DOI: 10.1002/JLB.4AB0919-432R

JLB JOURNAL OF LEUKOCYTE BIOLOGY

BRIEF CONCLUSIVE REPORT

Vancomycin-induced gut dysbiosis during *Pseudomonas aeruginosa* pulmonary infection in a mice model

Caio Pupin Rosa[1] | Jéssica Assis Pereira[1] | Natália Cristina de Melo Santos[1] | Gustavo Andrade Brancaglion[1] | Evandro Neves Silva[2] | Carlos Alberto Tagliati[3] | Rômulo Dias Novaes[4] | Patrícia Paiva Corsetti[2] | Leonardo Augusto de Almeida[1]

[1]Department of Microbiology and Immunology, Federal University of Alfenas, Alfenas, Minas Gerais, Brazil

[2]Laboratory of Infectious and Chronic Diseases (LIDIC), José do Rosário Vellano University, Alfenas, Minas Gerais, Brazil

[3]Laboratory of Toxicology (LabTox), Department of Clinical and Toxicological Analysis, Pharmacy Faculty, Federal University of Minas Gerais, Belo Horizonte, Brazil

[4]Department of Structural Biology, Federal University of Alfenas, Alfenas, Minas Gerais, Brazil

Correspondence
Leonardo Augusto de Almeida, Universidade Federal de Alfenas, Depto. Microbiologia e Imunologia. Rua Gabriel Monteiro da Silva, 700 Centro, Alfenas/MG 37130-001, Brazil.
E-mail: leonardo.almeida@unifal-mg.edu.br

Abstract

Pseudomonas aeruginosa is one of the most common opportunistic pathogens causing respiratory infections in hospitals. Vancomycin, the antimicrobial agent usually used to treat bacterial nosocomial infections, is associated with gut dysbiosis. As a lung-gut immunologic axis has been described, this study aimed to evaluate both the immunologic and histopathologic effects on the lungs and the large intestine resulting from vancomycin-induced gut dysbiosis in the *P. aeruginosa* pneumonia murine model. Metagenomic analysis demonstrated that vancomycin-induced gut dysbiosis resulted in higher *Proteobacteria* and lower *Bacteroidetes* populations in feces. Given that gut dysbiosis could augment the proinflammatory status of the intestines leading to a variety of acute inflammatory diseases, bone marrow-derived macrophages were stimulated with cecal content from dysbiotic mice showing a higher expression of proinflammatory cytokines and lower expression of *IL-10*. Dysbiotic mice showed higher levels of viable bacteria in the lungs and spleen when acutely infected with *P. aeruginosa*, with more lung and cecal damage and increased *IL-10* expression in bronchoalveolar lavage. The susceptible and tissue damage phenotype was reversed when dysbiotic mice received fecal microbiota transplantation. In spite of higher recruitment of CD11b+ cells in the lungs, there was no higher CD80+ expression, DC+ cell amounts or proinflammatory cytokine expression. Taken together, our results indicate that the bacterial community found in vancomycin-induced dysbiosis dysregulates the gut inflammatory status, influencing the lung-gut immunologic axis to favor increased opportunistic infections, for example, by *P. aeruginosa*.

KEYWORDS
Gut dysbiosis, Lung infection, *Pseudomonas aeruginosa*, Vancomycin

1 | INTRODUCTION

Pseudomonas aeruginosa is an aerobic Gram-negative bacterium responsible for skin, ear, and pulmonary infections.[1] In particular, the latter occur as ventilator-related pneumonia in intensive care units (ICUs), representing one of the most common respiratory infections in these health settings.[1,2] This pathogen also causes disease in immunocompromised individuals and cystic fibrosis patients.[3] In order to treat *P. aeruginosa*-associated pneumonia, patients have to take broad-spectrum antibiotics,[2] which is followed by the development of dysbiosis, especially in the intestines,[4,5] with systemic repercussions.[6] The changes in commensal communities alter their interaction with intestinal mucosa, enhancing not only the production of certain T cell subsets, but also altering the cytokine expression in immune innate and adaptive cells.[7] These effects have also been recognized in the lungs, highlighting gut-lung crosstalk.[8] The available data suggest that changes in the operational taxonomic unit (OTU) load and/or diversity plays a significant role in predisposing patients to

Abbreviations: BAL, Bronchoalveolar lavage; BMDM, Bone marrow-derived macrophages; CFU, colony-forming unit; FMT, Fecal microbiota transplantation; ICU, Intensive care unit; OTU, Operational taxonomic units; VAN, Vancomycin.

Received: 26 January 2019 | Revised: 27 September 2019 | Accepted: 23 October 2019

