

## ABSTRACT

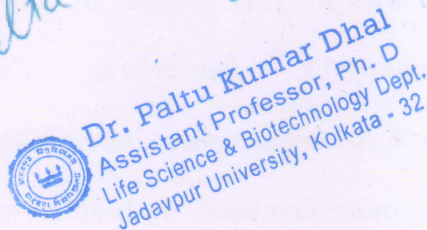
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**Title: Characterization of gut microbiota of the Indian Type 2 Diabetic patients:  
Sustainability of Human Health**

Type 2 Diabetes (T2D) is a severe global public health issue due to the rising incidence of overweight/obesity and poor lifestyles in the twenty-second century. The relationship between changed gut flora and a higher incidence of T2D is well addressed by several epidemiological studies. Understanding of the causative gut microbiota and their interaction with host as well as important host physiological parameters for early detection of disease are emerging research topic for the better management of T2D. With this view this study aimed to develop efficient models for identifying essential physiological markers for improved T2D classification using machine learning algorithms. In addition to that using amplicon metagenomic approaches, an effort has also been made to understand the alterations in core gut microbial members in Indian T2D patients with respect to their control (NGT). Our data indicate the level of fasting blood glucose (FBG) and glycated hemoglobin (HbA1c) were the most useful physiological indicators while Random Forest (SEN: 1.00; ACC: 0.76) and Support Vector Machine with RBF kernel (SEN: 1.00; ACC: 0.67) were effective predictions models for identifications of T2D. *Prevotella\_9*, *Alloprevotella*, *Bacteroides*, *PrevotellaIncertaeSedis*, *Rikenellaceae RC-9 gut group*, *Eubacterium*, *UCG-002*, *Phascolarctobacterium*, and *Asteroleplasma* genera were the most dominant gut microbial members in T2D disease. In contrast *Prevotella*, *Roseburia*, *LachnospiraceaeIncertaeSedis*, *Butyrivibrio*, *Faecalibacterium*, *Klebsiella*, *Succinivibrio*, *Megasphaera*, *SelenomonadaceaeIncertaeSedis*, *Treponema*, and *Akkermansia* genera were the most dominant in healthy individuals. The

dominating gut microbial members *Alloprevotella*, *Rikenellaceae RC9 gut group*, *Haemophilus*, *Ruminococcustorques group*, etc. in Indian T2D patients showed a strong association with both FBG and HbA1c. These members have been reported to have a crucial role in gut barrier breakdown, blood glucose, and lipopolysaccharide level escalation, or as biomarkers. While the dominant NGT microbiota (*Akkermansia*, *Ligilactobacillus*, *Enterobacter*, etc.) in the colon has been shown to influence inflammatory immune responses by acting as an anti-inflammatory agent and maintaining the gut barrier. The co-occurrence network analysis indicates that changes in network complexity in T2D lead to variations in the different gut microbial members compared to NGT. *Firmicutes*, *Bacteroidota*, *Proteobacteria*, *Actinobacteriota* and *Spirochaetota* gut microbial phyla network were identified as keystone taxa in T2D co-occurrence network. In contrast, *Bacteroidota*, *Firmicutes*, *Proteobacteria*, *Patescibacteria* and *Desulfobacterota* as keystone microbial phyla for healthy. The metabolic pathway prediction revealed that abundant microbial metabolic pathways in T2D diseases condition are mostly associated with insulin resistance and inflammation. This study may provide a better understanding of the gut-microbial diversity in Indian T2D patients and show the way for the development of valuable diagnostics strategies to improve the prediction and modulation of the T2D.

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