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Immuno-metabolic dysregulation in autoimmune diseases and potential therapeutic interventions

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The functional and molecular integration between immune and metabolic system is crucial for homeostasis of an organism. Defective immunometabolism has been implicated in many aspect of biology including cancer, autoimmune and infectious diseases although the underlying mechanisms remain largely elusive. TREX1 is an endoplasmic reticulum (ER)-associated exonuclease that digests viral or host DNA in the cytosol and prevent accumulation and activation of cytoplasmic DNA sensing pathway. TREX1 mutations are associated with a broad spectrum of autoimmune and inflammatory phenotypes, including Aicardi-Goutieres syndrome (AGS), familial chilblain lupus (FCL), systemic lupus erythematosus (SLE) and retinal vasculopathy with cerebral leukodystrophy (RVCL). Recently, we discovered that TREX1 regulates lysosomal biogenesis through a mechanism involving master regulator of cellular metabolism, mTORC1. Using various TREX1 mutant/truncation constructs and also animal models, we have identified the molecular cause that is associated with TREX1-deficiency/mutations. We also identified unique pathomechanisms associated with RVCL due to misregulated oligosaccharyl transferase (OST) activity and glycan metabolism. Most importantly, we identified target specific small molecule inhibitors for the treatment of TREX1 associated autoimmune diseases and potential other interferonopathies.

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Antioxidant enzymes in saliva of patients with systemic lupus erythematosus

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Atypical autoimmune disease with chronic systemic inflammation is systemic lupus erythematosus (SLE). The pathogenesis of SLE includes a number of internal and external factors. However, it is suggested that oxidative stress may play an important role in this regard. Therefore, either increase of Reactive Oxygen Species (ROS) or impaired antioxidant defense system can cause oxidative stress in SLE. We have previously studied variations in antioxidant activity in serum of SLE patients. To the best of our survey, however, salivary antioxidant enzymes have not been evaluated. Saliva, the non-invasive biological fluid, could be a reflection of the state of health. Therefore, the purpose of this study was evaluation of peroxidase (POD), superoxide dismutase (SOD) and catalase (CAT) activity in the saliva of patients with SLE. In practice, 30 patients with SLE and 30 healthy controls were selected to enter the research and donate their saliva samples. Their un-stimulated saliva was centrifuged and the biological activity of POD, CAT and SOD were evaluated and the results were statistically analyzed. According to the results, the biological activities of antioxidant enzymes SOD and CAT were significantly reduced in saliva of SLE patients as compared to controls. It is suggested that antioxidant status is impaired in the saliva of SLE patients and antioxidant status of saliva could be one of the non-invasive markers for SLE.

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