Bighorn Sheep Leukocyte Receptor for Leukotoxin Secreted by *Mannheimia (Pasteurella) haemolytica*

WEIGUO LIU, Department of Veterinary Microbiology and Pathology, Washington State University, Pullman, WA 99164, USA
WILLIAM C. DAVIS, Department of Veterinary Microbiology and Pathology, Washington State University, Pullman, WA 99164, USA
JOHN LAGERQUIST, Department of Veterinary Microbiology and Pathology, Washington State University, Pullman, WA 99164, USA
WILLIAM J. FOREYT, Department of Veterinary Microbiology and Pathology, Washington State University, Pullman, WA 99164, USA
S. SRIKUMARAN,[1] Department of Veterinary Microbiology and Pathology, Washington State University, Pullman, WA 99164, USA

Abstract: *Mannheimia (Pasteurella) haemolytica* is an important etiological agent of pneumonia, a highly fatal disease of bighorn sheep (*Ovis canadensis*). *M. haemolytica* produces an exotoxin which is cytolytic to all subsets of bighorn sheep leukocytes. This leukotoxin is regarded as the most important virulence factor of this organism. Hence identification and characterization of the receptor for leukotoxin on bighorn sheep leukocytes is an important prerequisite for understanding the pathogenesis of this disease. Antibodies specific for CD18, the β subunit of β_2-integrins, inhibit leukotoxin-induced cytolysis of bighorn sheep leukocytes suggesting that CD18 may serve as a receptor for leukotoxin on bighorn sheep leukocytes. Confirmation of bighorn sheep CD18 as a receptor for leukotoxin requires demonstration that the recombinant expression of bighorn sheep CD18 in leukotoxin-non-susceptible cells renders them susceptible to leukotoxin. Therefore, we cloned and sequenced the cDNA encoding CD18 of bighorn sheep, and transfected a leukotoxin-non-susceptible murine cell-line. Cell surface expression of bighorn sheep CD18 on the transfectants was tested by flow cytometry with anti-CD18 antibodies. Transfectants stably expressing bighorn sheep CD18 on their surface were subjected to a cytotoxicity assay with leukotoxin. In this assay, the transfectants were effectively lysed by leukotoxin in a concentration-dependent manner, whereas the parent cells were not. These results indicate that leukotoxin utilizes CD18 as a receptor on bighorn sheep leukocytes. Identification of CD18 as a receptor for leukotoxin on bighorn sheep leukocytes should enhance our understanding of the pathogenesis of pneumonia, which in turn should help in the development of control measures against this fatal disease of bighorn sheep.

BIENN. SYMP. NORTH. WILD SHEEP AND GOAT COUNC. 15: 90

Key words: Bighorn sheep, leucocytes, leukotoxin receptor, *Ovis canadensis*, pneumonia.

[1] *Corresponding author e-mail: ssrikumaran@vetmed.wsu.edu*