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Seven of the top 10 causes of death in the US are due to chronic diseases such as cancer, cardiovascular disease, and type 2 diabetes. Altered gut bacterial ecosystems due to environmental factors have been associated with greater risk for chronic diseases. To counter the global epidemic of chronic diseases, it is critical to understand the interaction between environmental factors (e.g., high-calorie diet, HCD), gut microbiota, and intestinal mucosa in a human-relevant model during health and disease. We show that pigs, which have gut bacterial profiles and immune systems similar to humans, also maintain two distinct colonic stem cell populations (ASCL-2 and BMI-1). Mice lack colonic BMI-1 stem cells that play a critical role in colon carcinogenesis. Additionally, we discovered that when exposed to HCD, stem cells move up along the colon crypt – an early marker of colon carcinogenesis. Observed changes in stem cells are independent of food intake, body weight, and serum iron levels, and they occurred before the onset of insulin resistance. Given that colonic stem cell kinetics play a central role not only in colon carcinogenesis but also in gut inflammation and permeability and endotoxemia, we correlated this to the gut bacterial phyla and colonic inflammatory markers. Changes in the stem cell position (stem cell zone) and their function (proliferative index) positively correlated with proteobacteria phylum levels and inflammatory markers, which are associated with type 2 diabetes, colitis, and colon cancer. The figure on the cover shows a correlation heat map between bacterial phylum levels and colonic stem cell/epithelial cell kinetics markers. Red and blue represents positive and negative correlations, respectively. In the central insert, a BMI-1 stem cell is seen in green at the bottom of pig colon crypt. See article by Charepalli, Reddivari, et al. (beginning on page 442) for more information.



# Cancer Prevention Research

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*Cancer Prev Res* 2017;10:431-487.

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