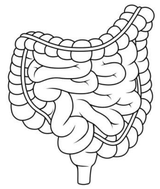

The Genetic Groundwork of Crohn's Disease

Chloe Drorbaugh, Dr. EC Cline (Mentor)

TBIOMD 492

UNIVERSITY of WASHINGTON TACOMA

INTRODUCTION

- Crohn's Disease is a chronic inflammatory bowel disease characterized by relapsing episodes of intestinal inflammation, which significantly affects patients' quality of life (Baumgart & Sandborn, 2012).
- While the specific etiology of Crohn's Disease remains unknown, both genetic predisposition and epigenetic modifications play crucial roles in its pathogenesis (Jostins et al., 2012; Howell et al., 2018).
- Advances in genetic research have identified key mutations, such as those in NOD2 and ATG16L1, that are strongly associated with disease susceptibility and progression (Hugot et al., 2001; Hampe et al. 2006).
- Emerging evidence highlights the role of epigenetic modifications, including DNA methylation and histone modifications, in regulating gene expression and contributing to immune dysregulation (Karatzas et al., 2014; Ventham et al., 2016).
- Understanding the complex interactions between genetic and epigenetic factors may pave the way for novel, personalized therapeutic approaches (Cleynen et al., 2016; Howell et al., 2018).

OBJECTIVE

In this literature review I aimed to examine how genetic mutations, specifically NOD2 and ATG16L1, as well as epigenetic modifications, like DNA methylation and histone alterations, contribute to the pathogenesis of Crohn's Disease. I also explored the ways in which these molecular mechanisms interact with environmental factors that trigger disease progression and the development of personalized therapies.

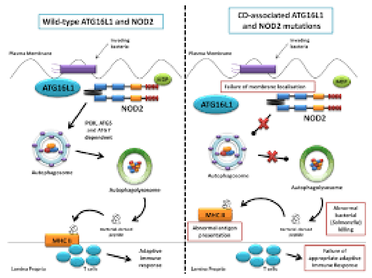

Figure 1: This figure compares the roles of wild-type and Crohn's Disease associated mutant ATG16L1 and NOD2 in bacteria sensing, authophagy process, and antigen presentation. In CD-associated mutations, defective membrane localization and impaired authophagy lead to abnormal bacterial clearance, disruption of antigen presentation, and failure to activate appropriate immune responses (Henderson et al., 2012).

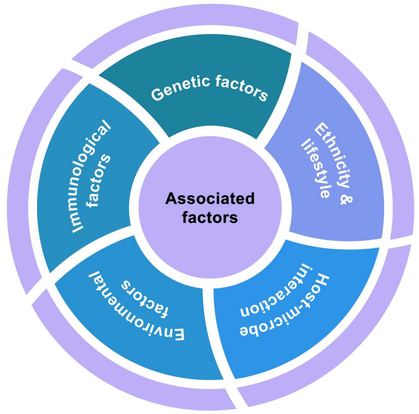

Figure 2: This figure illustrates how the nature of disease susceptibility can be due to many factors, and highlights key associated factors including genetic, immunological, environmental, host-microbe interactions, and ethnicity and lifestyle influence. These interconnected factors all collectively can contribute to the risk, onset, and progression of Crohn's Disease (Prabhu et al., 2025).

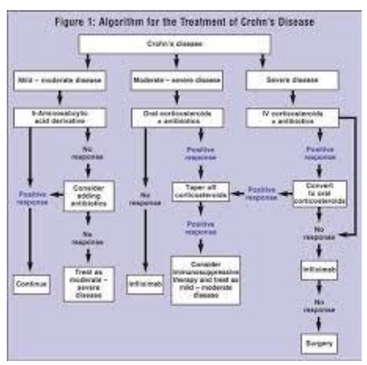

Figure 3: This figure displays the differences in treatments of Crohn's Disease, outlining the different therapeutic approaches based on disease severity in this case: mild-moderate, moderate-severe, and severe. It details stepwise management strategies based off of patient response, highlighting how therapeutic approaches differ each case (Chan et al., 2007).

RESULTS

- *NOD2* and *ATG16L1* mutations are strongly associated with increased susceptibility to Crohn's Disease and contribute to immune dysfunction (Hugot et al., 2001; Hampe et al., 2006; Rioux et al., 2007; Murthy et al., 2014).
- Epigenetic changes, including abnormal DNA methylation and histone modifications, alter gene expression patterns crucial for intestinal barrier function and immune regulation (Karatzas et al., 2014; Ventham et al., 2016; Howell et al., 2018).
- Environmental factors (e.g., diet, smoking, microbiota composition) interact with genetic and epigenetic tendencies to worsen disease severity and progression (Ananthakrishnan et al., 2017; Chassaing et al., 2015; Singh et al., 2017)
- The interaction of genetic and epigenetic disruptions leads to chronic inflammation and compromised intestinal health (Cleynen et al., 2016; Jostins et al., 2012)
- Personalized medicine approaches, including biologic therapies and emerging epigenetic modulators, show promise for targeting individual molecular profiles (Howell et al., 2018; Ventham et al., 2016)
- Further research is needed in order to validate epigenetic targets and assess long-term safety and efficacy of tailored therapeutic interventions (Ventham et al., 2016; Karatzas et al., 2014)

METHODS

To research information needed to complete the literature review on Crohn's Disease, scholarly primary and secondary articles were collected from academic databases such as PubMed and Google Scholar. These articles were to be peer reviewed and were selected based on relevance to the topic and credibility.

REFERENCES

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