別紙２

平成 27 年度　全体研究開発報告書 Progress Report FY2015

１．研究開発領域：　疾患における代謝産物の解析および代謝制御に基づく革新的医療基盤技術の創出
２．研究開発課題名：腸内細菌叢制御による代謝・免疫・脳異常惹起メカニズムの解明と治療応用
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４．研究開発の成果 The summary of research achievements made in FY2015 (about the Whole Group)

The objectives of our research are to uncover how a specific immune deficiency limited to T cells affects the gut microbiota and how together the microbiota and immune disregulation causes metabolic and brain disorders (see general scheme). We performed targeted metabolomic studies in WT and PD-1 deficient mice focusing on small compounds, particularly aminoacids and their catabolic pathways for the serum and brain. To evaluate the impact of gut microbiota on metabolism we generated and analysed mice in germ-free conditions. The analyses of germ-free and colonized mice side by side allowed us to identify the bacteria-dependent or immune-dependent metabolic changes. Such analyses were preceded by behavioral analyses and whenever possible we also performed immunologic tests. We also generated gnotobiotic mice that were subsequently analysed in a similar manner. Thus germ-free WT mice were transplanted with fecal microbiota from either WT or PD-1 deficient mice. Reversely, PD-1 deficient germ-free were transplanted with microbiota from WT or PD-1 deficient mice. Metagenomic analyses from the gnotobiotic mice are still ongoing and aiming to directly assess the contribution of specific bacterial groups or species to immune, metabolic and behavioral changes.

General scheme for the project