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Bifidobacterium Genus in Colorectal Carcinoma Tissue in relation to Tumor Characteristics and Patient Survival

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Evidence suggests that members of the *Bifidobacterium* genus may not only inhibit colorectal carcinogenesis, but also enhance the anti
immune response and efficacy of immunotherapy. We hypothesized that the amount of bifidobacteria in colorectal carcinoma tissue m
associated with distinctive clinical features, higher immune response to colorectal cancer, and favorable clinical outcome.

Using 1,313 rectal and colon carcinoma cases in the Nurses' Health Study and Health Professionals Follow-up Study, we measured the am
Bifidobacterium DNA in carcinoma tissue by a quantitative polymerase chain reaction assay. Multivariable logistic and Cox proportional H
regression models were used to adjust for potential confounders, including microsatellite instability status, CpG island methylator phenotyp
interspersed nucleotide element-1 methylation, *KRAS*, *BRAF* and *PIK3CA* mutations.

Intratumor bifidobacteria were detected in 393 (30%) cases. The amount of bifidobacteria was associated with the extent of signet ring cel
0.002, with adjusted α of 0.002). Compared with signet ring cell-absent cases, multivariable odds ratios for the amount of bifidobacteri
1.45 (95% confidence interval 0.98-2.14) for cases with 1-50% signet ring cell components and 2.21 (95% confidence interval 1.05-4.
cases with ≥51% signet ring cell components (P_{trend} = 0.011). The amount of bifidobacteria was not significantly associated with any
densities, histological lymphocytic reaction patterns, or colorectal cancer survival.

The amount of detectable *Bifidobacterium* DNA in colorectal cancer tissue is associated with the extent of signet ring cells.