Adaptive Immunity

KV1.3 EXPRESSION ON SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) URINARY LEUKOCYTES

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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 dalazatin. 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 leukocytes 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 leukocytes were defined as non-epithelioid cells by morphology. Leukocyte subsets were defined as CD3^+ T lymphocytes, CD20^+ B lymphocytes, or CD14^+ macrophage.

Results In the urine, leukocytes expressing Kv1.3 were found in samples from every subject studied. Overall, Kv1.3 expression was detected on a mean of 3.5% of leukocytes (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 leukocytes 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 dalazatin.

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