# RESEARCH PROPOSAL

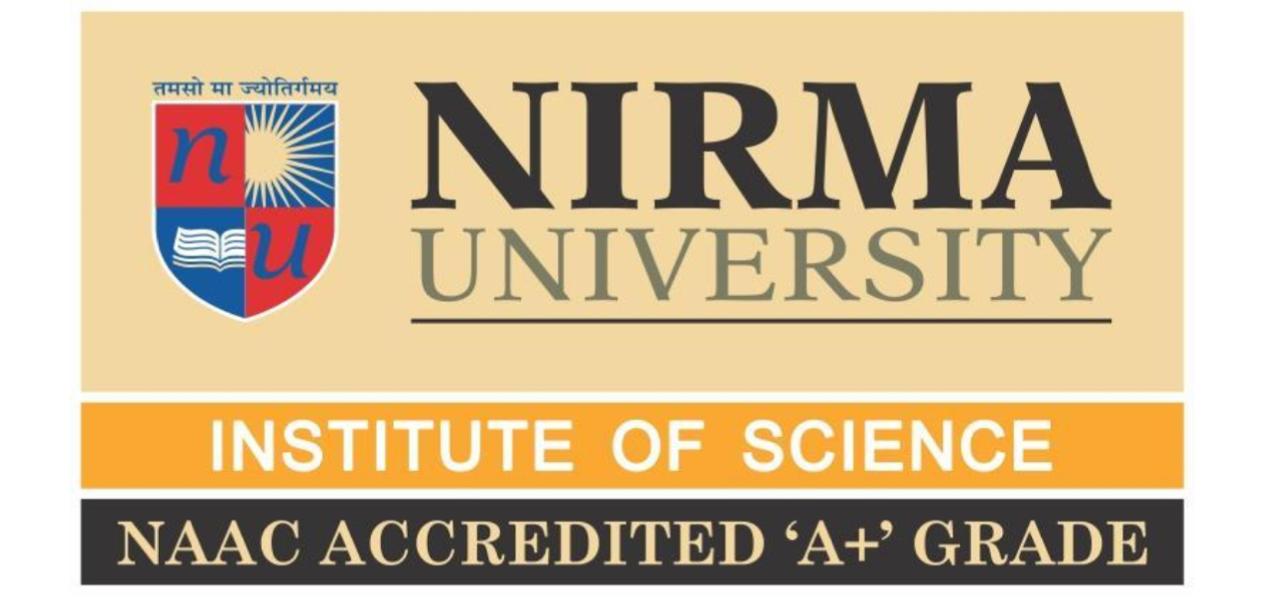
**TITLE: Gut Microbiota and Colorectum Cancer**

A Multi-Omics Approach for Microbial Biomarker Discovery and Therapeutic Insights

**SUBMITTED BY:**

**Akansha Rai**

**SUBMITTED TO:**

**Institute Of Science, NIRMA University**

# 1. INTRODUCTION

The digestive system plays a crucial role in the breakdown and absorption of nutrients and the elimination of waste. It comprises the gastrointestinal (GI) tract, which includes the mouth, esophagus, stomach, intestines, and associated organs such as the liver and pancreas. Among these, the colon is a major site of microbial colonization, hosting trillions of microorganisms that collectively form the gut microbiota.

According to the World Health Organization (WHO), CRC is the third most common cancer worldwide and the second leading cause of cancer-related mortality. The burden of CRC is steadily rising in low- and middle-income countries due to changes in lifestyle, dietary patterns, and inadequate screening programs. With most CRC cases detected at advanced stages, there is an urgent need for improved strategies for early detection and prevention.

# 2. BACKGROUND AND RATIONALE

The human gut harbors over 100 trillion microbes, including bacteria, archaea, viruses, and fungi. These microorganisms play essential roles in digestion, immune regulation, and metabolic homeostasis. Dysbiosis—a disruption in the microbial balance—has been implicated in various diseases, including inflammatory bowel disease, obesity, and cancers such as CRC.

Studies have identified specific microbes, such as *Fusobacterium nucleatum, Bacteroides fragilis*, and colibactin-producing *Escherichia coli,* as contributors to colorectal tumorigenesis. These bacteria can promote inflammation, produce genotoxins, and interfere with host cell signaling. Thus, characterizing the gut microbiome in CRC patients holds promise for discovering biomarkers for early diagnosis and designing microbiome-targeted therapies.

# 3. AIM OF THE STUDY

To investigate the alterations in gut microbiota composition and metabolic profiles associated with colorectal cancer and identify potential microbial and metabolic biomarkers for early detection and therapeutic intervention.

# 4. OBJECTIVES

* To compare gut microbiota composition between CRC patients and healthy controls using 16S rRNA gene sequencing.
* To identify differentially abundant microbial taxa and associated metabolic pathways.
* To analyze fecal and serum metabolomic profiles to identify significant metabolites linked to CRC.
* To evaluate the correlation between microbial shifts and host immune response.

**5. METHODOLOGY**

1. **Study Design:** A case-control study can be conducted involving CRC patients and healthy controls. Ethical approval and informed consent may be obtained prior to sample collection.
2. **Sample Collection:** Faecal, tissue, and serum samples can be collected under sterile conditions and stored at -80°C.
3. **Microbiome and Metabolomic Analysis:** Microbial DNA can be extracted and sequenced (16S rRNA V3-V4) using the Illumina Sequencing platform. Data may be analyzed using various software such as QIIME2 and taxonomic classification of bacterial species might be performed using one of the databases for example; SILVA database.
4. **Immune Response and Data Analysis:** Cytokine levels (IL-6, IL-10, TNF-α) can be measured by ELISA. Multi-omics data may be integrated and analyzed using PCA (Principal Component Analysis) and PLS-DA (Partial Least Squares Discriminant Analysis), and correlation networks and cluster patterns may be visualized and interpreted using R software for further results.

# 6. EXPECTED OUTCOMES

* Identification of microbial and metabolic biomarkers specific to CRC.
* Insights into the mechanistic link between dysbiosis, metabolism, and tumorigenesis.
* Development of a microbial/metabolic signature for early screening.
* Potential targets for microbiota-modulating therapies.

# 7. SIGNIFICANCE OF THE STUDY

The proposed research bridges microbiology, oncology, and bioinformatics to uncover novel aspects of CRC pathogenesis. The identification of gut microbial and metabolic biomarkers will support the development of non-invasive diagnostic tools. Furthermore, understanding host-microbe interactions may lead to personalized interventions, improving patient outcomes and reducing disease burden.

# 8. REFERENCES

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