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A Longitudinal Fludarabine–Lipopolysaccharide Induced Mouse Model for Studying Immunosuppression and Inflammatory Responses: A preliminary Study

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Abstract

Immunosuppressive therapy, particularly fludarabine-based chemotherapy, profoundly alters hematopoietic and immune balance, heightening vulnerability to bacterial infections. Exposure to bacterial endotoxin lipopolysaccharide (LPS) can trigger an exaggerated inflammatory response, such as fludarabine-based chemotherapy, significantly increases susceptibility to bacterial infections by disrupting hematopoietic and immune homeostasis. In particular, exposure to bacterial endotoxin lipopolysaccharide (LPS) can provoke an exaggerated inflammatory response in immunocompromised hosts, leading to hematological dysregulation and hepatic stress. Establishing a fludarabine–LPS mouse model enables the characterization of these complex interactions between chemotherapy-induced immunosuppression and secondary inflammation. A longitudinal study

performed on mice receiving fludarabine followed by LPS administration. Hematological parameters [leukocyte, erythrocyte, and platelet indices) and hepatic enzyme markers (SGOT and SGPT) were measured at baseline, day 1, day 3, day 7, and day 14. Data were analyzed using ANOVA followed by Tukey's post-hoc test [$p < 0.05$). Fludarabine induced a gradual decline in red blood cell count and hemoglobin, indicating persistent anemia, while mean corpuscular volume [MCV) and red cell distribution width (RDW) increased significantly, reflecting macrocytosis and anisocytosis. Leukocyte parameters showed transient leukocytosis dominated by neutrophils and monocytes on day 3 post-LPS, followed by a marked decline on day 7, consistent with myelosuppression and immunosuppressive nadir. Platelet indices [PDW and P-LCR) demonstrated significant fluctuations reduced at day 7 and recovered at day 14 indicating temporary inhibition of megakaryopoiesis and subsequent compensatory thrombopoiesis. SGOT levels increased moderately (from ~135 U/L to ~200 U/L on day 7), while SGPT remained stable (45–65 U/L), suggesting transient hepatic stress without overt cytolysis. The fludarabine–LPS model successfully reproduces the dual phenomena of immunosuppression and inflammation that underlie infection vulnerability in chemotherapy-treated hosts. The longitudinal hematological and hepatic changes highlight MCV, RDW, PDW, and P-LCR as sensitive indicators of erythropoietic and platelet disturbances, while elevated SGOT supports mild hepatic mitochondrial stress. This model provides a valuable tool for investigating infection susceptibility and evaluating immunomodulatory or hepatoprotective interventions in immunocompromised conditions.