each group). *P*<0.05 Student t test. B, Migration capacity was not significantly different between *ApoE<sup>−/−</sup>* macrophages (black bar) and *BubR1<sup>L/L</sup>-ApoE<sup>−/−</sup>* macrophages (white bar; n=5 in each group) in chemotaxis assay. MCP-1 concentration was 10 ng/mL; *P*<0.05 Student t test. C, Migration capacity was not significantly different between *ApoE<sup>−/−</sup>* macrophages (black bar) and *BubR1<sup>L/L</sup>-ApoE<sup>−/−</sup>* macrophages (white bar; n=4 in each group). Student t test, NS, not significant. ApoE<sup>−/−</sup> indicates apolipoprotein E-deficient; BrdU, bromodeoxyuridine; *BubR1*, Budding uninhibited by benzimidazole-related 1; MCP-1, monocyte chemotactic protein-1; M-CSF, macrophage colony-stimulating factor.
Deficient Mice

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