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# Rejuvenation of intestinal microbiota via microbiota transfer in aged mice: effects on local expression of proteins and function

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We have previously shown that microbiota transfer from aged donors into young recipients triggered a series of event leading to changes at systemic level, including the nervous central system<sup>1</sup>. Here we sought to evaluate the effects of the rejuvenation of intestinal microbiota via microbial transfer from young donors into aged recipient mice on the intestinal expression of proteins and function.

Aged (20 month) mice were colonized with microbiota from young (3-4 month) syngeneic donors and protein expression of the colon were evaluated by proteomic approach that enabled us to assess the expression of 2453 proteins. We observed that 24 proteins were up regulated while 14 were down regulated. Interestingly, these proteins were associated to a variety of signalling pathways including Integrin-linked Kinase (ILK), Integrin, Leukocyte extravasation and IL-1 pathways and others with an overall anti-inflammatory effect.

Also, the rejuvenation of the microbiota led to a significant increase in bacterial species (such as *Lachnospiraceae*, and *Ruminococcaceae*) involved in the production of short-chain fatty acid (SCFAs) the decline of which is considered highly detrimental for the aging organism. Further, histological analyses showed that at least some aspects of innate immunity were affected. Indeed, we observed that aged recipients showed an increased expression and production on angiotensin IV, an important mediator of immunity to pathogens produced by Goblet cells. Colonization of the ageing gut with "young-like" microbiota also triggered local changes at morphological level. Importantly, these included

significant changes in the number of mucus producing cells, another critical component contributing to the integrity of the intestinal barrier.

Currently, the effects of the rejuvenation of intestinal microbiota on innate immunity (IgA to orally and nasally delivered antigens) is under evaluation. Taken together, these data show that maintaining a young-like microbiota late in life might contribute to achieve and healthy ageing.

## References

- 1 D'Amato et al. Microbiome 2020;8:140. doi: 10.1186/s40168-020-00914-w2020

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