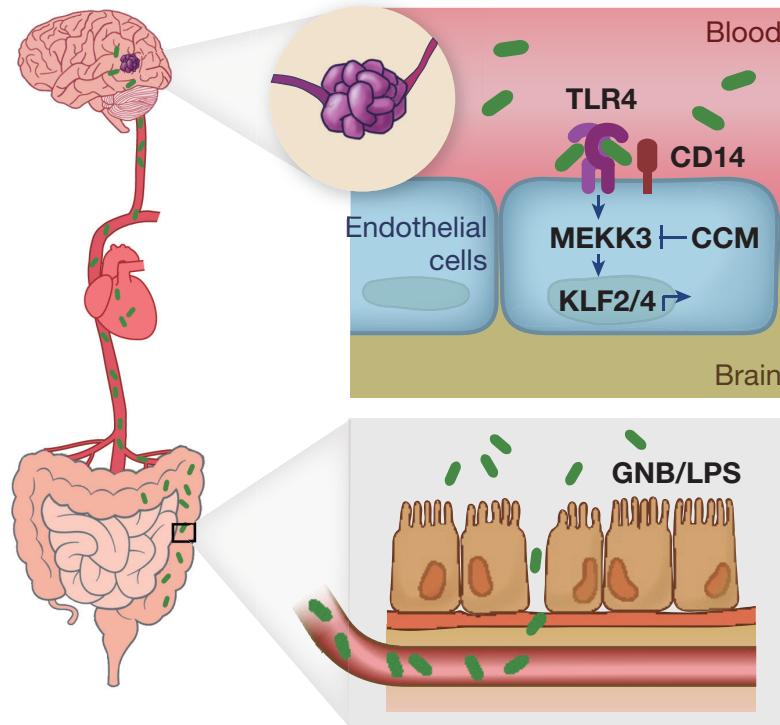


Endothelial TLR4 and the microbiome drive cerebral cavernous malformations

Tang et al, Nature 2017 (Upenn)

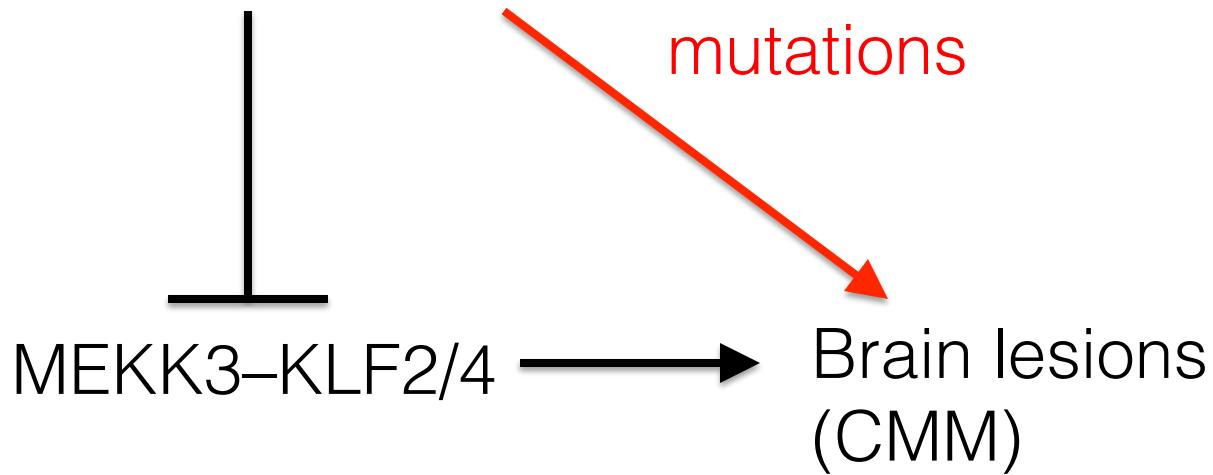


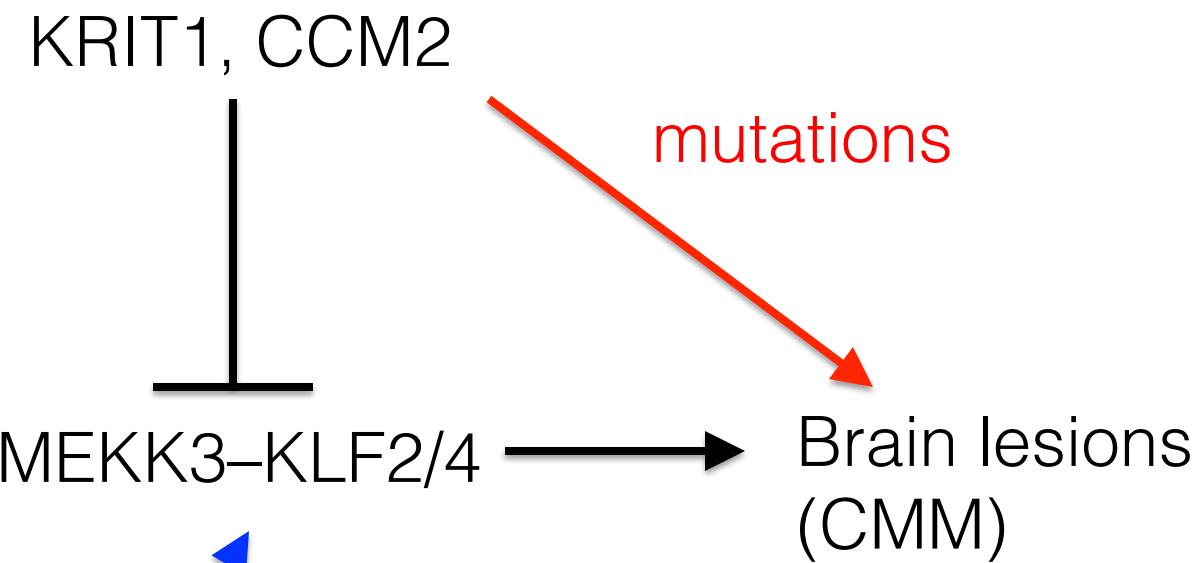
KRIT1, CCM2

mutations

Brain lesions
(CMM)

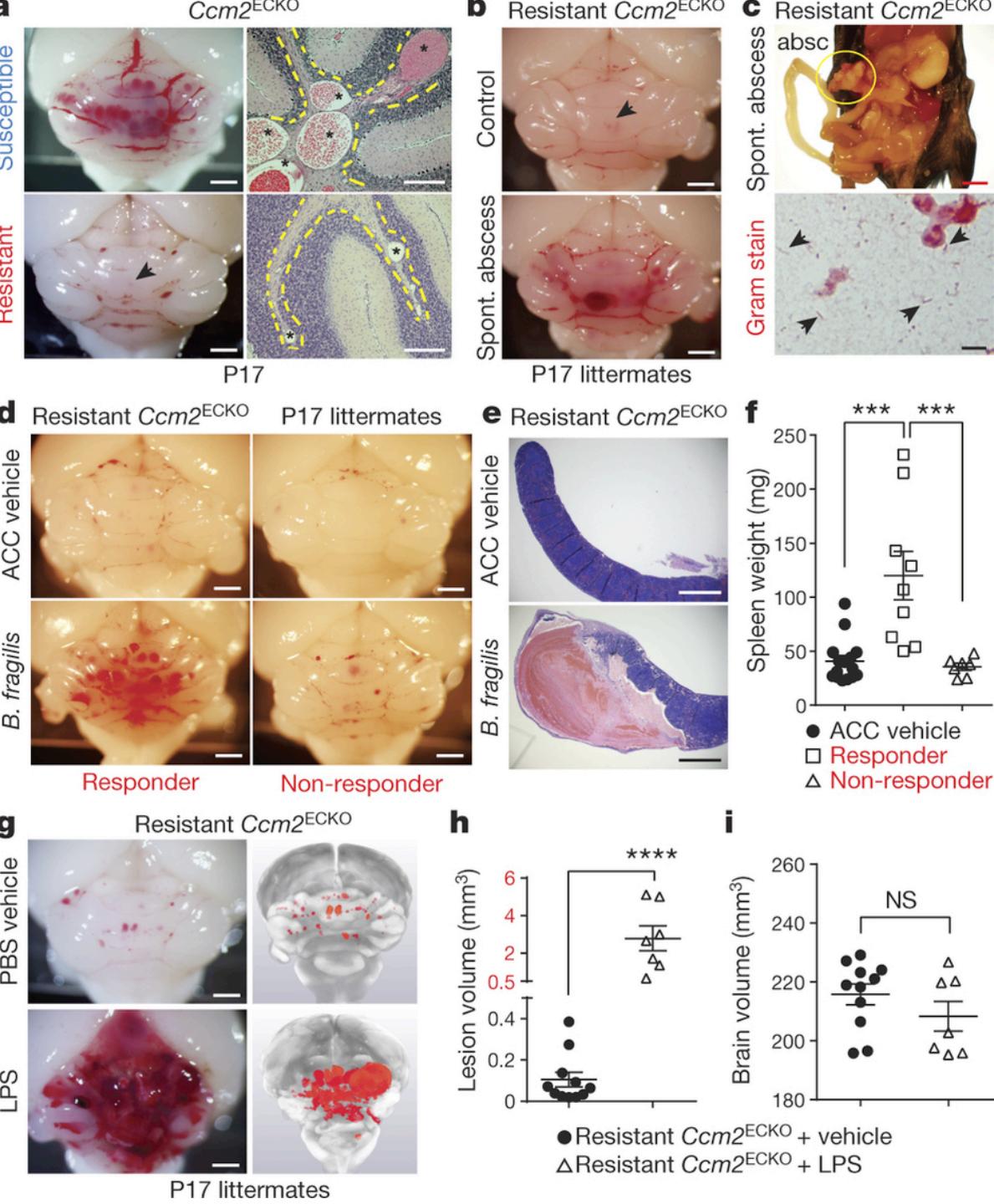
KRIT1, CCM2

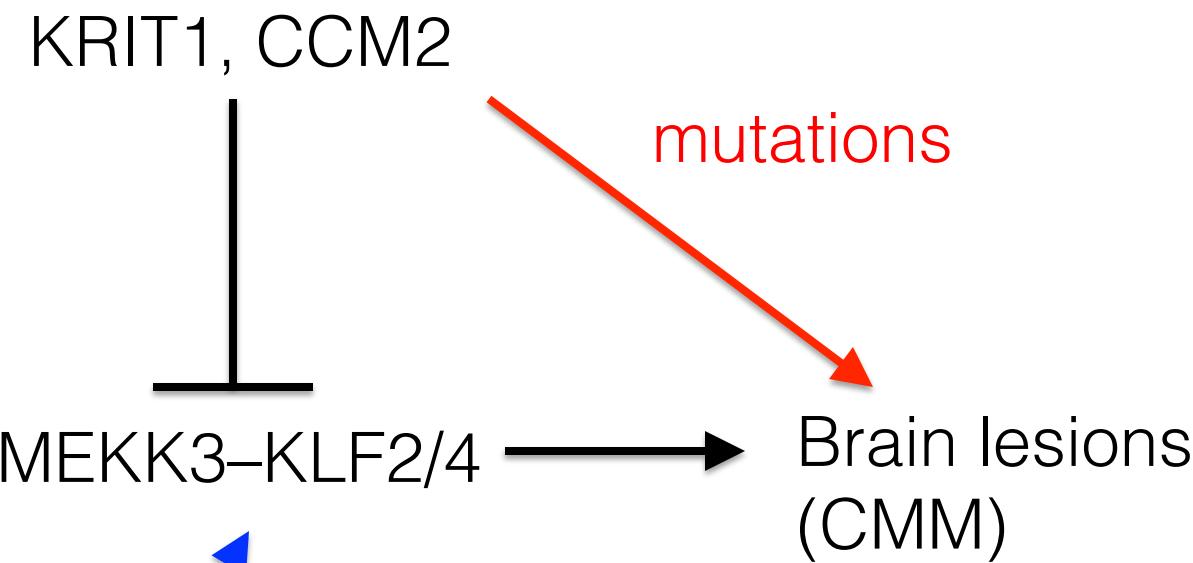




What
stimulates
this
pathway?

Figure 1 | CCM formation is stimulated by GNB infection and intravenous LPS injection.

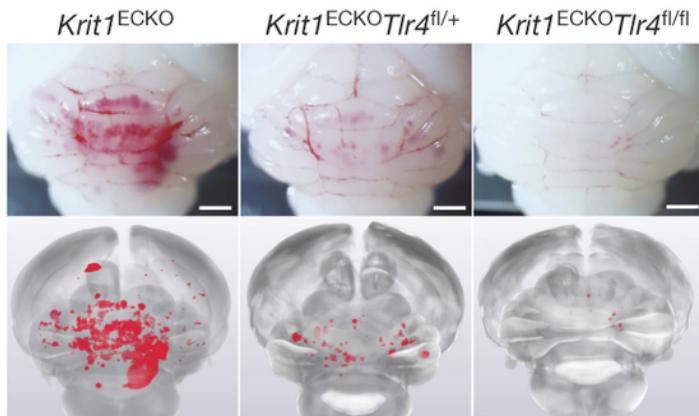




What
stimulates
this
pathway?

Figure 2 | CCM lesion formation requires endothelial TLR4/CD14 signaling.

c



d

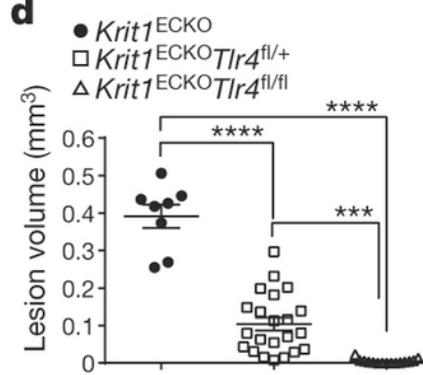
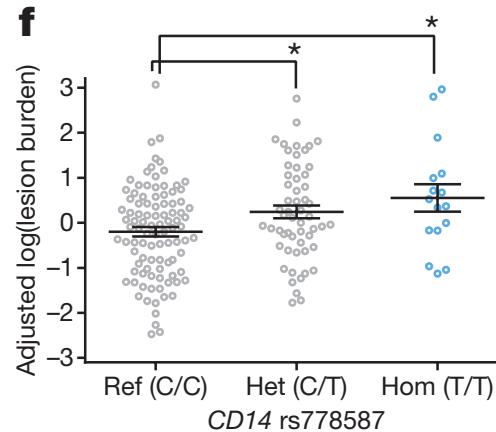
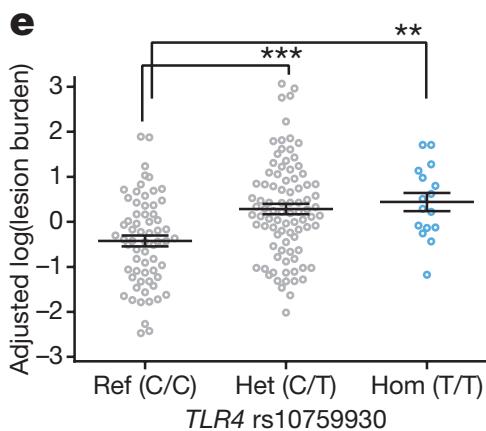
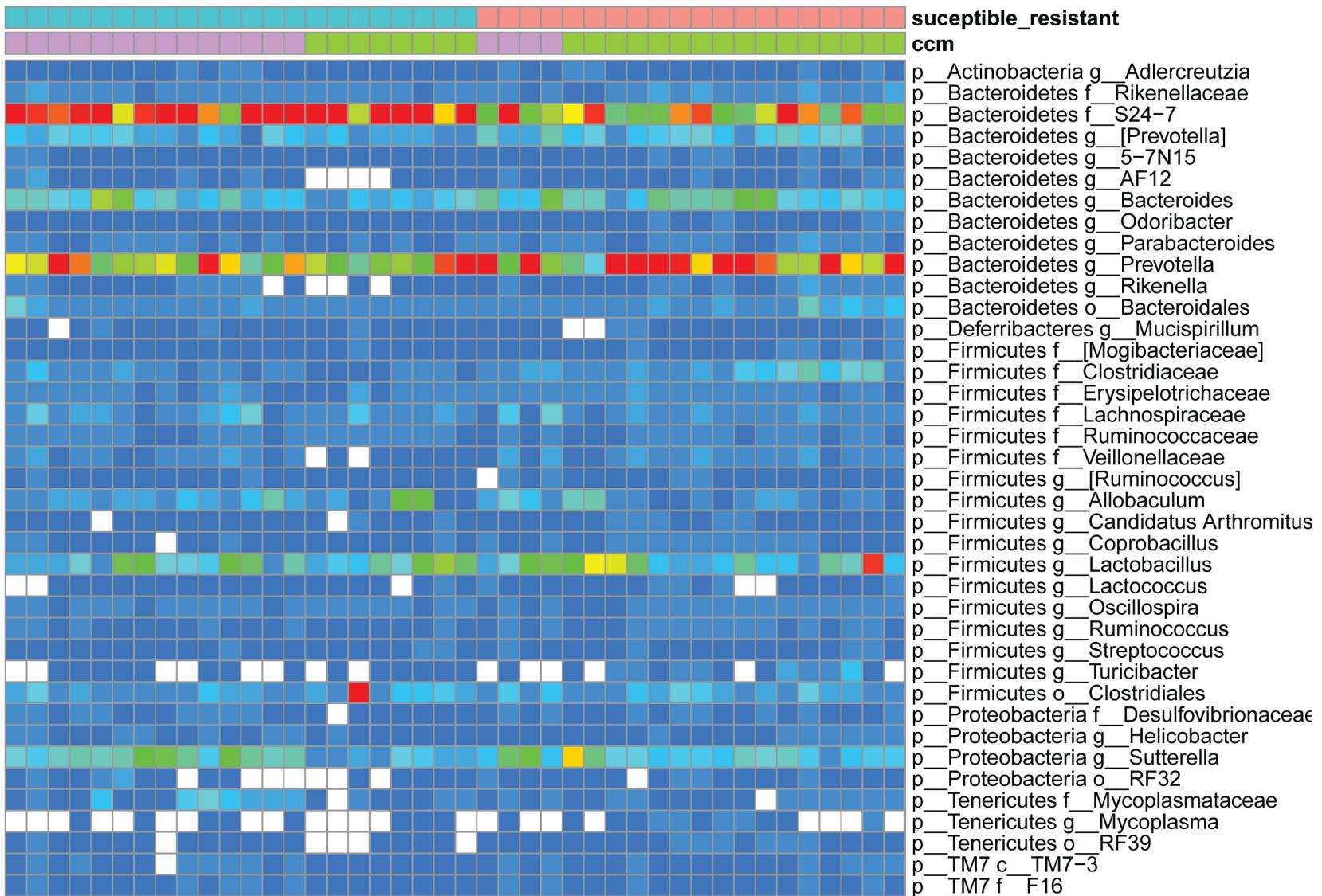


Figure 3 | Increased TLR4 or CD14 expression is associated with higher lesion number in familial CCM patients.





Extended Data Figure 7 | 16S rRNA sequencing results from susceptible and resistant Krit1fl/fl and Ccm2fl/fl dams

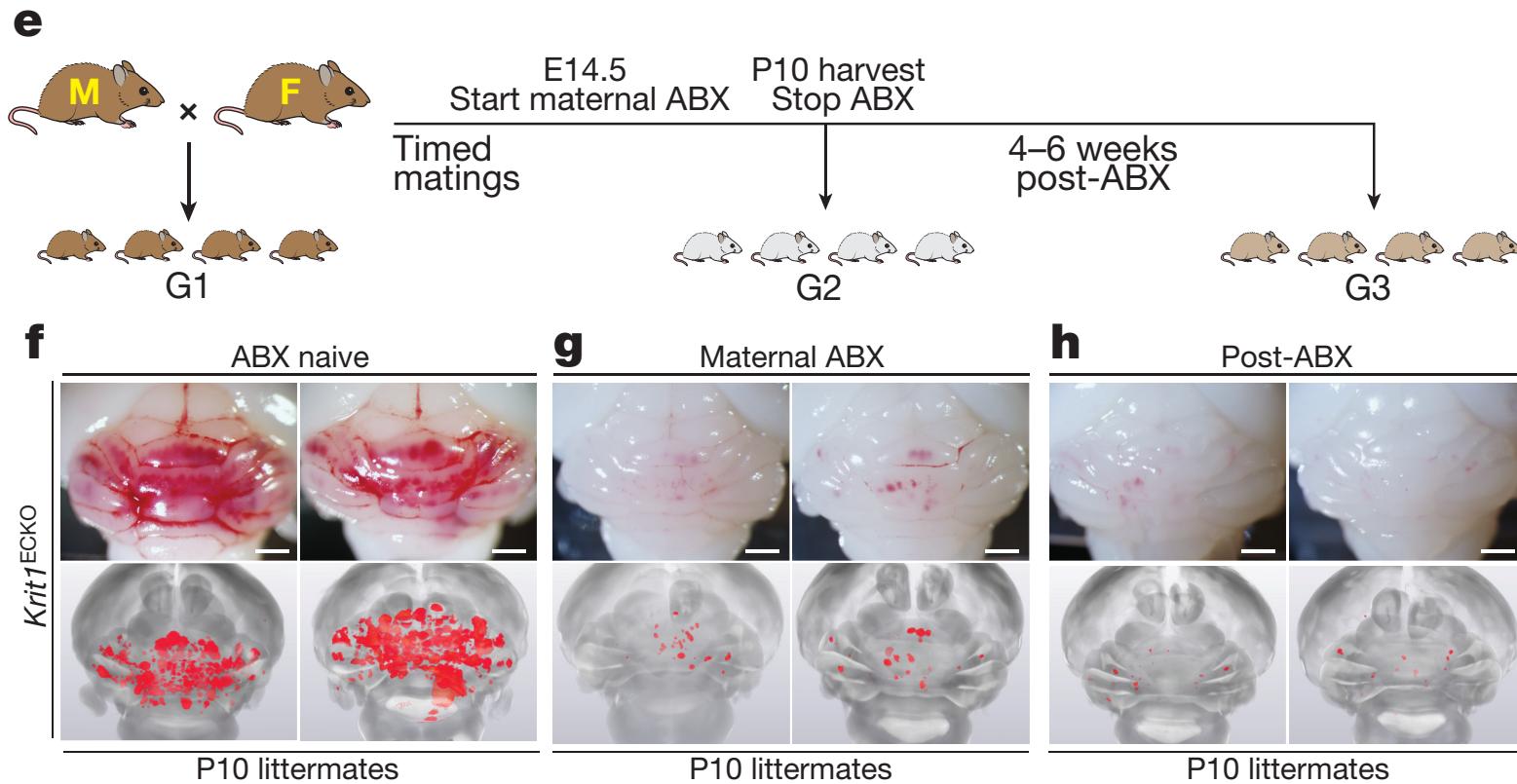
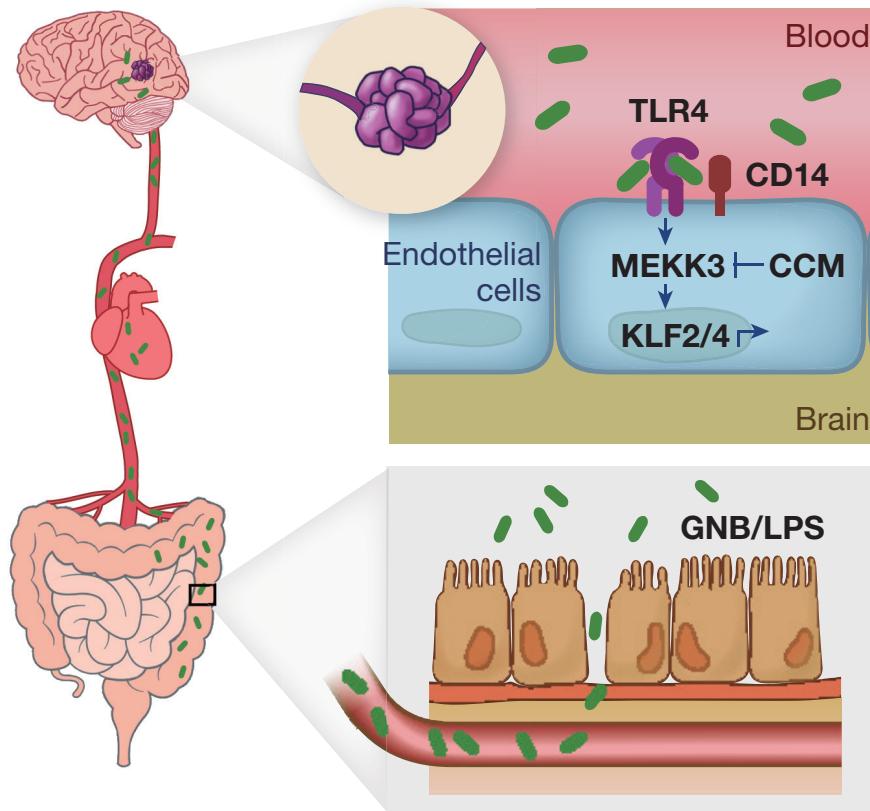
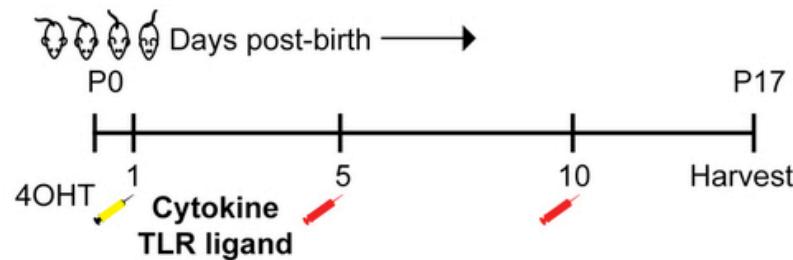


Figure 6 | Preventing CCM formation by TLR4 antagonism and microbiome manipulation.

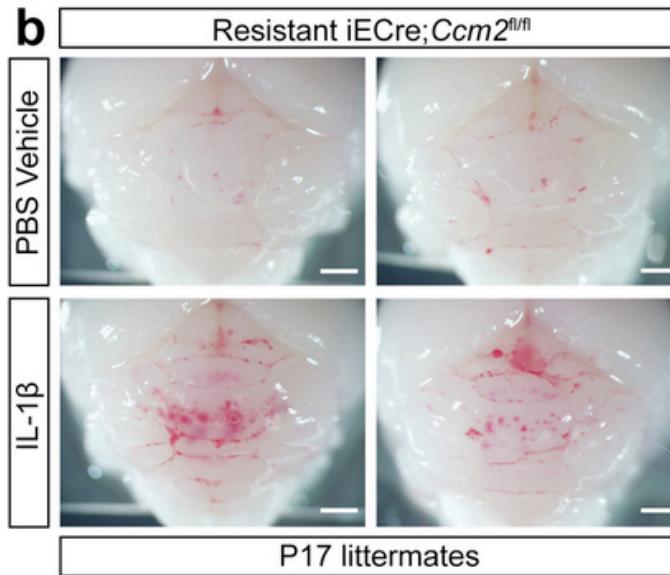


Big caveat: Other cytokines can make CCM lesions

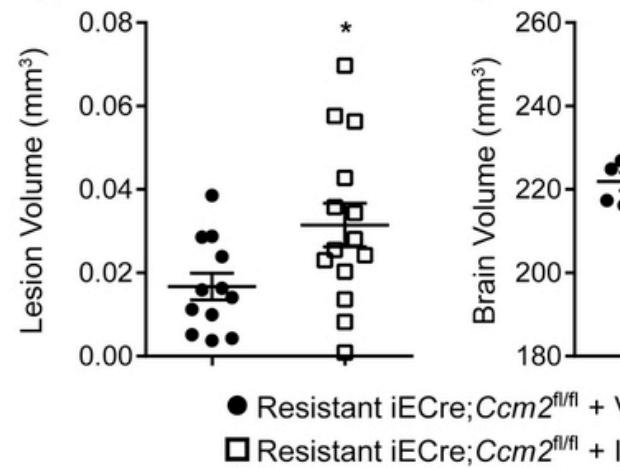
a



b



c



d

