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BECKER'S
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20 bold predictions on the ASC industry over the next 5 years

What will the ASC industry look like in 2025? Likely more consolidation, collaborative relationships with hospitals and payers, and more cardiology procedures. Twenty ASC owners, operators and industry leaders share their predictions in this article.

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How CMS' proposals could affect ASCs in 2021

CMS proposed several drastic pay cuts for both general and specialty surgeons in 2021. The agency is also considering removing 266 orthopedic procedures from the inpatient-only list.

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Walmart Health is expanding: 5 things for ASC execs to know

Walmart plans to add six health clinics in Atlanta through the end of the year and continue expanding in Illinois and Florida in 2021.

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"Invisible" diseases will soon have no place to hide.

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Bridging the divide between disease understanding and treatment approach in gastroenterology

By Jan Wehkamp, MD, Vice president, Gastroenterology disease area leader, Janssen Research & Development, LLC

It may be alarming at first to discover that the human body is made up of more bacteria cells than human cells, especially in the gut.[i] However, research over the years has shown us how bacteria interacts with our immune system and the dynamic role it can play in diseases such as inflammatory bowel disease (IBD).

IBD was originally considered to be a classic autoimmune disease, driven by immune dysfunction (e.g., T and B cell dysregulation) and, as such, treatment approaches aimed to broadly suppress the systemic immune system.[ii] In more recent years, as our understanding of the disease evolved, it became clear that IBD is also a complex variety of different barrier disorders, and the mucosal interface plays a critical role.[iii] As a result of this expanded perspective, treatment goals for the different types of IBD have shifted from immune suppression to immune protection and immune homeostasis (a return of the natural balance).[iv] This disruption of the barrier is key, as its breakdown/impairment has been implicated as a critical determinant in the predisposition to several gastrointestinal diseases, including IBD.[v]

Some interventions aimed to modify the microbiota of IBD patients by means of dietary approaches, administration of live microbials such as probiotics and/or antibiotics, or fecal microbiota transplants.[vi] However, we at Janssen are pursuing another approach: restoration of the healthy microbiome by restoration of the epithelial barrier. The simplified, but not mutually exclusive, concept aims to restore barrier function, which would directly target the inflammatory trigger and re-establish immune homeostasis. Since the microbiome is, in large part, controlled by epithelial host defense and immune function, this strategy ultimately allows the microbiome to be restored/rebalanced.

When I was in medical school and after starting to work in an IBD research lab, I listened to a surgical talk regarding how patients do better after ileostomy: preventing the presence of stool in the distal part. In contrast, after surgical restoration of the intestinal continuity with the microbial stool being reinstalled, the inflammation recurred. For me, this was such a compelling argument; and this was one of my personal initiators for more than two decades of research in this area.

The intestinal mucosa represents the largest surface within the human body and the most important physical barrier between external and internal environments.[vii] This barrier consists of a monolayer of epithelial cells lining the gut lumen (intestinal epithelial cells) coated by a protective, hydrophobic mucus layer. Epithelial cells actively secrete host defense antimicrobial peptides such as defensins, which control the composition of luminal microbes. Also present within the epithelial barrier are adaptive and innate immune cells which, with the epithelial layer, constitute the mucosal immune system.[viii]

The mucosal immune system is the primary defense against resident intestinal microbes (called the microbiota), which are estimated to number in the trillions in healthy individuals.[ix,x] The microbiome provides an abundant source of potentially pathogenic organisms, toxins and antigens, leading to continuous dynamic and complex interactions with the mucosal immune system.[xi] In a healthy setting, the intestinal epithelial barrier protects the body from such bacterial threats, however, defects in barrier function can lead to exposure of underlying immune cells in the lamina propria to resident bacteria, thereby activating the immune cells, triggering the inflammatory cascade and, ultimately, leading to consecutive dysregulation of the mucosal immune system.[xii] Similarly, dysbiosis, or an unbalancing or alteration of the gut microbiome, can disrupt intestinal barrier integrity and subsequently activate mucosal immune responses.

IBD, which consists of two major subtypes, Crohn's disease (CD) and ulcerative colitis (UC), are chronic, relapsing-remitting inflammatory diseases believed to be triggered by environmental factors in genetically susceptible individuals.[xiii] While CD impacts the entire bowel wall, UC is restricted to the surface lining of the gut. It has been reported that CD patients with clinically active disease have increased intestinal permeability and that such increased permeability is predictive of clinical relapse in patients with inactive disease.

Restoration of barrier function/mucosal healing, and thereby immune homeostasis, is critical, as evidence suggests that inflammation in the gut may contribute to inflammation/immune dysfunction outside the gastrointestinal tract.[xiv] For example, CD is associated with various inflammatory diseases, including asthma, bronchitis, pericarditis, psoriasis, rheumatoid arthritis and multiple sclerosis.[xv] Experts recommend that treatments target mucosal healing, which population-based studies and meta-analyses have demonstrated to result in improved outcomes, including decreased risk of requiring surgery, lower relapse rates and improved quality of life.[xvi] Therefore, it is our hope that by understanding how the mucosal barrier controls tolerance to the microbiome and prevents the inflammatory cascade from being activated in IBD, we may someday move beyond treating IBD to also impact these other associated inflammatory conditions. What we learn by expansion to other disease spaces may also provide more insight and further inform our approach to restoring this function within the gastrointestinal tract.

Evidence suggests that several pathways and players contribute to the integrity of the epithelial barrier, providing many possible approaches to targeting barrier integrity. Excessive T helper 1 (Th1) and Th17 cell responses, characteristic to IBD, secrete the proinflammatory cytokines IL-17, IFN-γ and TNF-α, which stimulate the production of other downstream cytokines (e.g.,

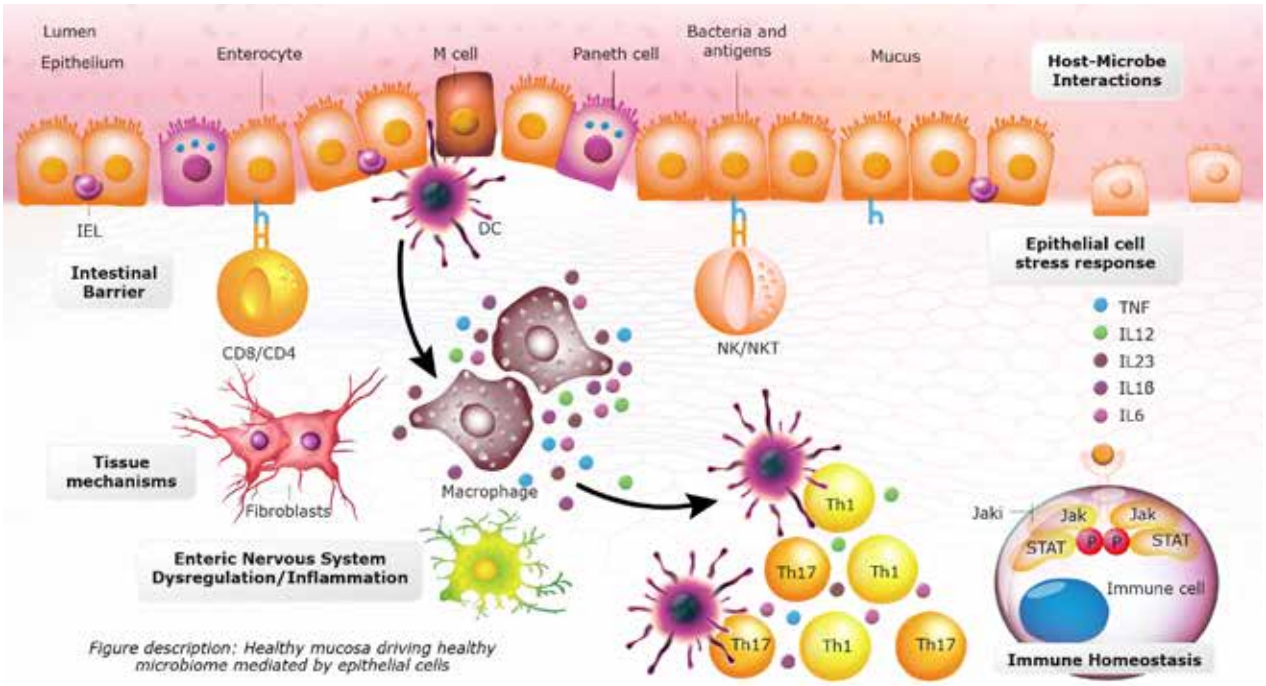

Figure description: Healthy mucosa driving healthy microbiome mediated by epithelial cells

TNF, IL-1, IL-6, IL-8, IL-12 and IL-18) by other cell types such as macrophages, endothelial cells and monocytes.[xvii] The role of proinflammatory cytokines interferon-γ (IFN-γ) and tumor necrosis factor-α (TNF-α) have been well-established as being central to mediating IBD, but more recent data have implicated the IL-23/Th17 axis as also being a pivotal player.[xviii] In fact, a genetic variant of the IL-23R has been found to be significantly associated with CD. Additionally, other types of mediators are known to play a role, such as the Janus kinases (JAKs), which play a central role in innate and adaptive immunity and are utilized by nearly all cytokines as a common signaling pathway, and NKG2D, a critical mediator of communication between intraepithelial cells and innate and adaptive immune cells. As the players and pathways involved in IBD pathogenesis are elucidated, new treatment strategies are being developed targeting different points within the disease.[xvii]

Janssen is committed to exploring treatments targeting the mucosal barrier and interface. We recognize that every part of the body is different, and no two diseases or their patient populations are alike (e.g., CD and UC, despite similar/overlapping symptoms). As an example, ileocecal CD can be viewed as a separate disease with a distinct genetic- and non-genetic pathophysiology, which translates into distinct clinical burden with high unmet medical need.[xix] Our development strategy recognizes important differences within each disease and aims to find specific differentiated treatments for different phenotypic classifications. In addition to insight regarding common pathways and mechanisms of inflammation, each disease requires special considerations and a specific, thorough, deep disease understanding. In terms of the GI tract, we are committed to investigating the role of various players involved in barrier maintenance and repair in each disease state (rather than assuming a role for one disease based on that in another). Janssen is actively exploring such roles in diseases such as UC, CD, and Celiac disease. Recognizing the burden of distinct patient populations and differences in clinical outcome and pathophysiology enables us to develop differentiated therapies.

At Janssen, we're working to deliver transformational and accessible therapies and regimens to patients with gastrointestinal disease and know that we can't go it alone. We continue to seek bright and passionate minds to help us in our vision in restoring the immune balance for the millions of people living with immune-mediated diseases. ■

i. Fields, H. (2015). The Gut: Where Bacteria and Immune System Meet. Johns Hopkins Medicine. https://www.hopkinsmedicine.org/research/advancements-in-research/fundamentals/in-depth/the-gut-where-bacteria-and-immune-system-meet.

ii. Fakhoury, M., Negrulj, R., Mooranian, A., & Al-Salami, H. (2014). Inflammatory bowel disease: clinical aspects and treatments. Journal of inflammation research, 7, 113–120. Pg. 114. https://doi.org/10.2147/JIR.S65979

iii. Wehkamp, J., Götz, M., Herrlinger, K., Steurer, W., & Stange, E. F. (2016). Inflammatory Bowel Disease. Deutsches Arzteblatt international, 113(5), 72–82. pg. 74. https://doi.org/10.3238/arztebl.2016.0072

iv. Groschwitz, K. R., & Hogan, S. P. (2009). Intestinal barrier function: molecular regulation and disease pathogenesis. The Journal of allergy and clinical immunology, 124(1), 3–22. pg. 12. https://doi.org/10.1016/j.jaci.2009.05.038

v. Groschwitz, K. R., & Hogan, S. P. (2009). Intestinal barrier function: molecular regulation and disease pathogenesis. The Journal of allergy and clinical immunology, 124(1), 3–22. pg. 12. https://doi.org/10.1016/j.jaci.2009.05.038

vi. Schreiner, P., Neurath, M. F., Ng, S. C., El-Omar, E. M., Sharara, A. I., Kobayashi, T., Hisamatsu, T., Hibi, T., & Rogler, G. (2019). Mechanism-Based Treatment Strategies for IBD: Cytokines, Cell Adhesion Molecules, JAK Inhibitors, Gut Flora, and More. Inflammatory intestinal diseases, 4(3), 79–96. pg. 88. https://doi.org/10.1159/000500721

vii. Lin, L., & Zhang, J. (2017). Role of intestinal microbiota and metabolites on gut homeostasis and human diseases. BMC immunology, 18(1), 2. https://doi.org/10.1186/s12865-016-0187-3, pg 2.

viii. Lin, L., & Zhang, J. (2017). Role of intestinal microbiota and metabolites on gut homeostasis and human diseases. BMC immunology, 18(1), 2. https://doi.org/10.1186/s12865-016-0187-3, pg 10.

ix. Schreiner, P., Neurath, M. F., Ng, S. C., El-Omar, E. M., Sharara, A. I., Kobayashi, T., Hisamatsu, T., Hibi, T., & Rogler, G. (2019). Mechanism-Based Treatment Strategies for IBD: Cytokines, Cell Adhesion Molecules, JAK Inhibitors, Gut Flora, and More. Inflammatory intestinal diseases, 4(3), 79–96, pg 88. https://doi.org/10.1159/000500721

x. Lin, L., & Zhang, J. (2017). Role of intestinal microbiota and metabolites on gut homeostasis and human diseases. BMC immunology, 18(1), 2, pg 1. https://doi.org/10.1186/s12865-016-0187-3

xi. Groschwitz, K. R., & Hogan, S. P. (2009). Intestinal barrier function: molecular regulation and disease pathogenesis. The Journal of allergy and clinical immunology, 124(1), 3–22, pg. 10. https://doi.org/10.1016/j.jaci.2009.05.038

xii. Roda, G., Chien Ng, S., Kotze, P.G. et al. Crohn's disease. Nat Rev Dis Primers 6, 22 (2020), pg. 4. https://doi.org/10.1038/s41572-020-0156-2

xiii. Groschwitz, K. R., & Hogan, S. P. (2009). Intestinal barrier function: molecular regulation and disease pathogenesis. The Journal of allergy and clinical immunology, 124(1), 3–22. pg. 14. https://doi.org/10.1016/j.jaci.2009.05.038

xiv. Roda, G., Chien Ng, S., Kotze, P.G. et al. Crohn's disease. Nat Rev Dis Primers 6, 22 (2020). Pg. 4. https://doi.org/10.1038/s41572-020-0156-2

xv. Roda, G., Chien Ng, S., Kotze, P.G. et al. Crohn's disease. Nat Rev Dis Primers 6, 22 (2020). Pg. 7. https://doi.org/10.1038/s41572-020-0156-2

xvi. Roda, G., Chien Ng, S., Kotze, P.G. et al. Crohn's disease. Nat Rev Dis Primers 6, 22 (2020). Pg. 11. https://doi.org/10.1038/s41572-020-0156-2

xvii. Roda, G., Chien Ng, S., Kotze, P.G. et al. Crohn's disease. Nat Rev Dis Primers 6, 22 (2020). Pg. 5. https://doi.org/10.1038/s41572-020-0156-2

xviii. Groschwitz, K. R., & Hogan, S. P. (2009). Intestinal barrier function: molecular regulation and disease pathogenesis. The Journal of allergy and clinical immunology, 124(1), 3–22. pg. 7. https://doi.org/10.1016/j.jaci.2009.05.038

xvii. Schreiner, P., Neurath, M. F., Ng, S. C., El-Omar, E. M., Sharara, A. I., Kobayashi, T., Hisamatsu, T., Hibi, T., & Rogler, G. (2019). Mechanism-Based Treatment Strategies for IBD: Cytokines, Cell Adhesion Molecules, JAK Inhibitors, Gut Flora, and More. Inflammatory intestinal diseases, 4(3), 79–96. pg. 84. https://doi.org/10.1159/000500721

xix. Wehkamp, J. & Stange, E. F. (2020) An Update Review on the Paneth Cell as Key to Ileal Crohn's Disease. Frontiers in Immmunolgy, 11: 646. https://doi.org/10.3389/fimmu.2020.00646

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