SESSION 3. ANIMAL GENETICS

Chair Filipe Costa and Jorge Vieira

Microbial evolution in the long-lived gut

Rita Melo-Miranda, Ana Pinto, Ana Sousa

Institute of Biomedicine (iBiMED), Department of Medical Sciences, University of Aveiro, Aveiro, Portugal

Aging, one of the biggest health challenges of our time, is associated with several occurrences, including an increase in inflammation and gut microbial dysbiosis. These events contribute to aging by rising intestinal permeability and inflammation, but how they influence microbiota evolution and pathobiont selection remains poorly understood.

Previous work described the adaptation of an *E. coli* commensal strain to the gut of young animals (6-9 weeks old) and showed that it acquires metabolism-related mutations, whereas, in old mice (19 months old), the pattern is shifted towards stress-related mutations, and metabolic adaptations arise slower.

Here, to further understand features associated with longevity, we compared the microbial evolution in the guts of these two age groups with very old animals (25 months old).

Remarkably, while very old mice were the frailest, they did not show higher intestinal inflammation than any of the two. Also, when compared with the other age groups, very old mice showed an increase in health-associated bacteria, e.g., *Akkermansia muciniphila* and *Oscillospira sp*.
Interestingly, *E. coli* evolution in the gut of very old mice resembled the pattern found in young animals, as it displayed more metabolic than stress-related mutations. Also, it shared certain mutational targets with young mice that are absent in the old, and conversely, it shared mutations with the old that are absent in young animals. Additionally, *E. coli*'s evolutionary signature potentially targeted different phenotypes, such as motility and biofilm formation, according to the parallel gene-inactivating mutations observed in fimE.

These findings suggest that the microbial evolution signature in the guts of long-lived mice shares similarities with both young and old mice, while also bearing unique features that may be associated with longevity.

Keywords: *aging, microbial evolution, longevity*