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Title: Plasma cells live for decades in the human small intestine

Abstract: The intestinal mucosa contains 80% of all plasma cells in the human body that produce several grams of secretory immunoglobulins (mostly IgA) every day and IgA play an important protective role in the defense against pathogens and toxins. More recently it was shown that IgA also interacts with the microbiota. A large fraction of resident commensal bacteria is coated by IgA, which affects their growth and microbial functions. Moreover, blocking the transepithelial transport of secretory antibodies into the intestinal lumen disturbs the stability of the microbiota and compromises gut homeostasis. In order to control the composition of the microbiota there are data to suggest that generation of microbial-specific IgA responses is persistent. However, whether long-lived plasma cells exist in the gut has been an open question for many years. Recently we studied the phenotype, immune repertoire and functions of human small intestinal plasma cells as well as their dynamics by cell-turnover analysis in organ transplants and by retrospective cell birth dating measuring carbon-14 in genomic DNA. We found that the plasma cells consist of three distinct subsets with very different survival rate. Importantly, a large fraction are extremely long-lived with a mean lifespan of more than 20 years. This finding represents an important shift in the concept of gut humoral immunity and shows that IgA responses can be extremely persistent. Long-lived plasma cells may be particularly important in order to reinforce a stable, diverse and healthy microbiota and such cells may be attractive targets for vaccination and for treatment of dysbiosis-mediated disorders.

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