



The potential role of the circadian rhythm in immune repertoire formation and pathogenesis of immune disorders

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ABSTRACT

The incidence of immune disorders such as autoimmunity and hypersensitivity reactions has been increasing in industrialized countries recently. Although some hypotheses based on epidemiological studies have been proposed to evaluate this increase among the immune disorder cases such as "Hygiene Hypothesis", the underlying mechanism is not clear yet. It has been well studied that impairments in immune repertoire, total diversity among the antigenic receptors such as B cell receptor, T cell receptor and antibodies, may be causative factors of several immune disorders. Although genetic aspects of these immune disorders are well established, elucidating the responsible mutations in the genes encoding the molecules having key role in the formation of immune repertoire, we still lack knowledge on what kind of environmental factors take role in the pathogenesis of these diseases. Establishment of the diversity of immune repertoire depends on the recruitment of V(D)J re-arrangement which is basically Non-Homologous End Joining (NHEJ), one of the DNA repair mechanisms, mediated pathway. Circadian rhythm which DNA repair mechanisms may have effects on V(D)J recombination through NHEJ pathway especially in the early stages of life when immune repertoire is formed. The proteins recruited in the circadian regulation of the cells and regulation of DNA repair mechanisms such as Per1, Cry1, Parp-1 ve Tim are candidate molecules which may regulate V(D)J rearrangement. We suggested in our hypothesis that a novel molecular pathways linking circadian rhythm to immune system functioning and environmental factors disrupting circadian rhythm may have potential role in the pathogenesis of several immune disorders through epigenetic control of V(D)J recombination.

KEY WORDS: Circadian rhythm; Immune repertoire; Allergy; Autoimmunity

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