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Short Communication
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Intestinal Stem Cell Regulation via Glycolytic Activity of Neighboring Paneth Cells

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The epithelial lining of the small intestine (SI) is regenerated in its entirety at a rapid pace of every three to five days [1,2]. In order to perpetuate normal physiological functions of digestion and absorption provided by the SI epithelium, regeneration of this magnitude is required and must be properly maintained [3]. In tissues of high turnover such as the intestinal epithelium, stem cells are crucial regulators of tissue homeostasis. In the gastrointestinal tract, crypt base columnar (CBC) stem cells, a population of rapidly dividing cells at the crypt base expressing leucine-rich-repeat-containing G-protein coupled receptor 5 ($Lgr5^+$), give rise to all terminally differentiated intestinal epithelial cell types (enterocytes, Paneth, goblet, enteroendocrine, tuft, and M cells) [4]. Local conditions in which the $Lgr5^+$ CBCs reside, called the stem cell niche, regulate cell proliferation, differentiation, and stem cell self-renewal [1]. Paneth cells are long-lived secretory cells that migrate into the crypt base and reside between $Lgr5^+$ CBCs where they produce and secrete antimicrobial peptides and stem cell factors such as epidermal growth factor, Wnt3, and Notch ligand D114 that sustain the stem cell niche [3,5-7]. Maintenance of crypt homeostasis is well documented in the literature; however, Rodriguez-Colman et al. [2] have recently highlighted the role of mitochondrial activity in $Lgr5^+$ CBC maintenance. Compared to other differentiated intestinal epithelial cells and relatively quiescent stem cell populations in the adult, such as hematopoietic stem cells [8] and neural stem cells [9,10], $Lgr5^+$ CBCs show higher mitochondrial oxidative phosphorylation activity [7,11]. Rodriguez-Colman et al. [2] revealed that in support of increased demand for mitochondrial oxidative phosphorylation for $Lgr5^+$ CBCs to maintain the immense amount of cell turn over in the small intestine, lactate from Paneth cells is fed into neighboring $Lgr5^+$ CBCs fueling their oxidative phosphorylation processes. Inhibition of glycolysis, and subsequently lactate production, in Paneth cells affects $Lgr5^+$ CBC function and hinders crypt maturation [2]. Therefore, the glycolytic phenotype in Paneth cells is crucial for lactate production, which drives increased oxidative phosphorylation in $Lgr5^+$ CBCs. Mechanistically, Rodriguez-Colman et al. [2] demonstrated that mitochondrial-derived reactive oxygen species produced in $Lgr5^+$ CBCs during oxidative phosphorylation stimulate activation of p38 MAP kinase, which in turn regulates $Lgr5^+$ CBC self-renewal and differentiation. These results show that the glycolytic phenotype in Paneth cells and increased OXPHOS in $Lgr5^+$ CBCs are required in supporting both stem cell niche and function. Provision of lactate from Paneth cells is therefore another critical aspect of the interdependent relationship between $Lgr5^+$ CBCs and Paneth cells, essential to the maintenance and differentiation of SI epithelium.

Alteration of crypt homeostasis affects $Lgr5^+$ CBC and Paneth cell function leading to ramifications for the small intestine as a whole. Inflammation, intestinal dysbiosis, radiation, spontaneous genetic mutations and consumption of a diet composed of 45% to 60% fat are all documented examples of such alterations [7,12-14]. Aside from impending weight gain, high fat diets (HFD) cause changes in both Paneth and $Lgr5^+$ CBCs. Gou et al. [13] recently demonstrated that Paneth cell-derived immune health regulation is impaired following prolonged implementation of a HFD as the mRNA expression of antimicrobial peptides significantly decreased in these cells. Decreased antimicrobial peptide secretion from Paneth cells leads to less pathogen defense and detrimental changes in microbiome composition [1]. In addition, chronic HFD exposure reduces Paneth cell numbers themselves not only decreasing immune defense but also $Lgr5^+$ CBC support [12]. In the face of decreased Paneth cell support, Beyaz et al. [12] reports that proliferating $Lgr5^+$ CBCs exposed to HFD lack differentiation of progenitor cells resulting in diminished villi

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length. Adverse effects induced by prolonged HFD intake upsets the epithelial regeneration and innate immunity sustained by efficiently functioning symbiotic relationship between Paneth cells and $Lgr5^+$ CBCs. Without this Paneth/$Lgr5^+$ CBC relationship, a decline in effective absorptive digestive function is observed.

References

1. Clevers HC, Bevins CL. Paneth cells: maestros of the small intestinal crypts. Annu Rev Physiol. 2013;75:289-311.
2. Rodriguez-Colman MJ, Schewe M, Meerlo M, Stigter E, Gerrits J, Pras-Raves M, et al. Interplay between metabolic identities in the intestinal crypt supports stem cell function. Nature. 2017;543:424-7.
3. Henning SJ, von Furstenberg RJ. GI stem cells - new insights into roles in physiology and pathophysiology. J Physiol. 2016;594:4769-79.
4. Barker N, Clevers H. Leucine-rich repeat-containing G-protein-coupled receptors as markers of adult stem cells. Gastroenterology. 2010;138:1681-96.
5. Elphick DA, Mahida YR. Paneth cells: their role in innate immunity and inflammatory disease. Gut. 2005;54:1802-9.
6. Srinivasan T, Than EB, Bu P, Tung KL, Chen KY, Augenlicht L, et al. Notch signalling regulates asymmetric division and inter-conversion between lgr5 and bmi1 expressing intestinal stem cells. Sci Rep. 2016;6:26069.
7. Umar S. Intestinal stem cells. Curr Gastroenterol Rep. 2010;12:340-8.
8. Passegue E, Wagers AJ, Giuriato S, Anderson WC, Weissman IL. Global analysis of proliferation and cell cycle gene expression in the regulation of hematopoietic stem and progenitor cell fates. J Exp Med. 2005;202:1599-611.
9. Morshead CM, Reynolds BA, Craig CG, McBurney MW, Staines WA, Morassutti D, et al. Neural stem cells in the adult mammalian forebrain: a relatively quiescent subpopulation of subependymal cells. Neuron. 1994;13:1071-82.
10. Khacho M, Clark A, Svoboda DS, MacLaurin JG, Meghaizel C, Sesaki H, et al. Mitochondrial dynamics impacts stem cell identity and fate decisions by regulating a nuclear transcriptional program. Cell Stem Cell. 2016;19(2):232-47.
11. Chandel NS, Jasper H, Ho TT, Passegué E. Metabolic regulation of stem cell function in tissue homeostasis and organismal ageing. Nat Cell Biol. 2016;18:823-32.
12. Beyaz S, Mana MD, Roper J, Kedrin D, Saadatpour A, Hong SJ, et al. High-fat diet enhances stemness and tumorigenicity of intestinal progenitors. Nature. 2016;531:53-8.
13. Guo X, Li J, Tang R, Zhang G, Zeng H, Wood RJ, et al. High fat diet alters gut microbiota and the expression of paneth cell-antimicrobial peptides preceding changes of circulating inflammatory cytokines. Mediators Inflamm. 2017;2017:9474896.
14. Anitha M, Reichardt F, Tabatabavakili S, Nezami BG, Chassaing B, Mwangi S, et al. Intestinal dysbiosis contributes to the delayed gastrointestinal transit in high-fat diet fed mice. Cell Mol Gastroenterol Hepatol. 2016;2:328-39.