



Title	Comparison of Japanese and Indian intestinal microbiota shows diet-dependent interaction between bacteria and fungi
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## 論文内容の要旨

## Synopsis of Thesis

氏 名 Name	Siddhika Pareek
論文題名 Title	Comparison of Japanese and Indian intestinal microbiota shows diet-dependent interaction between bacteria and fungi (日本人とインド人の腸内細菌叢解析により明らかとなった食事依存的な細菌と真菌の腸内共生関係)
<p>論文内容の要旨</p> <p>〔目 的(Purpose)〕</p> <p>The composition of microbiota varies tremendously amongst individuals in response to environmental stimuli, especially diet. Human microbiome studies have extensively characterized bacterial population for its links with diet and metabolism. However, the potential association of other less abundant microorganisms such as fungi, protists or viruses with the bacteria in this regard remains poorly understood. In this study we showed that dietary polysaccharides impact growth of major fungal and bacterial species which are found abundantly in the intestines of Indians. We show that a dietary metabolite, relevant to the Indian diet, is produced by the fungus and facilitates growth of the bacterium. Thus, our study highlights the importance of lesser studied microorganisms, particularly fungi, in order to understanding the complex interactions of intestinal microorganisms.</p> <p>〔方法ならびに成績(Methods/Results)〕</p> <p>Methods:</p> <p>To analyze the composition of bacterial and fungi, fecal samples, collected from 47 healthy Japanese adults (n=47) from Osaka and healthy Indians (n=50) from Delhi area were analyzed for bacteria and fungi using 16S rRNA gene sequencing and PacBio RS II system, respectively. In vitro culture assays were designed to determine the impact of dietary polysaccharides and monosaccharides on the growth of the major fungal and bacterial species found in the two populations. <i>Candida albicans</i>, <i>Candida tropicalis</i> and <i>Prevotella copri</i> (individually) were cultured in a defined medium supplemented with different dietary polysaccharides, including arabinoxylan or starch or CMC. The interactions between <i>Candida spp.</i> and <i>P. copri</i> were assessed by culturing <i>P. copri</i> in the culture supernatants of <i>Candida spp.</i> grown with arabinoxylan. The growth-inducing factor in <i>Candida</i> culture supernatant was identified using HPLC, TLC and LC-MS-MS analysis. Finally, in vivo gnotobiotic mice model were generated by oral administration of fungi <i>C. albicans</i> and <i>P. copri</i> independently and together in the germ-free mice.</p> <p>Results:</p> <p>Next generation sequencing of fecal samples from Japanese and Indian adults revealed differential patterns of bacterial and fungal composition. In particular, Indians, who consume more plant polysaccharides than Japanese, harbored increased numbers of <i>Prevotella</i> and <i>Candida</i>. <i>Candida spp.</i> showed strong growth responses to the plant polysaccharide arabinoxylan in vitro. Furthermore, the culture supernatants of <i>Candida spp.</i> grown with arabinoxylan promoted rapid proliferation of <i>P. copri</i>. Arabinose was identified as a potential growth-inducing factor in the <i>Candida</i> culture supernatants. <i>Candida spp.</i> exhibited a growth response to xylose, but not to arabinose, whereas <i>P. copri</i> proliferated in response to both xylose and arabinose. <i>Candida spp.</i>, but not <i>P. copri</i>, colonized the intestine of germ-free mice. However, <i>P. copri</i> successfully colonized mouse intestine already harboring <i>Candida</i>.</p> <p>〔総 括(Conclusion)〕 These findings demonstrate a proof of concept that fungal members of gut microbiota can facilitate a colonization of the intestine by their bacterial counterparts, potentially mediated by a dietary metabolite.</p>	

## 論文審査の結果の要旨及び担当者

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## 論文審査の結果の要旨

近年、腸内微生物叢がさまざまな宿主の健康状態、疾患に関連することが報告されてきているが、主に細菌叢のみの解析であり、腸内細菌叢と腸内真菌叢の共生メカニズムの詳細についてはほとんど明らかになっていない。

Pareek氏の学位論文は、食生活の違う日本人とインド人の腸内細菌叢ならびに腸内真菌叢を解析することで、日本人と比較しインド人の糞便では、*Prevotella*属菌が非常に多いこと、また真菌叢においてはカンジダ属菌が多いことを見出した。さらに同氏はその違いが摂取する食物繊維の違いによってもたらされことに着目し、インド人糞便中に多く存在する*Prevotella copri*と*Candida albicans*を用いて、食物繊維の一つであるアラビノキシランを*C. albicans*が代謝し、産生されたアラビノースが*P. copri*の増殖を促すという共生関係を同定し、これまで知られていなかった腸内細菌叢と腸内真菌叢の共生メカニズムの一つを証明した。本研究は、博士（医学）の学位授与に値する。