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RESEARCH ARTICLE

DECIPHERING HEALTH INSIGHTS: INVESTIGATING METABOLOME INTERACTIONS FOR BIOMEDICAL APPLICATIONS

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Abstract

Metabolic regulations form the intricate web of diverse pathways within the human body, orchestrating the execution of vital physiological and biological processes. This study explores the potential of therapeutic interventions through the manipulation of novel metabolic pathways, showcasing the emerging field of metabolic engineering.Metabolic regulations encompass the diverse and numerous metabolic pathways within the human body. The interplay of these pathways is crucial for the proper execution of various physiological and biological processes. Addressing the challenges posed by diseases, the manipulation of novel metabolic pathways highlights the potential of metabolic engineering in therapeutic interventions. A comprehensive grasp of metabolic functions in the human body can be gleaned through simulated yeast models. These models provide insight into the intricate interactions among molecular metabolomes, shedding light on their complexity.By providing a comprehensive grasp of these interactions, simulated yeast models serve as invaluable tools for researchers seeking to decipher the intricacies of metabolic regulationsThe article concludes by highlighting the broader implications of this knowledge in advancing our comprehension of metabolic processes and its transformative potential in addressing various health conditions.

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Introduction:-

As a central hub or an area concentrated with majority of metabolic reactions, it can be understood from the studies of the gut that systemic metabolism in human is not just regulated by their genes and their personal dietary habits but also by gut microbes [1].If the gut microbiota present in the body is in a state of intestinal dysbiosis, certain micro-organisms like *E.coli*can be engineered and modelled metabolically to improve the functioning and growth of the indigenous microbiome [2].The role of microorganism is widely being known and explored in the recent years due to their exploitable advantages and disadvantages that are meant to be kept in check [3]. Apart from different cohorts and divisions of microbiota present, a decent understanding and knowledge about the gut microbiota present in the human digestive system is required to evaluate, explore and treat the different diseases related to the human intestine tract [4]. A proper balance in the growth and bioactivity of different intestinal flora is required for the

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homeostasis of the human biological system [5]. A metabolic pathway is basic for every disease or any biological function that takes place in the body [6]. So, study about these metabolic pathways and identifying the metabolites involved in them as markers helps in easy diagnosis and treatment of different diseases [7]like Non-small cell lung cancer and Anaplastic large cell lymphoma (ALK), Alpha-fetoprotein (AFP) - Liver cancer andgerm cell tumours, Beta-2 – microglobulin (B2M) - Multiple myeloma, chronic lymphocytic leukemia, and some lymphomas and problems faced by the organism [8].

Role Of Metabolites In Precision Medicine

It is known from statistics that out the many people who are being treated with a disease only few of them are responding to the treatment and some are not. As an example, when it comes to the radiotherapy and immunotherapy for the treatment of different cancers, only a handful people are being cured. This is because not every individual's body responds in the same way. So, this is where the concept of precision medicine comes in to picture [9]. With the required biomarkers and companion (diagnostic tests used as a companion to a therapeutic drug to determine its applicability to a specific patient), researchers based on the patient's disease progression and other key factors can stratify patients in to subsets [10]. This facilitates in the better prediction of disease outcomes so that appropriate treatment regimens can be formulated for the different sub groups identified. In turn, stratified medicine can give rise to precision medicine, where treatment is tailored for each patient according to their medical history, results from other tests, their response to medication and other clinical features [11].In this respect there are a set of plant derives secondary metabolites like Vinblastine [12], Capsaicin [13], Curcumin[14] which are of medicinal impotence. These metabolites can be harnessed by modifying their respective metabolic pathways so that these metabolites are produced in large amounts. As a result, they can be commercially produced in large amounts and aid in the treatment of different diseases [15].

Gut Microbiota – Impacting Flora In Human Body

The fluctuation seen in the growth of different gut microbiota can be due to host genotypes, physiological status, diet, drugs, and living conditions. The system formed as a combination of both the gut microbiota and the human system is called a "Superorganism" [16]. Based on the effects they induce; gut microbiota can be divided into 3 groups: - 1) beneficial bacteria 2) conditional pathogenic bacteria 3) pathogenic bacteria. As per the growth and functioning of different classes of gut microbiota listed above it results in the different diseases and ill effects of the gut and organs concerned to it like the liver and the gall bladder.

Scfa And Gut Microbiota

In general, the food that enters into the digestive system is partly digested by the digestive enzymes and partly by the gut microbiota. The complex carbohydrates that entering the human gut is fermented into SCFA (small chain fatty acids) via the gut microbiota which further promotes the process of intestinal gluconeogenesis, and the formation of lipids [17]. This SCFA produced is known to play certain significant role in host organisms by improving the intestinal functioning, increases the resistance against pathogenic microorganisms, fight tumours, maintaining the electrolyte balance of the host and they also provide energy to the host epithelial cells [19]. Anotherintriguing factor about the gut microbiota is found out through a study that the peroxisome proliferation receptor-ɣ (PPAR-ɣ) signal induced by them is the one responsible for maintaining homeostasis. The compound that is responsible for the transduction of PPAR-ɣ is butyrate which is mainly produced by the metabolism of Clostridia. Butyrate also decreases the production of TGF-β1 and IL-6, increases the activity of cytokines (anti-inflammatory) and by inducing the T cells enhances body immunity through anti-inflammatory effects [19].

It was further known that the *Bifidobacteriaceae*in the intestine of the mice have started to increase in number after the treatment with oligofructose weakened the weight gain, fat accumulation and ameliorated metabolic disorders induced due to high fat diet in mice [20]. *Akkermansiamuciniphila*is microbewhose abundance in the gut is closely related with the health of the host. It majorly survives on the intestinal mucin as the only carbon and nitrogen source with its main metabolite being propionate (SCFA) and its intestinal abundance is around 1-3%. These bacteria with its metabolite are seen to have their effect in the inflammatory responses of obese and diabetic patients, improve adverse symptoms such as insulin resistance and glucose tolerance [21].

Gut Microbiota- A Regulative Biome For Many Diseases

A comprehensive study on gut microbiota can give us a idea about different diseases on which the gut microbiota can have their effect [22]. If seen every disease has its own specific microbial markers for the targeted treatment of diverse diseases. In this point of view Louis et al. found out that, in a weightloss problem conducted the

Firmicutes/Bacteroidetes was high in obese patients [23] and the *Akkermansia*an intestinal microbiota abundance was found in successful weight loss patients [24]. Additionally, it was also found that the *Lactobacillus* additives maintain homeostasis and reduced body weight considerably [25].Similarly, when it comes to liver diseases and liver cirrhosis, compared to healthy individuals the significant increase in the number of *Enterobacteriaceae*, *Enterococcus* species and *Proteus* species were found in patients with liver cirrhosis [26]. Seen at the pathogenesisof gastrointestinal diseases the microorganisms like Enteritoxigenic*B. fragilis* induced inflammatory responses in colorectal cancer (CRC) mouse models [27]. In this disease model it was also found out that the colon epithelial regeneration was hindered to an extent due to the low availability or absence of *Bifidobacterium*[28].

Conclusion:-

From above mentioned strategies using metagenomics it is clear that it has become a powerful technology in analyzing the gut microbiota and in understanding its relationship with host. But there are some limitations. It is not an easy task to know the expression of microbial systems and it also requires higher sequence coverage. The time and cost are also considerable constraints for limitations.Among above all limitations mentioned above getting highly purified and high-quality DNA samples is important because there may be 50% of human contaminants in DNA sample selected

References:-

1. Milani C, Duranti S, Bottacini F, Casey E, Turroni F, Mahony J, Belzer C, Delgado Palacio S, Arboleya Montes S, Mancabelli L, Lugli GA. The first microbial colonizers of the human gut: composition, activities, and health implications of the infant gut microbiota. Microbiology and molecular biology reviews. 2017 Dec 1;81(4):e00036-17.
2. Kumar VP, Prasanthi S, Lakshmi VR, Santosh MS. Cancer vaccines: a promising role in cancer therapy. Acad J Cancer Res. 2010;3(2):16-21.
3. Zhang L, An R, Wang J, Sun N, Zhang S, Hu J, Kuai J. Exploring novel bioactive compounds from marine microbes. Current opinion in microbiology. 2005 Jun 1;8(3):276-81.
4. Marchesi JR, Adams DH, Fava F, Hermes GD, Hirschfield GM, Hold G, Quraishi MN, Kinross J, Smidt H, Tuohy KM, Thomas LV. The gut microbiota and host health: a new clinical frontier. Gut. 2016 Feb 1;65(2):330-9.
5. Soetan KO, Olaiya CO, Oyewole OE. The importance of mineral elements for humans, domestic animals and plants-A review. African journal of food science. 2010 May 31;4(5):200-22.
6. Fadeel B, Orrenius S. Apoptosis: a basic biological phenomenon with wide-ranging implications in human disease. Journal of internal medicine. 2005 Dec;258(6):479-517.
7. Mamas M, Dunn WB, Neyses L, Goodacre R. The role of metabolites and metabolomics in clinically applicable biomarkers of disease. Archives of toxicology. 2011 Jan;85(1):5-17.
8. Padmavathi G, Bordoloi D, Banik K, Kunnumakkara AB. Cancer biomarkers: important tools for cancer diagnosis and prognosis. InNext Generation Point-of-care Biomedical Sensors Technologies for Cancer Diagnosis 2017 (pp. 1-29). Springer, Singapore.
9. Collins FS, Varmus H. A new initiative on precision medicine. New England journal of medicine. 2015 Feb 26;372(9):793-5.
10. Trusheim MR, Burgess B, Hu SX, Long T, Averbuch SD, Flynn AA, Lieftucht A, Mazumder A, Milloy J, Shaw PM, Swank D. Quantifying factors for the success of stratified medicine. Nature reviews Drug discovery. 2011 Nov;10(11):817-33.
11. Trusheim MR, Berndt ER, Douglas FL. Stratified medicine: strategic and economic implications of combining drugs and clinical biomarkers. Nature reviews Drug discovery. 2007 Apr;6(4):287-93.
12. Wright JR. Almost famous: E. Clark Noble, the common thread in the discovery of insulin and vinblastine. Cmaj. 2002 Dec 10;167(12):1391-6.
13. Olatunji TL, Afolayan AJ. Comparison of nutritional, antioxidant vitamins and capsaicin contents in Capsicum annuum and C. frutescens. International Journal of Vegetable Science. 2020 Mar 3;26(2):190-207.
14. Nelson KM, Dahlin JL, Bisson J, Graham J, Pauli GF, Walters MA. The essential medicinal chemistry of curcumin: miniperspective. Journal of medicinal chemistry. 2017 Mar 9;60(5):1620-37.
15. Tatsis EC, O’Connor SE. New developments in engineering plant metabolic pathways. Current opinion in biotechnology. 2016 Dec 1;42:126-32.
16. Salvucci E. The human-microbiome superorganism and its modulation to restore health. International journal of food sciences and nutrition. 2019 Oct 3;70(7):781-95.

17. Morrison DJ, Preston T. Formation of short chain fatty acids by the gut microbiota and their impact on human metabolism. Gut microbes. 2016 May 3;7(3):189-200.
18. Woting A, Blaut M. The intestinal microbiota in metabolic disease. Nutrients. 2016 Apr;8(4):202.
19. Arpaia N, Rudensky AY. Microbial metabolites control gut inflammatory responses. Proceedings of the National Academy of Sciences. 2014 Feb 11;111(6):2058-9.
20. Vemuri PK, Velampati RH, Tipparaju SL. Probiotics: a novel approach in improving the values of human life. Int J Pharm Pharm Sci. 2014;6(1):41-3.
21. Vemuri PK, Dronavalli L, Nayakudugari P, Kunta A, Challagulla R. Phytochemical Analysis and Biochemical Characterization f Terminalia Chebula Extracts For its Medicinal use. Biomedical and Pharmacology Journal. 2019 Sep 25;12(3):1525-9.
22. Shen TC. Diet and gut microbiota in health and disease. Intestinal microbiome: functional aspects in health and disease. 2017;88:117-26.
23. Magne F, Gotteland M, Gauthier L, Zazueta A, Pesoa S, Navarrete P, Balamurugan R. The Firmicutes/Bacteroidetes ratio: a relevant marker of gut dysbiosis in obese patients?. Nutrients. 2020 May;12(5):1474.
24. Peat CM, Kleiman SC, Bulik CM, Carroll IM. The intestinal microbiome in bariatric surgery patients. European Eating Disorders Review. 2015 Nov;23(6):496-503.
25. Kalavathy R, Abdullah N, Jalaludin S, Ho YW. Effects of Lactobacillus cultures on growth performance, abdominal fat deposition, serum lipids and weight of organs of broiler chickens. British Poultry Science. 2003 Mar 1;44(1):139-44.
26. Grąt M, Wronka KM, Krasnodębski M, Lewandowski Z, Kosińska I, Grąt K, Stypułkowski J, Rejowski S, Wasilewicz M, Gałęcka M, Szachta P. Profile of gut microbiota associated with the presence of hepatocellular cancer in patients with liver cirrhosis. InTransplantation proceedings 2016 Jun 1 (Vol. 48, No. 5, pp. 1687-1691). Elsevier.
27. Leystra AA, Clapper ML. Gut microbiota influences experimental outcomes in mouse models of colorectal cancer. Genes. 2019 Nov;10(11):900.
28. Sela DA, Price NP, Mills DA. Metabolism of bifidobacteria. Bifidobacteria: genomics and molecular aspects. 2010 Dec 20:45-70.