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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

腸管内には常在細菌叢が存在し、腸内恒常性維持や感染防御として作用している。眼結膜にも同様に固有細菌叢が存在し、その破綻が眼表面疾患発症に関与すると仮説を立て、健常者と結膜MALTリンパ腫において細菌叢の変化を4ヶ所で比較検討した。細菌叢同定には次世代シーケンサーを用い、16Sメタゲノム解析、主成分分析、LEfSe programを用いた分類学的比較解析を行った。結膜では体表面から独立した固有細菌叢が確認でき、種類は半数程度で、恒常性を認めた。疾患群結膜での細菌存在比率は、pathogenと考えられるDelftiaの有意な上昇、Bacteroides、Clostridiumなどの有意な低下を認めた。細菌叢変化に伴う環境変化を疑い、疾患群にて涙液採取し、pHの酸性化及び涙液中IgA濃度低下を認め、結膜環境変化を見い出した。結膜における常在細菌叢のバランス変化が、疾患発症に関わると考えられる。本研究は他疾患にも応用可能で、疾患発症予防や有効な加療に繋がる可能性があり、本研究は学位に値すると考える。

論 文 内 容 の 要 旨
Synopsis of Thesis

氏 名 Name	浅尾 和伸
論文題名 Title	Conjunctival dysbiosis in mucosa-associated lymphoid tissue lymphoma (結膜MALTリンパ腫における結膜細菌叢の変異)

Abstract of Thesis

〔Purpose〕

The ocular surface, a part of the conjunctiva-associated lymphoid tissue (CALT), is continuously exposed to the external environment, such as temperature changes, ultraviolet light and oxidative stress. This stress has been implicated in the development of pterygium, dry eye, corneal dystrophy and Fuch's endothelial dystrophy. It is likely that changes in the microenvironment at the ocular surface lead to alteration of the microbiota, resulting in disease development. We hypothesized that mucosal microbial dysbiosis could contribute to immunological changes in the conjunctival mucosa and might be associated with the development of conjunctival MALT lymphoma. The purpose of this study is to investigate the conjunctival microbiota and the association between the development of conjunctival mucosa-associated lymphoid tissue (MALT) lymphoma and dysbiosis.

〔Methods/Results〕

Samples were collected to compare the microbiota from the following four body locations: conjunctiva, meibomian gland, periocular skin and hand. Extracted DNA was analyzed by 16S rRNA sequences, and libraries were sequenced on an Illumina MiSeq sequencer. The differences in bacteria were characterized by using principal coordinate analysis of metagenomics data, and the differences in bacterial compositions were evaluated by linear discriminant analysis effect size. The conjunctival microbiota of MALT lymphoma patients was compositionally different from that of healthy controls. For the conjunctival MALT lymphoma patients, alterations in the microbial composition were detected, and a remarkable change was detected at the conjunctiva.

〔Conclusion〕

Detailed analysis showed that a specific population of the microbiota, the genus Delftia, was significantly more abundant in conjunctival MALT lymphoma patients, and the genera Bacteroides and Clostridium were less abundant in the MALT lymphoma patients. A specific microbiota on the ocular surface in conjunctival MALT lymphoma patients was detected, and dysbiosis may play an important role in the pathophysiology of conjunctival MALT lymphoma.