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INFECTION

Go wild?

Much of our understanding of the immune system has come from studying laboratory mice, which are typically housed in specific-pathogen free (SPF) barrier facilities. A major drawback of this approach is that such abnormally clean facilities are not reflective of the environment in which the human immune system develops. Two independent groups now show that the immune systems of mice raised under 'dirty' conditions are markedly different from those of SPF mice and, importantly, are more representative of the adult human immune system.

Initial experiments by Beura *et al.* showed that, compared with adult humans, laboratory mice that are maintained under SPF conditions have markedly reduced frequencies of memory $CD8^+$ T cells in the cervical mucosa and lack tissue-resident memory T (T_{RM}) cells. Furthermore, although most memory $CD8^+$ T cells isolated from human cervical tissue showed an effector memory phenotype (T_{EM}), almost all of the memory $CD8^+$ T cells from the cervix of adult SPF mice showed a central memory (T_{CM}) phenotype. Indeed, memory $CD8^+$ T cells from adult SPF mice were more similar to those of human neonates in that they lacked differentiated effector and mucosally distributed populations.

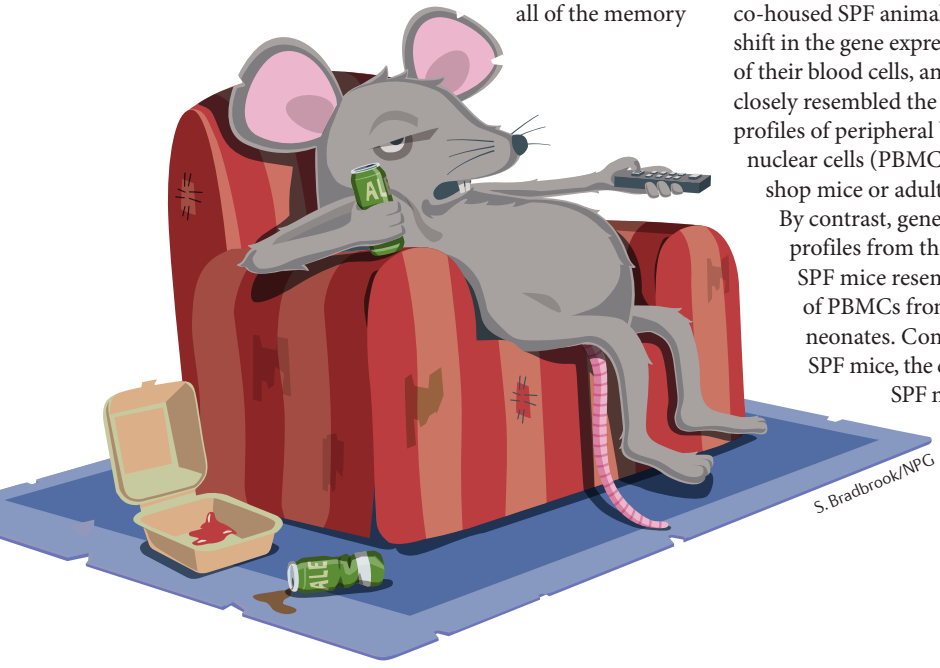
To test whether these differences were a result of genetic or environmental factors, the authors examined memory $CD8^+$ T cell compartments in free-living feral mice and in pet shop animals. Notably, feral and pet shop mice had higher frequencies of T_{EM} cells, and their memory $CD8^+$ T cells more closely resembled those of adult humans. To explore how exposure to a dirtier environment affects $CD8^+$ T cell development, the authors co-housed adult SPF mice with pet shop mice. This resulted in the death of 22% of the SPF mice, but the animals that survived showed increased frequencies of T_{EM} cells in the blood and markedly increased numbers of T_{RM} cells in non-lymphoid tissues. Furthermore, co-housed SPF animals showed a shift in the gene expression profiles of their blood cells, and these more closely resembled the immune profiles of peripheral blood mononuclear cells (PBMCs) from pet shop mice or adult humans. By contrast, gene expression profiles from the PBMCs of SPF mice resembled those of PBMCs from human neonates. Compared with SPF mice, the co-housed SPF mice showed increased protection in models of *Listeria monocytogenes* or *Plasmodium berghei* infection, suggesting that previous microbial exposure increases innate resistance to these infections.

The study by Reese *et al.* also examined how immune gene signatures are altered by the infection history. The authors found that co-infection of SPF mice with several viruses and a helminth induced gene signatures in the peripheral blood of the mice that were similar to those seen in the blood of adult humans or in the blood of pet shop mice. By contrast, SPF mice that were mock infected showed gene expression signatures that resembled those of human neonates. Similarly to Beura *et al.*, Reese *et al.* found that co-housing SPF mice with pet shop animals shifted the gene expression profiles of the SPF animals to more closely match those seen in dirty animals.

In summary, these studies suggest that mice raised in a microbial-rich environment have immune systems that more closely reflect those of adult humans. Both sets of authors suggest that conducting experiments in dirty mice could help increase the translational potential of immunological findings that are made in SPF mice.

Yvonne Bordon

> "conducting experiments in dirty mice could help increase the translational potential of immunological findings that are made in SPF mice"



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ORIGINAL ARTICLES Beura, L. K. *et al.* Normalizing the environment recapitulates adult human immune traits in laboratory mice. *Nature* **532**, 512–516 (2016) | Reese, T. A. *et al.* Sequential infection with common pathogens promotes human-like immune gene expression and altered vaccine response. *Cell Host Microbe* http://dx.doi.org/10.1016/j.chom.2016.04.003 (2016)