Involvement of Galectin-3 in Maintaining Barrier Integrity of Lung Vasculature

Author Block: M. Han, R. Rancourt, D. L. Laskin, and J. Andres. *Rutgers, The State University of New Jersey, Piscataway, NJ.*

Galectin-3 (LGALS3; Gal-3) is a 35-kDa carbohydrate-binding protein used as a diagnostic biomarker for cardiovascular disease. Recently, a role for Gal-3 in the pathophysiology of heart failure and lung fibrosis has been suggested. Histological examination of lung sections from unchallenged Gal-3 -/- KO mice revealed elevated levels of perivascular inflammation relative to wild type mice. Normal lung vasculature typically exhibits a size selective permeability that permits small solutes to enter the airway but limits the influx of large plasma molecules. We hypothesized that Gal-3 -/- mice would also exhibit a disruption in airway vascular barrier function. To assess for "leakiness", we analyzed bronchoalveolar lavage for high molecular weight IgM (900 kDa) and performed immunohistochemical analysis to screen for the presence of plasma-derived fibrinogen and inflammatory cells in lung tissue. Both Gal-3 -/- and corresponding wild-type (WT) C57/bl6 mice were exposed to nitrogen mustard or phosphate buffered saline (PBS) by intratracheal instillation. Fourteen days after exposure, mice were terminally anesthetized and airway-capillary leak was estimated by the detection of IgM levels in bronchoalveolar lavage fluid (BALF). Left lung lobes from these mice were also paraffin embedded, sectioned at 5 μm thickness, and immunostained for the plasma protein fibrinogen. Deposition of fibrinogen in airways was assessed by use of an Allred scoring system. Additional sections were also immunostained for myeloperoxidase (MPO) to assess numbers of activated inflammatory cells in lung. In contrast to PBS-treated wild type mice, immunohistochemistry performed on Gal-3 -/- mice after PBS treatment, revealed prominent perivascular fibrin deposition, increased numbers of MPO-expressing inflammatory cells, and a four-fold elevation IgM plasma protein in BALF. GAL-3 may be an essential factor for maintaining hemostasis and barrier integrity of lung vasculature. *This work supported by Rutgers University CounterACT Center of Excellence - U54AR055073, and pilot grant funding from the Center for Environmental Exposures and Disease (CEED).*