Oral-Gut Microbiome Axis Influence Mortality and Disease progression in Colorectal Cancer

Rizwana Hasan[1], Taha Mustafa Shaikh[2], Saumitra Rawat[3], Sangeeta Choudhury[1]*

1. Department of Biotechnology & Research

2. Department of General & Laproscopic Surgery

3. Department of Surgical Gastroenterology & Liver Transplant

Background: The causal factors of Colorectal Cancer is yet not deciphered. Emerging evidences suggests oral-gut axis associated pathogens can translocate to distant sites including colon. Herein, we explored the plausible role of Periodontal microbiome in CRC progression and if yes, then can oral microbiome be a suitable CRC screening panel?

AIM: To decipher the CRC tumor-tissue derived microbiota and whether this microbial dysbiosis is linked to periodontal conditions

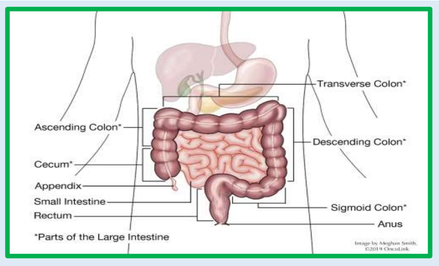


Fig. 1: Large intestine, colon and rectal

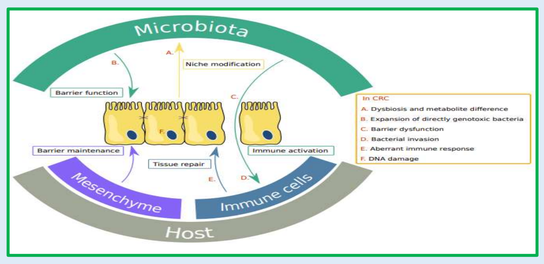


Fig.2: Molecular mechanism of colorectal cancer & dysbiosis

METHODOLOGY

Study design

Identification of CRC patient based on clinical & histopathological criteria (H & E) CRC n=25 & n=25, total No. 50

↓

CRC patients enrolled as per Inclusion/exclusion criteria

↓

Tissue sample collection (Tumor & AN)

↓

Bacterial DNA isolation from ~ 25 mg [2x2] of tissue tissue

↓

16s amplicon libraries constructed using hypervariable regions V2 to V9

↓

Sequencing using Ion 5s system-ion reporter software, Elucidation of Phyla to species using respective analytical software(Qiime2 and R programming)

RESULT

Table 1 – Demographic of CRC patients

Characteristics	Category	CRC Patients N=25 (%)
Age (32-83)	Mean ± SD	53.84 ± 16.94
BMI (18.5-24.9)		25.83 ± 5.53
Mortality		15 (60%)
Sex	Male	13 (52%)
	Female	12 (48%)
Diet	Non Veg.	19 (76%)
	Veg.	6 (24%)
Tumor location	Colon	14 (56%)
	Rectum	11 (44%)
Histopathological Grade	Poorly	5 (20%)
	Moderately	17 (68%)
	Well	3 (12%)
TNM stage	I	1 (4%)
	II	3 (12%)
	III	16 (64%)
	IV	5 (20%)
Nodal involvement	Yes	17 (68%)
	No	8 (32%)

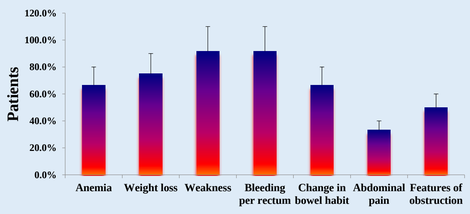


Fig. 3: Clinical symptoms

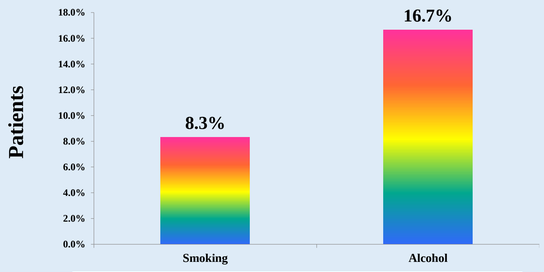
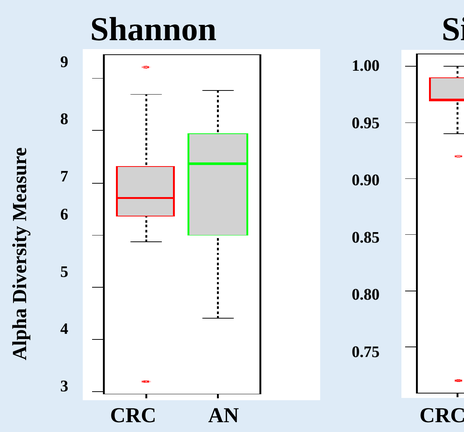


Fig. 4: Percentage of Smokers & alcoholic



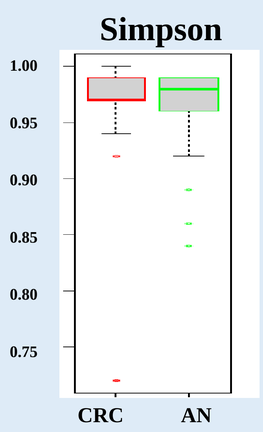


Fig.5: Alpha Diversity

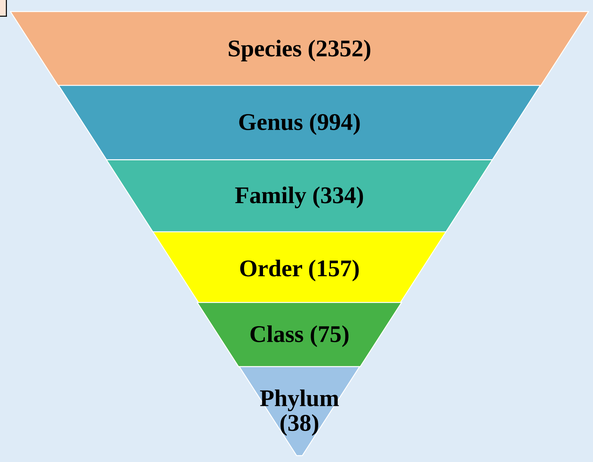


Fig. 6: Distribution of OTUs from Phyla to species

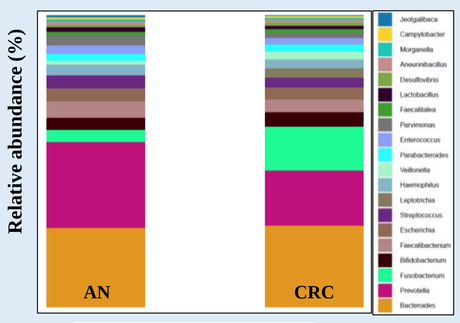


Fig.7: Genus

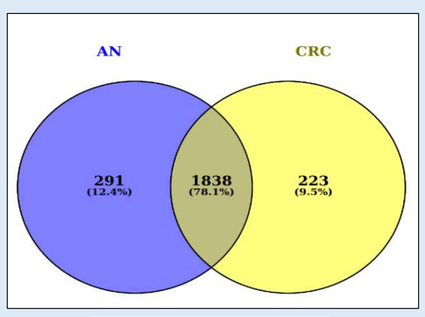


Fig.8: Venn Diagram

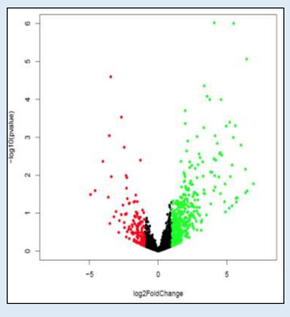


Fig.9: Volcano Plot

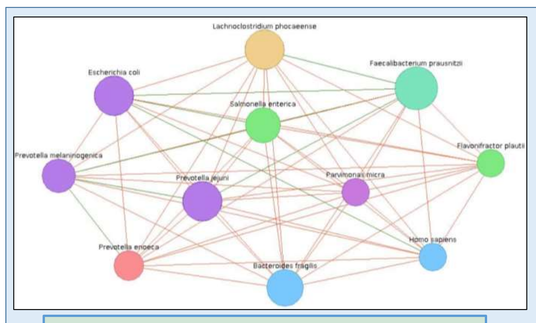


Fig. 10a: CRC species interactome

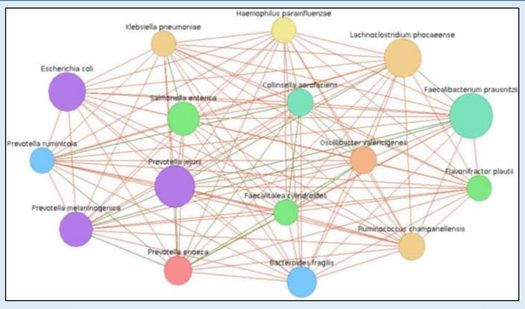


Fig. 10b: AN species interactome

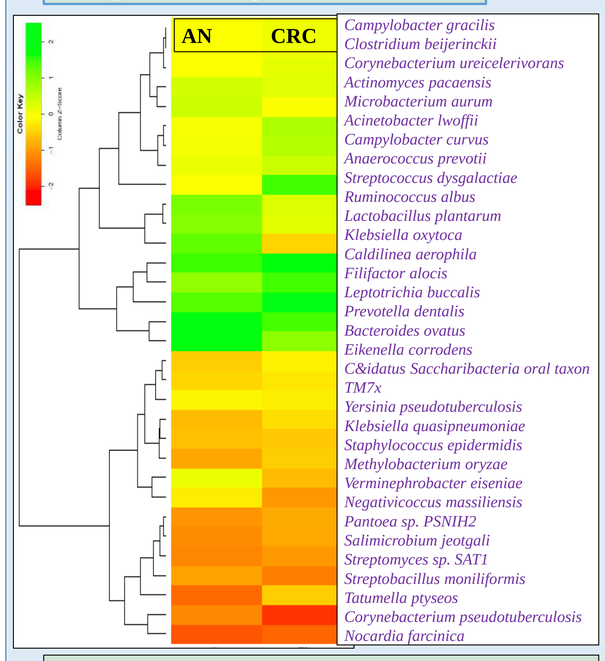


Fig. 11: Hierarchical heat-map distinguishing expression-32 significant species

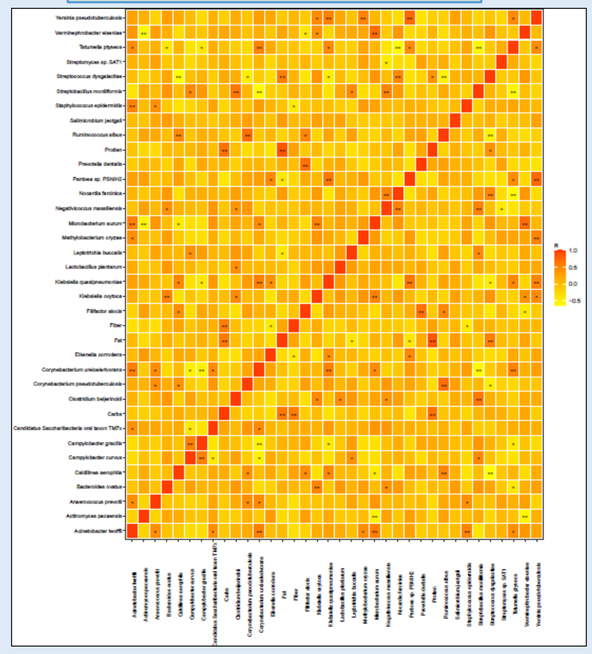


Fig. 12 Correlation Heatmap- Diet

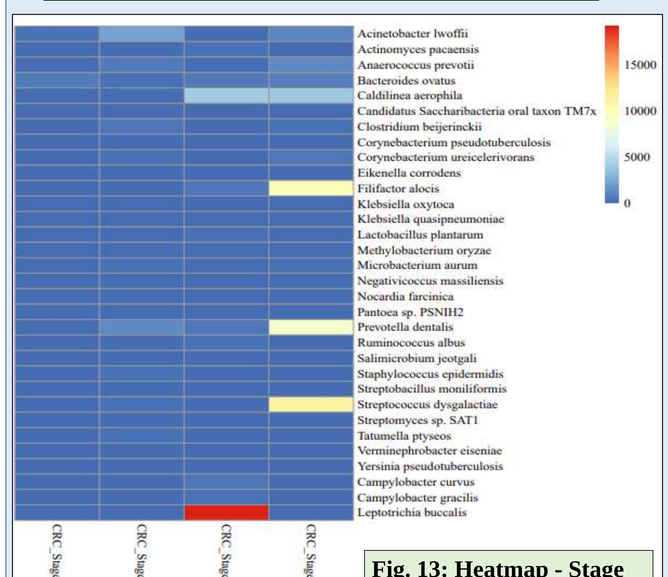


Fig. 13: Heatmap - Stage

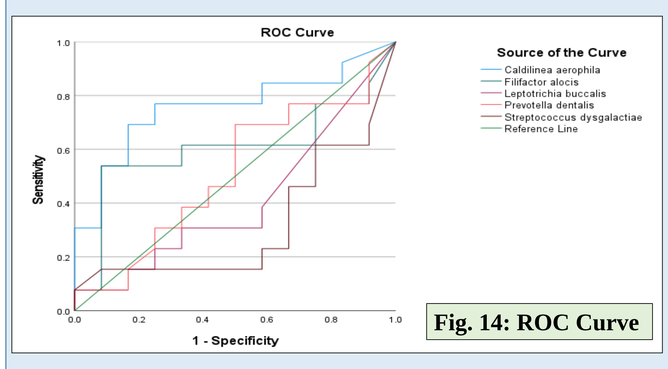


Fig. 14: ROC Curve

Species	AUC	Sensitivity	PPV	NPV	P value
Caldilinea aerophila	0.76	0.7	0.81	0.71	**0.01**
Filifactor alocis	0.6	0.53	0.88	0.647	**0.03**
Streptococcus dysgalactiae	0.68	0.23	0.27	0.28	**0.047**
Leptotrichia buccalis	0.59	0.08	0.5	0.48	1
Prevotella dentalis	0.51	0.69	0.6	0.6	0.42

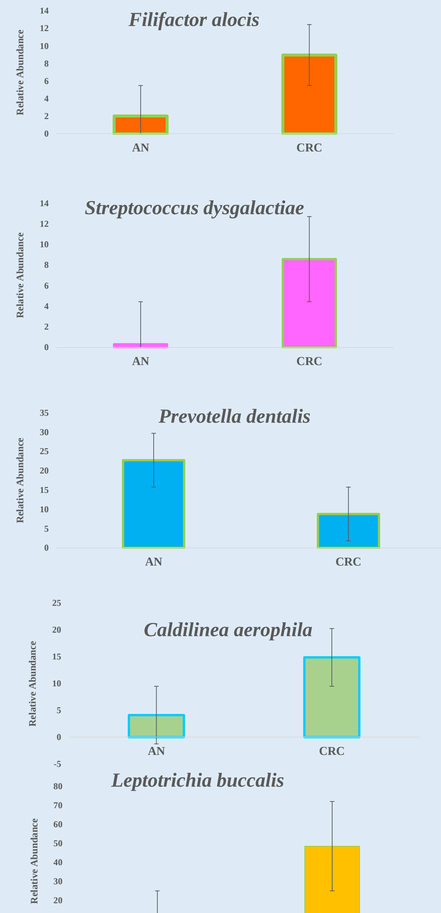
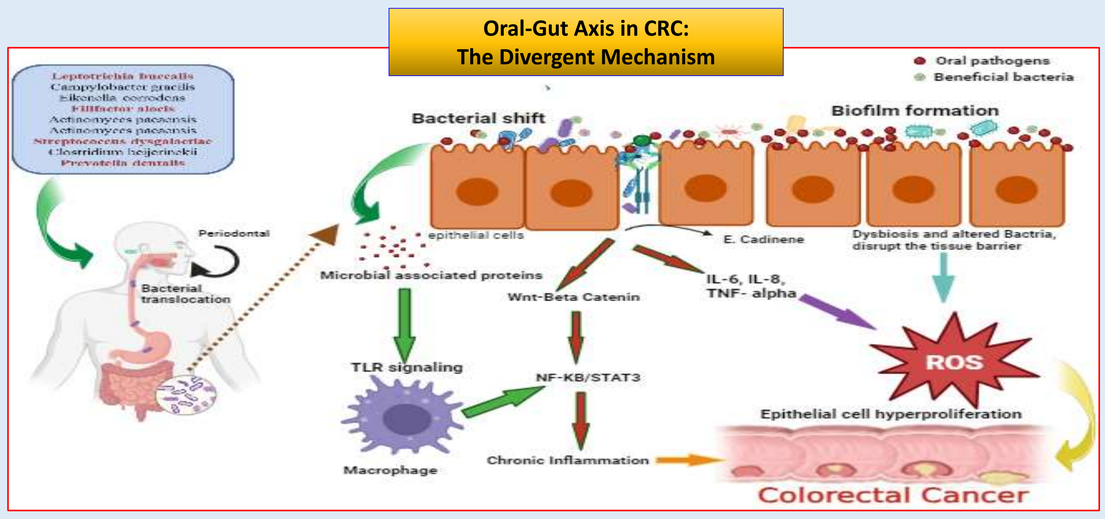


Fig. 15: Bar graphs

- ✓ Identification of *Caldilinea aerophila* & *Filifactor alocis*, & *Streptococcus dysgalactiae* as promising biomarkers for CRC prognosis.
- ✓ These species could aid in stratifying patients based on mortality risk.

Oral-Gut Axis in CRC: The Divergent Mechanism



Conclusion: Oral pathogens abundant in oral biofilms, such as Leptotrichia buccalis, Campylobacter curvus, Filifactor alocis, Streptococcus dysgalactiae, and Prevotella dentalis, may contribute to CRC development. These oral pathogens may enter the colon via saliva or the bloodstream, altering the intestinal microbiota and leading to dysbiosis. This dysbiosis triggers bacterial shifts, virulence factor production, and biofilm formation, which activate macrophages and disrupt the mucosal barrier. Pro-inflammatory cytokines like IL-6, IL-8, TNF-α, and IFN-γ enhance epithelial cell proliferation through STAT3 and NF-κB activation. Additionally, ROS release, DNA damage, and mutations occur, promoting chronic inflammation, aberrant immune responses, and further colonic epithelial damage ultimately leads to CRC.

❖ **Future:** Validate current findings in large no. of patient cohorts, for ensuring d robustness of d results.

❖ Explore interaction between host & microbiome, particularly between miRNA & mRNA.

Acknowledgement: Funding - Research development programe (4.9.36-012) (sgrh)