

# Global Prebiotic Association Young Researcher Awards - Entry #340

**Name**

Saurabh Kadyan

**Your Title**

Prebiotic mechanisms of resistant starches from dietary beans and pulses on gut microbiome and metabolic health in a humanized murine model of aging

**Your Affiliation**

Florida State University

**Email**

[sk21bq@fsu.edu](mailto:sk21bq@fsu.edu)

**Phone**

+18509662134

**Please indicate which category you're applying for:**

GPA Young Researcher Award for Applied Research (115 points possible)

**Please provide a link to your published paper (if open access) or abstract:**

<https://www.frontiersin.org/articles/10.3389/fnut.2023.1106463/full>

**Please provide a summary of your research(limit 250 words)**

WHO estimates that the proportion of people aged 60 years and above will double by the year 2050. This is alarming as elderly subjects are more vulnerable to nutritional risk leading to their predisposition to chronic cardiometabolic and neurocognitive diseases. Emerging scientific literature pinpointed the crucial role of gut microbiome architecture in modulating the pathogenesis of these chronic lifestyle diseases, whereas maintaining a fiber-rich diet in later life could ensure a healthy 'homeostatic' gut microbiome to promote healthy ageing. Pulses offer a 'perfect' food choice as they are cheap, readily available, and nutrient-dense loaded with high quality fiber. More specifically, pulses-derived resistant starch (RS) is major constituent of dietary fiber, however, its interaction with gut microbiome in regulating the metabolic health of aged host remains largely unexplored. Through our in-depth investigation using a humanized murine model of aging, we have unveiled the unique prebiotic-microbiome dynamics facilitated by RS derived from four commonly consumed pulse varieties: pinto beans, black-eyed peas, lentils, and chickpeas. The distinct effects of pulses-specific RS on the gut microbiome demonstrate a positive influence, effectively mitigating undesirable metabolic consequences such as postprandial hyperglycemia, gut hyperpermeability, and pro-inflammatory responses. These findings strongly

suggest the therapeutic potential of RS as innovative prebiotic candidates, offering a promising avenue for enhancing host health. Simultaneously, our research addresses the pressing issue of the 'dietary fiber gap' in the expanding global population.

**Please provide a summary of methods (limit 250 words)**

The prebiotic effects of pulses-derived RS on the gut microbiome and intestinal health were evaluated in aged (60-week-old) mice colonized with human microbiota. C57B6/J mice were subjected to a 20-week feeding regimen, with one group receiving a control western-style high-fat diet (CTL), and the other receiving the same diet supplemented with 5% w/w RS from pinto beans (PTB), black-eyed peas (BEP), lentils (LEN), chickpeas (CKP), or inulin (INU; reference control). Weekly measurements were taken for body weight and diet intake. At the study endpoint, mice were anesthetized with isoflurane and humanely euthanized, and tissues were promptly collected, flash-frozen in liquid nitrogen, and stored at  $-80^{\circ}\text{C}$  for subsequent analysis. Total body composition, distinguishing between lean mass and fat mass, was determined in live mice using the EchoMRI-130 Body Composition Analyzer. The gut microbiome was assessed using universal primers 515F (barcoded) and 806R to amplify the hypervariable V4 region of the bacterial 16S rRNA gene, and sequencing was carried out on an Illumina MiSeq sequencer. Microbiome bioinformatics analysis was performed using QIIME2 (ver. 2–2022.8). Post-prandial glycemic response and insulin sensitivity were evaluated through meal tolerance and insulin tolerance tests. Gut permeability was determined using the FITC-dextran assay. Gene expression analysis for tight-junction proteins and inflammatory markers was conducted on colonic and ileal tissues using the qPCR-based ddCt method, normalized against the 18S housekeeping gene.

**Please provide a summary of your results (limit 250 words)**

Our study revealed that the addition of pulses-derived RS had a sex-dependent impact on the modulation of the gut microbiome. Specifically, CKP enhanced  $\alpha$ -diversity exclusively in females, while  $\beta$ -diversity showed variations in both sexes. Moreover, distinct RS groups displayed specific differences in the microbiome at the levels of bacterial phyla and genera. Notably, LEN fostered an increase in Firmicutes and a decrease in Proteobacteria, while CKP and INU promoted Bacteroidota. The genus *Dubosiella* showed a dominant increase in males across all groups except PTB, while *Faecalibaculum* decreased in females within CKP and INU groups. The Linear Discriminant Analysis Effect Size (LEfSe) and correlational analyses unveiled RS-mediated upregulation of crucial bacterial genera associated with the production of short-chain fatty acids, particularly butyrate, and the suppression of specific pathobionts. Subsequent machine-learning analysis confirmed a reduced abundance of notorious genera, namely, *Enterococcus*, *Odoribacter*, *Desulfovibrio*, *Alistipes*, and *Erysipelatoclostridium* among RS groups. CKP and LEN groups partially shielded males from post-prandial glycemia. Importantly, RS ameliorated gut hyperpermeability induced by a high-fat diet and enhanced the expression of tight-junction proteins, notably claudin-1 and claudin-4, with LEN showing a more pronounced effect. Additionally, IL10 upregulation was more prominent for LEN, while TNF- $\alpha$  was downregulated by LEN, CKP, and INU. Collectively, these findings indicate that RS supplementation positively modulates the gut microbiome, reducing gut leakiness and inflammation, suggesting their prebiotic potential for functional food and nutritional applications.

**Please provide a statement about what, in your opinion, makes this paper outstanding and why it fits into the grant category you selected. (limit 250 words)**

Our research represents a pioneering effort in uncovering the unique prebiotic mechanisms associated with resistant starch (RS) derived from diverse dietary pulses, expanding beyond the traditional emphasis on cereals and tubers. What sets us apart is not just our choice of RS origins, but also our use of a humanized murine model

of aging, uniquely mimicking the gut microbiome of aged-matched healthy older adults. This leap in methodology opens doors to translational applications in clinical settings. Our findings showcase the distinctive prebiotic effects of RS across genders, shedding light on the intricate interplay of microbiome, immune response, and metabolism. This sexual dimorphism underscores the importance of recognizing individual differences in health responses, a pivotal factor in validating the broad-reaching health claims made by functional foods. While our observed effects are tailored to RS from specific beans and pulses, the nuances align with the inherent structural disparities among pulse varieties. This discernment is crucial for comprehending the unique contributions of each pulse type in promoting gut, metabolic, and intestinal health. The insights from this study not only pave the way for the development of nutraceuticals derived from natural sources but also hold promise in fortifying the health of our expanding elderly population.

**By typing your full name below and completing this application, you verify that you are the first author of this research and that this paper is original research.**

Saurabh Kadyan

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