Adaptive Immunity

Background Effector memory T lymphocytes (T_{EM}) implicated in the immunopathogenesis of SLE have been detected in the urine of patients with lupus nephritis. As T_{EM} depend on the voltage-gated potassium channel Kv1.3 for activation-induced calcium signalling, activated T_{EM} represents a potential target for the novel Kv1.3 blockade therapy dalazatide. In active SLE nephritis, Kv1.3 is upregulated on peripheral blood CD8^{+} T_{EM} and cytokine production was inhibited in SLE T lymphocytes. We therefore hypothesized that Kv1.3 is expressed on urinary leucocytes from patients with lupus nephritis.

Methods Urinary cells were isolated in 33 samples from patients with SLE ages 15–41 years, (mean 19, IQR 16.2–19.3). Immunofluorescence was performed to quantify and characterize cells expressing Kv1.3. Urinary leucocytes were defined as non-epithelial cells by morphology. Leucocyte subsets were defined as CD3^{+} T lymphocytes, CD20^{+} B lymphocytes, or CD14^{+} macrophage.

Results In the urine, leucocytes expressing Kv1.3 were found in samples from every subject studied. Overall, Kv1.3 expression was detected on a mean of 3.5% of leucocytes (range 0.1%–13.4%; IQR 0.8%–5.1%) with higher levels in patients with active disease (4.8%, IQR 1%–6.7%) compared to patients with inactive disease (2.1%, IQR 0.8%–2.7%, p=0.04). CD3^{+} lymphocytes expressing Kv1.3 were found in all subjects (mean 52% of CD3^{+} cells, IQR 33%–100%). In 90% of subjects, Kv1.3 was detected on CD20^{+} B lymphocytes (mean 68%, IQR 46%–100%), and in 90% of subjects CD14^{+} macrophages (mean 69%, IQR 46%–100%). Patients with class III or IV nephritis had increased frequencies of leucocytes expressing Kv1.3 (6%) compared to patients with Class V nephritis (2%, p=0.01) or no nephritis (1.8%, p=0.01).

Conclusions Kv1.3 is detectable on SLE urinary B lymphocytes, T lymphocytes, and macrophage, implying that inflammatory cells in the kidney may be targeted by this channel. Peripheral blood cell expression and functional data suggest that SLE activated T_{EM} lymphocytes may be susceptible to inhibition by dalazatide.

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