



Title	RpoN (sigma factor 54) contributes to bacterial fitness during tracheal colonization of Bordetella bronchiseptica
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論 文 内 容 の 要 旨
Synopsis of Thesis

氏 名 Name	MA XINGYAN
論文題名 Title	RpoN (sigma factor 54) contributes to bacterial fitness during tracheal colonization of <i>Bordetella bronchiseptica</i> (シグマ因子RpoNは気管支敗血症菌の気管内での適応増殖能力に関与する)
論文内容の要旨 〔目 的(Purpose)〕 The Gram-negative pathogenic bacterium <i>Bordetella bronchiseptica</i> is a respiratory pathogen closely related to <i>Bordetella pertussis</i>, the causative agent of whooping cough. Despite sharing <i>Bordetella</i> virulence gene (Bvg) system and homologous virulence factors, <i>B. bronchiseptica</i> infects a broad range of mammalian hosts, including laboratory animals, whereas <i>B. pertussis</i> is strictly adapted to humans. Therefore, <i>B. bronchiseptica</i> is often used as a representative model to explore the pathogenicity of <i>Bordetella</i> in infection experiments with laboratory animals. Although <i>Bordetella</i> virulence factors including toxins and adhesins have been studied well, our recent study implied that unknown virulence factors are involved in tracheal colonization and infection. Therefore, to seek novel factors involved in the <i>Bordetella</i> pathogenicity, we investigated bacterial genes contributing to tracheal colonization by high-throughput transposon sequencing (Tn-seq). 〔方法ならびに成績(Methods/Results)〕 In this study, we conducted an <i>in vivo</i> genome-wide screening for genes that support colonization/infection of <i>B. bronchiseptica</i> using Tn-seq and rat infection model of <i>B. bronchiseptica</i>. After screening, 151 genes of various functions were picked up and three genes: <i>rpoN</i>, <i>BB1983</i>, and <i>BB3242</i>, were selected because of their annotated functions. Then we evaluated their contributions to <i>B. bronchiseptica</i> RB50 infection by single infection experiment and co-infection with the wide-type (WT) strain. Consequently, no comparable differences in the colonization abilities of $\Delta rpoN$, $\Delta BB1983$, and $\Delta BB3242$ was observed. Defective competitive advantage was observed in $\Delta rpoN$ when competed against WT, but no apparent advantage was observed in co-infection of WT and $\Delta BB1983$ or $\Delta BB3242$. The assessment of growth rate of $\Delta rpoN$ and <i>in vitro</i> competition assay against WT excluded the possibility that growth retardation of $\Delta rpoN$ confer the fitness of tracheal colonization. RpoN is also known as sigma factor σ^{54}, which takes part in the transcription of varied genes and consequently regulates varied cell processes in several bacterial species. Although Bvg system is the master regulator in <i>Bordetella</i> species, we confirmed RpoN is independent of the Bvg system. The exploration of the functions of RpoN in <i>B. bronchiseptica</i> suggested that RpoN is involved in the bacterial motility and early biofilm formation. The prediction of RpoN-regulated genes in <i>B. bronchiseptica</i> indicates wide-ranging roles of RpoN in physiology and pathogenicity in <i>B. bronchiseptica</i>. 〔総 括(Conclusion)〕 Taken together, we identified RpoN of <i>B. bronchiseptica</i> as a factor conferring the fitness to colonize rat tracheas. <i>rpoN</i> encodes σ^{54}, a sigma factor that regulates the transcription of various genes, implying its contribution to various bacterial activities. In fact, we found RpoN of <i>B. bronchiseptica</i> is involved in bacterial motility and initial biofilm formation and has potential wide-ranging impacts on the expression of various genes. Therefore, we propose that RpoN coordinates the gene expressions to make bacteria adapt to the host environments.	

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

哺乳動物に気道感染するボルデテラ属には百日咳菌をはじめとしてパラ百日咳菌と気管支敗血症菌が代表種として知られている。そのなかで、百日咳菌やパラ百日咳菌が専らヒトにのみ感染するのに対し、気管支敗血症菌は広範な哺乳動物を宿主域に持つ。そのため、ボルデテラの病原性解析には気管支敗血症菌と汎用実験動物の組み合わせによる感染実験がしばしば行われる。申請者は本菌とラットの感染実験系において、気管支敗血症菌のトランスポゾン挿入変異株ライブラリーを用いた挿入失活遺伝子スクリーニング（トランスポゾン配列解析、Tn-seq）を行い、感染成立に寄与する本菌の遺伝子の候補151領域を同定した。さらに151遺伝子のうち真正細菌において環境適応型の遺伝子発現調節に関与することが知られている*rpoN* (σ^{54}) に着目し、この遺伝子が感染宿主内における本菌の適応応答に必要なことを見出した。さらに*rpoN*に制御される本菌の表現形質を解析し、*in silico*アプローチを駆使して気管支敗血症菌内で*rpoN*に制御されると予想される遺伝子を173種見出した。これらの成果は気管支敗血症菌の病原性制御には、*rpoN*から連なる遺伝子発現制御ネットワークが重要であることを初めて示したものである。以上のことから本研究内容は学位の授与に値するものと判断できる。