# Implications of gut bacterial capacity for *BUK*-mediated butyrate production on T2DM pathophysiology in a Community Enriched With Native Hawaiians

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## Purpose

The relationship between gut microbiome dynamics and type 2 diabetes mellitus (T2DM) risk in Native Hawaiian and Pacific Islanders (NHPIs) is not well-known. This gap in knowledge hinders efforts to comprehensively address health disparities in underserved NHPI communities, including those across Hawai`i. We characterized gut microbiome composition and butyrate production capacity in an NHPI-enriched cohort.

## Methods

Our cohort consisted of residents from predominantly NHPI communities on Oahu, Hawai`i (aged 16-70 years). Following their completion of a health-related survey, participants' height, weight, and A1c (%) were recorded. Blood and stool samples were collected and processed for downstream analyses of systemic inflammation, gut microbiome composition and capacity for butyrate production (via *BUK*-mediated pathways), and other T2DM risk factors. To control for age as a confounding variable, and to better visualize trends in relative bacterial abundance, we stratified our cohort into age groups: Early Adults (EA; 16-25 years), Young Adults (YA; 26-35 years), Mid-Adults (MA; 36-55 years), and Late Adults (LA; 56-70 years).

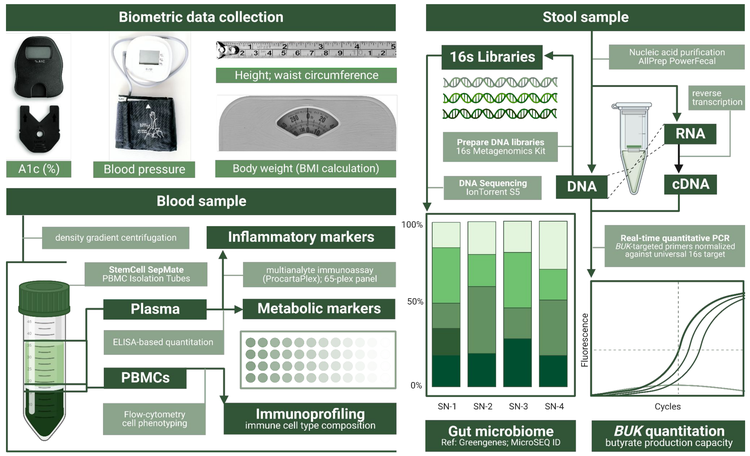


**Figure 1.** Overview of methods applied for data and sample processing.

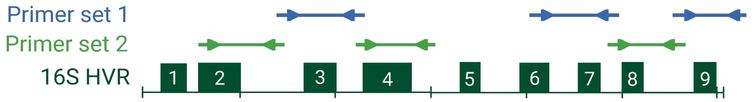


**Figure 2.** ThermoFisher 16s rDNA hypervariable region (HVR) PCR primer coverage.

## Results

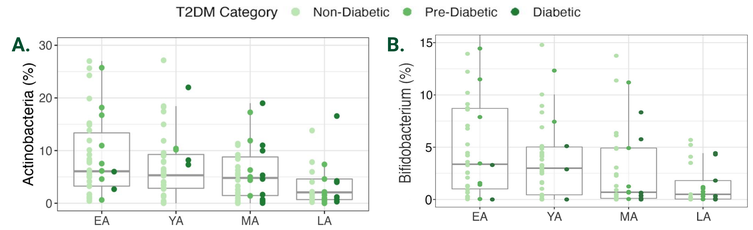


**Figure 3.** Relative abundance of **(A)** *Actinobacteria* and **(B)** *Bifidobacterium* across age and T2DM risk groups.

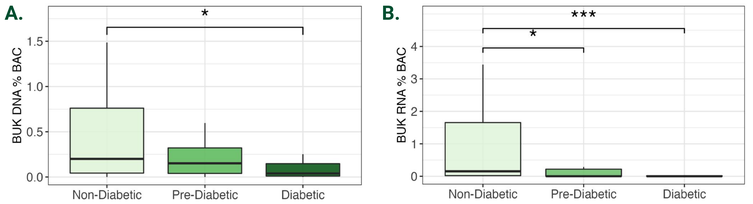


**Figure 4.** Relative abundance of **(A)** *BUK* DNA was significantly higher in non-diabetic individuals compared to diabetics (*P<0.05*). Similarly, that of **(B)** *BUK* RNA was significantly higher in non-diabetics compared to both pre-diabetics (*P<0.05*) and diabetics (*P<0.01*).

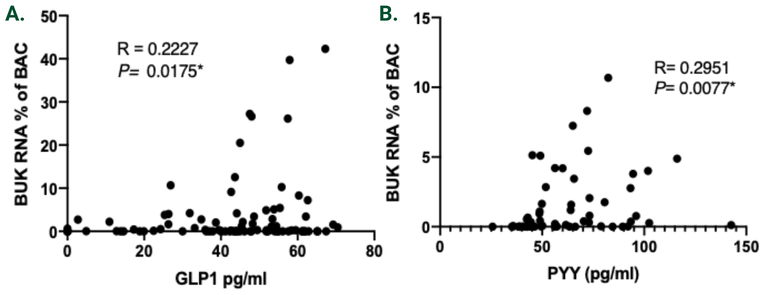


**Figure 5.** Relative abundance of *BUK* RNA correlated positively with **(A)** GLP-1 (*R=0.23; P=0.02*) and **(B)** PYY (*R=0.30; P=0.001*).

## Results

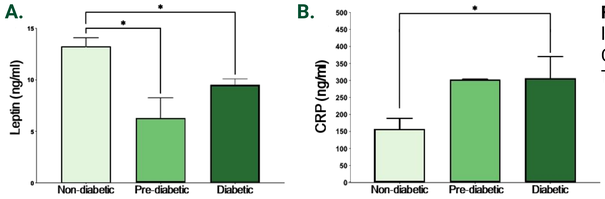


**Figure 6.** Comparative serum levels of **(A)** Leptin and **(B)** CRP across progressive T2DM risk groups.

## Conclusions

Major butyrate producers *Actinobacteria*, and corresponding genus *Bifidobacterium*, decreased in relative abundance across successive T2DM risk groups (**Figure 3**). *BUK* expression decreased with increasing T2DM risk (**Figure 4**). *BUK* activity corresponds with enhanced glucose homeostasis. Relative *BUK* RNA abundance correlated positively with metabolic hormones GLP-1 and PYY (**Figure 5**), implicating *BUK*-mediated metabolism as a partial determinant of insulin sensitivity and health outcomes.

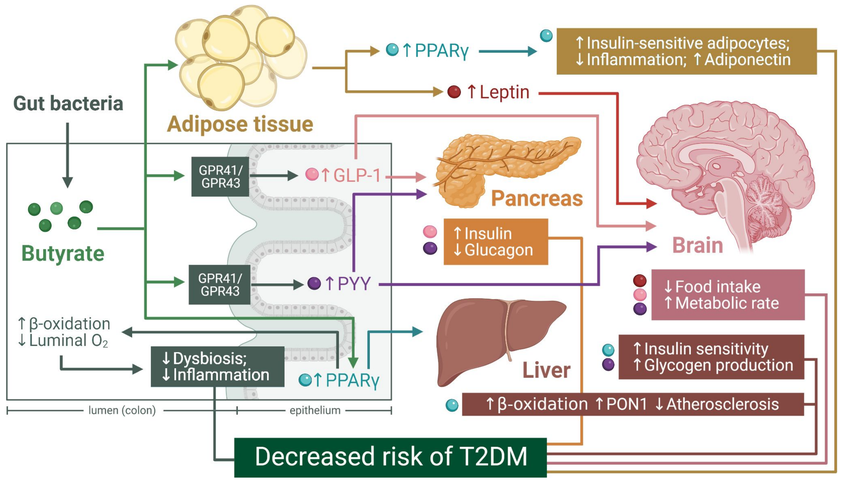


**Figure 7.** Proposed network of immunometabolic pathways affected by *BUK* activity in the gut.

In the next steps, we intend to investigate the epigenomic landscape of monocyte DNA in an NHPI-enriched cohort to clarify mechanistic links between gut bacteria and T2DM pathophysiology. Additionally, metabolomic profiling will be necessary to elucidate relationships among gut bacterial BUK gene capacity, inflammation factors, and host health outcomes.

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**References**

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