Role of Fecal calprotectin as a potential biomarker of intestinal inflammation

Sarita Garg[1,2], Isabelle R. Miousse[2], Junru Wang[1], and Martin Hauer-Jensen[1]

[1]Division of Radiation Health, Department of Pharmaceutical Sciences, College of Pharmacy, University of Arkansas for Medical Sciences, Little Rock, AR
[2] Department of Biochemistry and Molecular Biology, UAMS, Little Rock, AR

Background: Fecal calprotectin (CPN) is an unspecific marker for gut inflammation. Calprotectin constitutes up to 60% of neutrophil cytosolic proteins and its presence in the feces is directly proportional to neutrophil migration into the gastro-intestinal (GI) tract during times of inflammation. Due to its high sensitivity, specificity, and stability at room temperature, fecal CPN has been increasingly used in the diagnostic process for inflammatory bowel disease. To characterize biomarkers associated with GI disease onset and progression, the present study utilized a GI-specific acute radiation syndrome model in the non-human primate (NHP), where animals were exposed to partial body irradiation (PBI) at doses eliciting measurable changes in the GI-tract without concurrent hematopoietic related lethality.

Methods: Rhesus macaques were exposed to a single uniform dose of 0, 8. 11, 12.5 and 14Gy PBI using a 6 MV photon beam. Fecal samples were collected pre and post-radiation on days 3, 5, 10, 22, 30 and 60 to assess calprotectin levels by ELISA. Groups of animals were euthanized on days 10, 28 and 60 and segments of intestinal tissues were procured from proximal jejunum (PJ), ileum and colon to evaluate the expression of calprotectin by immunohistochemistry.

Results: Radiation induced a significant dose-dependent increase in fecal CPN levels noted as early as day 3 and remained elevated until day 10, in comparison to controls. These increases persisted even until D22 post radiation in the 12.5 and 14 Gy group. However, those exposed to 8 and 11 Gy reached baseline by day 22. Interestingly, animals exposed to 14 Gy PBI showed a robust time-dependent increase in CPN levels, which remained significantly elevated until day 28 (p=0.002) and reached baseline by day 60. Likewise, unlike controls, increased expression of calprotectin was noted both in jejunum and ileum sections by D10 post radiation. However, by day 30, the levels seemed to reach baseline.

Conclusion: Taken together these data suggest that high doses of radiation resulted in significant increase in fecal CPN levels. The CPN measurement in stool can serve as a useful biomarker marker for detecting and monitoring intestinal inflammation.