

**Background** Failure to properly dispose of self-DNA can inappropriately trigger anti-viral defense systems, leading to autoimmunity. Indeed, mutations in the DNA exonuclease TREX1 are causative for a spectrum of rare lupus-like autoimmune diseases in humans. These disorders involve triggering of the cytosolic dsDNA sensor cyclic GMP-AMP Synthase (cGAS) and the STimulator of INterferon Genes (STING), leading to chronic production of the anti-viral cytokine type I interferon (IFN-I) and the development of autoimmunity. Importantly, the exact cells in which the sensing of undegraded DNA and subsequent production of IFN-I occur remain unknown.

**Methods** We generated a mouse expressing the catalytically inactive TREX1 D18N allele, which causes familial chilblain lupus in humans. We examined anti-viral gene expression and the phenotype of these mice to study the immunological effects of losing TREX1 activity. We performed bone marrow transplants to determine if autoimmune pathogenesis in this model was dependent on hematopoietic or non-hematopoietic cells. Finally, we measured expression of type I interferon in various purified cell populations to identify specific cellular producers contributing to autoimmune pathogenesis.

**Results** In this study, we demonstrate that TREX1 catalytic inactivity induces IFN-I signaling and lupus-like autoimmunity in a mouse. Moreover, we show that TREX1 deficiency within bone marrow-derived cells causes IFN-I activation and the development of autoimmunity. We provide evidence of spontaneous IFN- production within both innate immune and T cells. T cell IFN- $\alpha$  expression was observed in all T cell populations, but was most enriched within naive T cells. We also demonstrate that D18N T cells express all components of the cGAS-STING pathways and generate IFN-I protein, both spontaneously and in response to small-molecule activation of STING.

**Conclusions** Our findings demonstrate that TREX1 enzymatic activity is crucial to prevent inappropriate DNA-sensing and IFN-I production. TREX1 inactivity within hematopoietic cells was both necessary and sufficient to induce lupus-like autoimmunity, indicating that TREX1 normally acts within immune cells to suppress inappropriate activation of anti-viral signaling. Both innate immune and T cells respond to TREX1 dysfunction by spontaneously synthesizing IFN-, a surprising result given that T cells are not canonically thought to be major IFN-producing cells. These results expand our understanding of the pathogenesis of lupus-like disease, and indicate that small molecule inhibition of TREX1 could represent an appealing strategy for anti-viral and cancer immune-therapies.

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## 285 LUPUS NEPHRITIS PRESENTING AS TUBERCULOSIS INFECTION: A CASE REPORT

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**Background** Lupus nephritis, a form of glomerulonephritis, is the inflammation of kidneys attributable to systemic lupus erythematosus (SLE). It is an autoimmune disorder in which kidney tissue insult is triggered predominantly by the

complement system. Herein, we report the case of a 24 years old female with atypical manifestations of SLE.

**Methods** Case Presentation: A female aged 24 years was presented with the complaint of fever, cough (with sputum) and dyspnea for the past one month. The preliminary physical examination was suggestive of pneumonia. Her laboratory investigations revealed anisocytosis and normochromic anemia (Hb 9.3 g/dL, HCT 30%). Lymphocytes (12%) were decreased while neutrophils (84%), platelets ( $439 \times 103/\mu\text{L}$ ) and ESR (75 mm/hr) were increased. A serum biochemistry test showed elevated urea (92 mg/dl), creatinine (1.5 mg/dl) and sodium (145 meq/L). The chest X-ray demonstrated a right sided pleural effusion which directed towards a possible Tuberculosis (TB) infection. However, pleural biopsy efficiently excluded an active TB infection. Nephrological investigations exhibited evidence of protein (0.3 g/L) and blood traces in the urine. Her proteinuria (2+) was within nephrotic range which was confirmed through qPCR (3.9 U). Moreover, serum TSH (8.054 mU/L) was also elevated and cardiolipin test was positive for IgM (1.10). SLE specific diagnostic tests anti-dsDNA was positive and ANA was also reactive. Left kidney biopsy exhibited characteristics of diffuse endocapillary proliferative glomerulonephritis. SLE diagnosis was established, and patient was treated with cyclophosphamide pulse therapy along with corticosteroid methylprednisolone and achieved complete remission.

**Results** CASE REPORT

**Conclusions** To date, this is the first case report of SLE simulating as a TB infection in a developing country. The patient did not display classic triad of SLE; joint pain and malar rash aside from fever. This case reiterates the implication of considering unusual case presentations of SLE and undertaking rigorous clinical workup to minimize the probability of missed cases and improve patient clinical outcomes.

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## 286 MATERNAL SYSTEMIC LUPUS ERYTHEMATOSUS AND THE RISK OF CRYPTORCHIDISM IN MALE OFFSPRING

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**Background** Background: Systemic lupus erythematosus (SLE) is one of the most prevalent autoimmune rheumatic diseases affecting young women of childbearing age. The disease is characterized by elevated levels of systemic inflammation and high levels of circulating autoantibodies, potentially affecting multiple organs and tissues. Women suffering from SLE have decreased fecundity, and increased risk of adverse pregnancy outcomes such as miscarriage and preeclampsia. This risk is further elevated with increasing disease activity, and seems less pronounced when disease is well managed. SLE is not in itself considered a risk factor for specific birth defects; however, not all congenital anomalies are diagnosed immediately after birth, and might thus be overlooked in most studies on reproductive outcomes. Cryptorchidism (undescended testis) is a common genital anomaly, often diagnosed throughout childhood. It arises from an imperfect genital development in the