Review Article

Gut microbiota: Succinct overview of impacts on human physique and current research status with future aspects

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Abstract

A human body is the excellent example of symbiosis in nature. About 10^{14} bacteria reside in the human physique as commensal. These microbes make a complex community in entrails is called "gut microbiota". It is estimated that the gut flora is composed more than thousand of different species. These species have various functions in human health and recent research reports on gut microbe's community those have role in the progress and development of major human disease include cancer, obesity, diabetes, autism, mental depression, hypertension etc. In this review we focused the succinct overview on gut microbe's origin, behavior, functions, role in major human disease and the current exploration circumstance with next generation perspective.

Keywords: *entrails, microbes, microbiota, parasite, immunity, probiotics, diversity, symbiotic, host, dysbiosis.*

Introduction

Like the other symbiotic relationships, human subsistent in a symbiotic relationship with entrails microbiota where human physique provide certain amount nutrition for exist microbes whilst exchange they help in various functions of host (Geurts *et al.* 2013). In this symbiotic relationship's microbiota ecosystem composed by bacteria, virus, fungi and various type of parasites (Hugon *et al.* 2015). The entrails microbes harbours at least 10^{11} to 10^{12} prokaryotes per gram in stool and it's structure varies with physiologic factor such as dietary habit, age etc(Sullivan *et al.* 2001).The research on human gut microbes has exploded during the last decade this microbiota has various role in metabolism, human health, immunity within host (Marchesi *et al.* 2015). Almost 70 disease including for irritable bowel syndrome(IBS)(Malinen *et al.* 2010), instance obesity (Ley *et al.* 2006), diabetes type1 (Fallani *et al.* 2010), cancer Arthur *et al.* 2012), autism and depression (De *et al.* 2019, Fond *et al.* 2015, Zhou and Foster 2015, Natividad and Verdu 2013, de Silva *et al.* 1991, Wang and Kasper 2014), hypertension (Yang *et al.* 2015), gout, arthritis,

ulcer, Alzheimer's disease etc. are directly and indirectly engaged with gut microbiota (Vogt *et al.* 2017). Moreover, this microbiota has been detected and proposed as a key modulator of human health (Kashyap *et al.* 2017, Wang *et al.* 2017).While certain amount changes of this microbiome composition known as "dysbiosis" has been explained the various kind of disease (Lloyd-Price *et al.* 2016). It is the aim of this work to critically review and summarize recent literature reports on gut microbiota characteristics, functions, role in disease and current research status with future perspectives.

Concise characteristics of entrails Microbiota:

In general, the human body remain fully sterile at birth, is starting to colonize various microbes is forthwith in contact with fecal,vaginal and skin microbiota of mother where a large amount of microbial community remain (Scaldaferri *et al.* 2012, Round *et al.* 2010).

The number of microbiota changes overtime during the dietary habit change, probiotics, prebiotics and various kind of antibiotic uses (Quigley E M 2013, Shen *et al.* 2016).

As high concentration acids are secreted on stomach and PH remain very low, the most microorganisms cannot survive there. Normally they inhabit in the last portion of small intestine and whole large intestine. Particularly, red shaped bacteria and gram-positive bacteria remain in large amount in the small intestine and the alkali environment remain in large intestine where gram negative bacteria is the dominant group (Sherwood *et al.* 2013).

The most part of entrails community inhabit on colon and about 60% dry mass of stool (UoG 2005).

The major microbes in entrails microbiota:

Prokaryotic diversity: Different species within genera *Bacteroidetes, Bifidobacterium, lactobacillus, fusobacterium, peptostreptococcus* were dominate at the entrails microbiome community (Mata *et al.*

1969). Pertaining prokaryotic diversity in host, at least 120 several prokaryotic phyla have been detected and only 31 phyla are cultured species. Moreover, a large number of several species isolated from entrails belong to four phyla *Fermicutes, Proteobacteria, Actinobacteria, Bacteroidetes* (Hugon *et al.* 2015).

The Archaeal diversity :

The archaea diversity constructed the third domain of life different from bacteria and eukarya (Woese *et al*1990). Finally 8 archaeal species have been identified in human entrails microbial community (Rajilic-Stojanovic and de Vos 2014). *Methanobrevibacter ruminantium* Nottingham and Hungate 1968), *Methanobrevibacter smithii* (Dridi *et al.* 2009), *Methanosphaera stadtmanae* (Millar *et al.* 1985), *Methanomas siliicoccus luminyensis (*Dridi *et al.* 2012) are the major species in human gut.

Human entrails virome diversity :

Bacteriophage with double stranded DNA that belong to the order *Caudovirales* are abundant in gut microbiota and *Microviridae* bacteriophage which is single stranded DNA are also remain large amount in human gut (Foca *et al.* 2015). Many viruses those are DNA or RNA including *Astorovirus, Rotaryvirus, Calcivirus* also found in human gut (Klein *et al.* 2006).

The Eukaryotic diversity :

In human gut the taxonomy of eukaryotic community is complex (Clarke *et al.* 2014, Gibson and Glenn 2004). The five major groups are *Amoebazoa, Opisthokanta, Sar, Archaeolastida* and *Excavata* are dominant group in gut microbial community (Adl *et al.* 2012). In general fungal species including Yeasts and Filamentous fungi are dominant group. The common eukaryotic organisms are *Candida albicans, Candida rugosa, Saccharinyces cerevisiae* etc also present here (Rajilic-Stojanovic and de Vos 2014, Adl *et al.* 2012).

Table 1: Prokaryotes and Eukaryotic in the human gut

Phyla	Family
Prokaryotes in human gut	
Actinobacteria	*Bogoriellaceae, Brevibacteriaceae, Dermacoccaceae, Dermatophilaceae, Dietziaceae, Geodermatophilaceae, Nocardioidaceae, Promicromonosporaceae, Propionibacteriaceae, Streptomycetaceae*
Bacteroidetes	*Flavobacteriaceae, Porphyromonadaceae, Prevotellaceae, Rikenellaceae, Sphingobacteriaceae*
Firmicutes	*Carnobacteriaceae, Catabacteriaceae, Christensenellaceae, Clostridiaceae, Clostridiales, Enterococcaceae, Erysipelotrichaceae Eubacteriaceae, Lachnospiraceae*
Proteobacteria	*Desulfovibrionaceae, Enterobacteriaceae, Francisellaceae, Halomonadaceae, Helicobacteraceae, Legionellaceae, Methylobacteriaceae, Moraxellaceae, Neisseriaceae, Oxalobacteraceae, Pasteurellaceae, Pseudomonadaceae, Rhizobiaceae, Rhodobacteraceae, Salinisphaeraceae, Shewanellaceae, Sphingomonadaceae, Succinivibrionaceae*
Eukaryotes in the human gut	
Fungi	*Candida albicans, Candida famata, Candida glabrata, Candida guilliermondii, Candid kefyr, Candida krusei, Candida lambica, Candida lusitaniae, Candida norvogensis, Candida parapsilosis, Candida pararugosa*
Helminths	*Ancylostoma duedonale, Necator americanus, Strongyloides stercorali*
Protozoa	*Endolimax nana, Entamoeba coli, Entamoeba dispar*

The major functions of entrails microbiota :

In metabolic system : Human would be unable to metabolize all consumed polysaccharide without gut microbiota. Because some important microorganism release some enzymes that breakdown these undigested certain type of polysaccharide (Clarke *et al.* 2014). Some bacteria convert the carbohydrate into short chain fatty acid by fermentation process (Gibson and Glenn 2004).

Braking the disease causing agent : By fully colonizing and secreting compounds the entrails flora play an important role in defending against the unwelcome microbes for human body (Yoon *et al.* 2014).

Improvement of protection in immune system : In human physique, the immune system produce the cytokines to create inflammation in order to protect from pathogen (Sommer and Bäckhed 2013).Several bacterial species such as Bacteroides fragilis and some Clostridia help to produce inflammatory cytokines (Reinoso *et al.* 2016). Gut microbes also play an important role in production of antibody (Mantis *et al.* 2011).

Bidrectional network Brain axis -gut microbiota: Entrails microbial community act as signaling system between Central Nervous System (CNS) and Gastrointestinal tract (GIT) (Wang *et al.* 2014). Through the bidirectional communication system, signal from the cerebrum increase the motor, secretory modalities of entrails and conversely the signal from entrails can increase the brain activity (Grenham *et al.* 2011, Montiel *et al. 2013).*

Table 02: Gut microbial products and their potential functions

Microbial Products Functions		References
Propionates, butyrates	Antineoplastic	Waldecker *et al.* 2008
LCA	Binds to the vitamin D receptor and acts as detoxifying agent	Sun *et al.* 2008
Endotoxin	Changes gut permeability, causes insulin resistance	Fei and Zhao 2013
SBA	Activates the nuclear famesoid X receptor (FXR) and protects against muscle fat deposition	Cipriani *et al.*2010
Capsular polysaccharides (PSA)	Prime T cell response	Mazmanian *et al.*2008
DCA	Causes gallstone formation	Thomas *et al.* 2000
Butyrates (SCFA)	Reduces inflammation and prevents ulcerative colitis	Machiels *et al.* 2013

Roles impact on human health disease :

Roles on Neuropsychiatric and depression:
The dysbiosis and consequent alteration of gut flora produce and spread within bloodstream a potent pro-inflammatory endotoxin, called "lipopolysaccharide(LPS).This small molecule have has an important role in modulation of Central Nervous System (CNS).increase the activity of emotionalism control such as amygdale (Haba *et al.* 2012). It also produce the cytokines that change the physiological activity of brain (Kastin and Pan 2010).

Involved in cancer: Gut microbiota have role in various cancer as carcinogenic agent (Mager 2006). Bacteroides fragilis which is enterotixigenic that associated with colorectal cancer (Goodwin *et al.* 2011, Marchesi *et al.* 2011). Fusobacterium nucleatem also play role in colorectal cancer (Castellarin *et al.* 2011).

Table 03: Gut microbiota and associated cancers.

Type of Cancer	Connected Microbe	References
Breast cancer	*Staphylococus, Enterobacter*	Ubraniak *et al.*2016
Gastric cancer	*Helcobacter pylori*	Huang *et al.* 1998
Liver cancer	Hepatitis B virus, hepatitis C virus	Parkin2016
Colon cancer	*Citrobacter rodentium*	Newman *et al.* 2001
Cervical cancer	*Human papillomavirus alpha type*	Bouvard *et al.* 2009
MALT lymphoma	*H. pylori*	Cavanna *et al.* 2008
Colorectal cancer	*Streptococcus bovis*	Burnett-Hartman *et al.* 2008

Role in Autism: Through some investigation on autistic children it exploded that some entrails microbial species is linked with autism Finegold *et al.* 2002, Song *et al.* 2004, Parracho *et al.* 2005. The alteration of gut microbiota is directly connected with this disease. Specially Fermicutesc,Bacteroidetes phyla as well as and other entrails commensal such as *Bifidobacterium, Sutterella, Prevotella, Lactobacillus,Ruminococcus* genera play major role in this disease (Finegold *et al.* 2010, Adams *et al.* 2011, Kang et al. 2013, Wang et al. 2013,Williams et al. 2012).

Role in obesity : Through the both in vitro and in vivo studies suggested that the entrails microbiome is directly connected with obesity and play the key role in development of obesity (Le *et al.* 2013, Sonnenburg and Backhed 2016). Imbalance of *Bifidobacterium,Lactobacillus,Enterococcus,Bacteroides,Prevotella* community develop the obesity of host (Zheng *et al.* 2018).

Role in Inflammatory Bowel Syndrome(IBS): Entrails microbiota is responsible for this disease specially *Firmicutes,Ruminococcus,Clostridium,Dorea,Bifidobacterium,Faecalibacterium* genera develop the IBS for being the alteration of normal level in gut (Rajilic-Stojanovic *et al.* 2011).

Role in Hypertension : Recent research evidence have claimed that entrails microbiome is the key modulator to maintain the physiological homeostasis. Dysbiosis particularly, increasing the diversity of *Fermicutes,Bacteroidetes* ratio are directly associated with development of hypertension (Yang *et al.* 2015).

Role in Diabetes Type 1: The alteration of *Clostridium* genus (Allin *et al.* 2018) and *Akkermanisa muciniphila* level in the gut microbiome is responsible for developing the type-1 diabetes (Hanninen *et al.* 2017).

Role in Gout: Comparism between normal human and gout patient, scientists revealed that the higher level *Bacteroides caccasae,Bacteroides* xylanisolvens are present in gout patient. Again *Bifidobacterium pseudocatenulatum* and *Faecalibacterium prausnitzii* were found in lower number in gout patient (Jie *et al.* 2017).

Cardiovascular disease : The entrails microbiota also have been associated with Atherosclerotic Cardiovascular Disease (ACVD),specially *Enterobacteriaceae* and *Streptococcus* species is associated with ACVD (Jie *et al.* 2017).

Alzheimer's disease(AD) : Through the investigation of Alzheimer's patient it revealed that the alteration of *Fermicutes, Bifidobacterium* and *Bacteroidetes* were connected and increased the AD(Vogt *et al.* 2017).
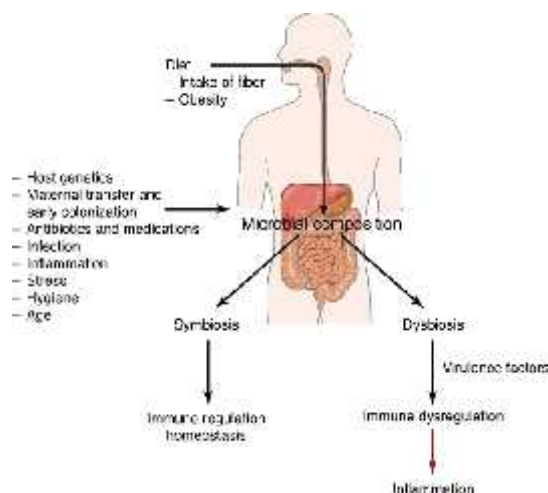

Figure 1:Process of gut microbiota impact on human health (Maslowski *et al.* 2011)

Current research status and future aspects on gut microbiota:

The current goal is to differentiate the host microbiota enabling the investigation of it's variation according to factors such as genotype,profile,nutrition, population as well as exposure to.mediation. The worldwide globally scientific and commercial interest on interaction between human and it's associated microbes (Seksik *et al.* 2006; Sokol *et al.* 2007; Penders *et al.* 2007). In the last decades, there has been a bulge in research on gut microbiota and revealed how microbiome community interfere on human health and disease progression (Fischbach MA 2018). Based on.analysing the interaction on synthetic entrails microbiota called a "bottom up" approach that using the Lota-voltermodel has been claimed the interaction pathway and mechanism of gut microbial community. Therefore, this is may be more appropriate to predict the ability of specific probiotics to persist in entrails (Abreu *et al.* 2018; Venturelli *et al.* 2018). In recent studies shown that the use of both symbiotics and multistrain probiotics confer the longer lasting effectiveness compared to single species probiotics. It could be an emarging and interesting research area in future (Bambury *et al.* 2018). Additionally, it could be also interesting to invent the safe and much beneficiable probiotics (Bafeta *et al.* 2018). Also it would be more effective against the various disease is manipulate the microbiome in entrails to improve the human health (Joglekar and Segre 2017).

Conclusion:

Albeit the symbiotic relationship of a human body with gut micorbes has been explored for decades, recent research on gut microbiota revealed the various unknown functions and role in human health. This community contains the ten fold more cells than the human body and 100 times the count of genes than the human genome. This entrails community play directly or indirectly almost all type of major severe human disease.   At present researchers finding the interaction pathway of gut microbes for establish the treatment procedure more efficient and effective than others conventional procedure by inhibiting or

regulating these metabolic intersection pathway.

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Conflicts of Interest: The authors declare that the research review was conducted in the absence of any commercial or economic associations that could be construed as a potential conflict of interest

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