CORRECTIONS & AMENDMENTS

CORRIGENDUM

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Corrigendum: NLRP10 is a NOD-like receptor essential to initiate adaptive immunity by dendritic cells

Stephanie C. Eisenbarth, Adam Williams, Oscar R. Colegio, Hailong Meng, Till Strowig, Anthony Rongvaux, Jorge Henao-Mejia, Christoph A. Thaiss, Sophie Joly, David G. Gonzalez, Lan Xu, Lauren A. Zenewicz, Ann M. Haberman, Eran Elinav, Steven H. Kleinstein, Fayyaz S. Sutterwala & Richard A. Flavell

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In this Letter, we reported that NLRP10-deficient mice had no defect in inflammasome function in macrophages or dendritic cells (DCs). Instead, a loss of T-cell-dependent immune responses was seen in these mice secondary to a defect in DC migration. We have since noticed a change in the phenotype of the NLRP10-knockout mice involving DC migration, after backcrossing them onto backgrounds such as FVB or BALB/c (see Supplementary Methods). We used whole-exome sequencing of these mice to determine whether loss of a different gene accounted for the observed phenotype. Six homozygous mutations/indels were found (sequence deposited in NCBI Sequence Read Archive under accession SRR1792904); one was a homozygous point mutation in the *Dock8* gene (Fig. 1a). DOCK8 is a guanine nucleotide exchange factor that has been shown to regulate the GTPase CDC42 in mouse DCs, and biallelic mutations in humans cause a severe immunodeficiency syndrome (OMIM 611432)[1,2]. This point mutation results in a premature stop codon in the second to last exon, and we believe results in nonsense-mediated decay of *Dock8* messenger RNA (Fig. 1b). *Dock8* mRNA is significantly reduced in DCs from the original *Nlrp10*$^{-/-}$ strain, but is restored when the mice are bred onto other wild-type backgrounds (Fig. 1c). The Bruce4 embryonic stem cells used to generate the NLRP10-deficient mice do not contain the mutation after sequencing (see Fig. 1a for primers and nucleotide change). It may have arisen spontaneously as a natural mutation early during the intercrossing of the knockout mice, and became fixed in our colony before the original phenotype analysis. From a previous proteomic screen, we identified DOCK8 as a candidate molecule involved in the loss of coordinated DC movement[3]. We tested whether this point mutation accounted for the loss of DC migration *in vivo* and adaptive immune responses. When mice were bred to isolate the NLRP10 deficiency, we found that DC migration was independent of NLRP10 (Fig. 1d). However, some aspects of the phenotype originally reported were maintained. For example, isolated NLRP10 loss does not result in enhanced NLRP3 inflammasome activation[3]. In addition, aberrant *Gdpd3* upregulation was due to *Nlrp10* loss and was not affected by the *Dock8* gene[3]. Notably, spontaneous *Dock* gene loss of function has been reported in many unrelated knockout mouse strains. For example, *Dock2* loss was recently reported in ASC-knockout mice[4,5]. In addition, *Dock2* mutations have been found in a subset of IRF5-deficient strains[6]. These separate instances suggest that the *Dock* gene family is prone to mutation, whether because of the large size (average of 275 kb across the 11 family members) or something more specific to these genes themselves, and that these mutations are readily discovered owing to the induction of a profound phenotype. Regardless of the aetiology of the mutations, these cases highlight the need for continual evaluation of genetic stability of inbred mouse strains, especially those expanded by sibling matings, as is common practice in many animal facilities. In addition, to limit accumulation of mutations in inbred strains as seen in our mice from the exome sequencing, periodically obtaining new breeding stock from founder lines or cryopreserved embryos from early generations has been recommended[7]. The original mouse phenotype reported in our Letter is correct and highly reproducible, but the conclusions must be reinterpreted in light of this new finding. We conclude that (1) DC migration is dependent on DOCK8 and not NLRP10; (2) NLRP10 deficiency is associated with aberrantly upregulated GDPD3; and (3) NLRP10 deletion does not alter NLRP3 inflammasome activity. We regret any confusion that this may have caused.

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Supplementary Information is available in the online version of the Corrigendum.

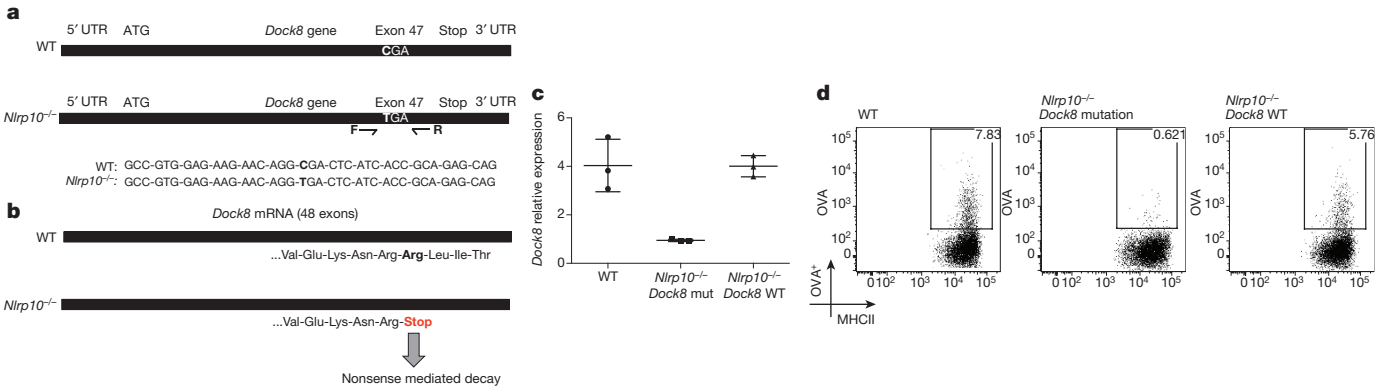

Figure 1 | NLRP10-deficient mice contain a *Dock8* point mutation resulting in failed DC migration. a, *Dock8* gene structure, highlighting homozygous point mutation in exon 47 in NLRP10-knockout mice. **b**, Resulting coding changes in DOCK8 induced by point mutation in **a**. **c**, Unstimulated bone-marrow-derived DCs from the original NLRP10-deficient mice with a *Dock8* mutation had significantly reduced *Dock8* mRNA. When the *Dock8* mutation was corrected through breeding, DCs from NLRP10-deficient mice showed no alteration in *Dock8* mRNA (relative to *Hprt*). **d**, *In vivo* DC migration to inguinal lymph nodes (see Supplementary Methods).