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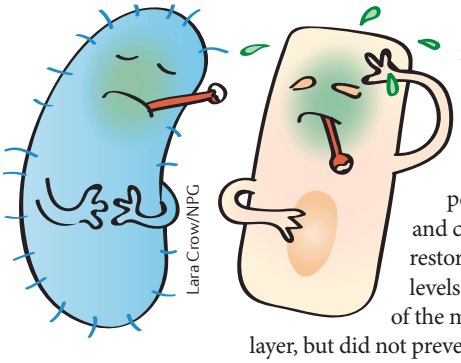
HYPERTENSION

Microbiota under pressure

Dysbiosis of the gut microbiota is involved in severe conditions such as chronic kidney disease but whether the gut–microbiome link is altered in hypertension has not been elucidated. A new study shows that hypertension is associated with altered gut function, changes in gut bacterial populations and altered gut–nervous system connectivity.

In their study, Mohan Raizada and colleagues found increased permeability and stiffness of the gut barrier, decreased levels of tight junction proteins, increased gut fibrosis, thickening of the gut muscularis layer, decreased villi length and goblet cell loss in spontaneously hypertensive rats (SHR) and in rats with angiotensin II (Ang-II)-induced hypertension. Treatment of SHR with captopril, an angiotensin-converting-enzyme inhibitor, lowered mean arterial pressure, reduced gut permeability, and completely restored fibrosis levels and thickness of the muscularis layer, but did not prevent goblet cell loss and only partially restored villi length.



Lara Crow/NPG

> Treatment of SHR with captopril … reduced gut permeability and completely restored fibrosis levels and thickness of the muscularis layer

Next, the researchers showed that SHR expressed higher levels of proinflammatory genes such as *CD68*, *IL-1β*, *HMGB1*, *TNF*, *TLR4* and *RAGE* than control rats. In addition, more T cells and macrophages were recruited, in part from the bone marrow, to the small intestine and colon of Ang II-treated rats.

The researchers previously showed that the ratio of *Firmicutes* to *Bacteroidetes* (F/B ratio) was increased in SHR. In this study, they found that prehypertensive SHR had the same F/B ratio as healthy rats, suggesting that the increased F/B ratio seen in SHR is linked to increased blood pressure. Consistent with those findings, SHR had altered bacterial populations (elevated *Streptococcaceae* and decreased *Bifidobacteriaceae* and several genera of the *Bacteroidetes* phyla).

Finally, the connectivity between the paraventricular nucleus of the hypothalamus and the gut was enhanced in both SHR and Ang II-treated rats and the sympathetic system was hyper-responsive in SHR.

"Currently we are conducting a clinical trial to validate the brain–gut dysfunction in hypertension," says Raizada. The researchers hope to address whether patients with hypertension have dysbiosis and increased gut permeability and if gut function and its link to the brain are different in drug resistant patients compared to drug sensitive patients.

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ORIGINAL ARTICLE Santisteban, M. M. *et al.* Hypertension-linked pathophysiological alterations in the gut. *Circ. Res.* http://dx.doi.org/10.1161/CIRCRESAHA.116.309006 (2016)