Ammonia and the gut-brain axis during viral infection

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Track: Adaptive Immunity
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Abstract text
Text: Viral infections impose vast immune, metabolic and behavioral changes to the host. Upon infection, mammals experience anorexia, lethargy, and other high-order adaptations collectively known as sickness behavior.
The gut microbiota has been increasingly recognized as a source of physiologically relevant metabolites. Nevertheless, we still lack an integrated view about how gut-derived metabolites influence infection pathophysiology, including sickness behavior.
Our group has reported that viral infection leads to an increase in blood ammonia levels (Lercher et al. 2019, *Immunity*). Despite being typically considered as a toxic waste product, ammonia is a small, gaseous molecule that might modulate cellular functions in distant tissues. Therefore, we hypothesized that infection-induced hyperammonemia might exacerbate sickness behavior in light of the documented effects of ammonia in the central nervous system.
We set out to identify potential physiological roles of hyperammonemia during infection using a mouse model of chronic viral infection by lymphocytic choriomeningitis virus (LCMV) combined with transcriptomics, imaging, behavioral tests and perturbations of the gut microbiota composition.
We observed that infection-induced hyperammonemia is dependent on bacterial metabolism in the gut, and that infection induces a higher ammonia uptake in the brain. Gut-derived ammonia signals through the paraventricular nucleus of the hypothalamus, which is involved in stress responses and behavioral adaptations.
These results suggest that ammonia signaling between the gut and the brain might influence stress responses and sickness behavior during viral infection. Our work aims to expand our understanding of how gut metabolism influences brain function in the context of infection.

Conflict of Interest statement
Do you have any conflict of interest to declare?: No

Affirmation
1. Consent to participate and present onsite: Yes
2. Consent to publication publication: Yes
3. Consent on treatment of contact details saved in this system: Yes