See related article, pages 2136–2141.

Apolipoprotein E (ApoE) is a protein related to the receptor-mediated removal of lipids from the bloodstream. When ApoE-deficient mice were introduced, these animals displayed hypercholesteremia and increased atherosclerosis, providing a new tool to study hypercholesteremia-related pathological mechanisms and have been used extensively ever since. With respect to the cerebral circulation, it is interesting to note that not until 1998 did the first study on ApoE deficiency and cerebral ischemia appear and only 5 more studies, mostly related to stroke and inflammation, followed to this date in this field.

Kitayama et al. are interested to study the effect of hypercholesteremia on pial arteriolar vasomotor responses. They used hemizygous (ApoE<sup>−/−</sup>) animals as their control (rather than homozygotes) and ApoE-deficient mice (ApoE<sup>−/−/−</sup>) that were fed normal or high-fat diets. The first observation is that the hemizygous control animals have similar cholesterol levels as homozygous mice, indicating that one functioning allele of ApoE may be sufficient to keep blood cholesterol at normal levels. After demonstrating that especially severe hypercholesteremia adversely affects pial arteriolar dilation, the group continues to show that scavenging oxygen radicals with Tempol or inhibiting NADPH oxidase with Apocynin can restore vessel dilation to Acetylcholine at the lower concentration tested. But at the higher concentration used, Acetylcholine did not achieve dilation comparable to control animals. This seems to indicate that another factor besides oxygen radicals affects the vascular dilation to Acetylcholine in severely hypercholesteremic arterioles. If there is another factor and what this factor could be need to be studied further. Lack of response to external nitric oxide, though, does not seem to be deficient.

Another aspect of the study of ApoE effects in mice is that we now have mouse models with the mouse ApoE gene replaced with human ApoE alleles. The study of such alleles has come to the forefront in many research areas including stroke and Alzheimer disease. Thus understanding and knowing the physiological effects of mouse ApoE will help us to determine the effects and consequences of introducing human ApoE alleles into this organism including vascular regulation. It is therefore possible that the observations and results provided by Kitayama et al. will have implications beyond the study of hypercholesteremia.

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**Disclosures**

None.

**References**

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