Evaluación del efecto de la infección viral por Epstein-Barr (EBV) en modulación de la respuesta autoinmune en células mononucleares de sangre periférica en pacientes con lupus eritematoso sistémico.

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Tesis Doctoral presentada como requisito para optar el título de:
Doctor en Genética y Biología Molecular

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RESUMEN

El lupus eritematoso sistémico (LES) es una enfermedad autoinmune compleja que aún plantea grandes interrogantes sobre su origen y progresión. En los últimos años, el virus de Epstein-Barr (EBV) ha cobrado especial interés como uno de los posibles desencadenantes y modulador de la respuesta inmune en estos pacientes. Con esta investigación buscamos comprender mejor esa relación, explorando cómo la infección viral y el ambiente inmunológico propio del LES influyen en la regulación de genes y en la actividad de las células inmunes.

Al estudiar a pacientes con LES y compararlos con controles sanos, encontramos que la mayoría de los casos presentaban enfermedad activa, con una alta frecuencia de daño renal. En ellos, la expresión de genes clave como TNF-α e IFN-γ estaba reducida, mientras que IL-10 aparecía aumentada y correlacionada de manera inversa con TNF-α, revelando un equilibrio alterado en la respuesta inflamatoria. Además, observamos que la mayoría de los pacientes mantenían una infección activa por EBV, asociada con la sobreexpresión de LMP1, una proteína viral capaz de favorecer la supervivencia de células B autorreactivas y de alterar importantes rutas de señalización inmunológica.

Otro hallazgo relevante fue la activación de retrovirus endógenos (HERV-E). En los ensayos con plasma heterólogo confirmamos, además, que el ambiente lúpico puede modificar directamente la conducta de células inmunocompetentes sanas, promoviendo cambios en IL-6. Finalmente, identificamos una reactividad cruzada entre EBNA1 y Ro60, lo que respalda

la hipótesis del mimetismo molecular como uno de los mecanismos que explican la pérdida de tolerancia inmunológica.
En conjunto, este estudio ofrece una visión más integrada del papel del EBV, los retrovirus endógenos y las alteraciones inmunorregulatorias en la patogénesis del LES. Más allá de ampliar la comprensión biológica de la enfermedad, estos hallazgos sugieren posibles biomarcadores y rutas terapéuticas que podrían contribuir en el futuro a un manejo más preciso y personalizado del lupus.

Palabras clave: Lupus eritematoso sistémico (LES); Virus de Epstein-Barr (EBV); Mimetismo molecular; Citocinas (TNF-α, IFN-γ, IL-10, IL-6); Retrovirus endógenos (HERV-E)

ABSTRACT

Systemic lupus erythematosus (SLE) is a complex autoimmune disease that continues to raise major questions regarding its origin and progression. In recent years, Epstein–Barr virus (EBV) has gained particular attention as a potential trigger and modulator of the immune response in these patients. This study aimed to better understand that relationship by exploring how viral infection and the immunological environment of SLE influence gene regulation and immune cell activity.
When comparing SLE patients with healthy controls, we found that most cases exhibited active disease, with a high frequency of renal involvement. In these patients, the expression of key genes such as TNF-α and IFN-γ was reduced, whereas IL-10 was increased and inversely correlated with TNF-α, indicating a disrupted balance in the inflammatory response. Moreover, most patients showed evidence of active EBV infection, associated with the overexpression of LMP1, a viral protein capable of promoting the survival of autoreactive B cells and altering critical immune signaling pathways.
Another relevant finding was the activation of endogenous retroviruses (HERV-E). In heterologous plasma assays, we also confirmed that the lupus environment can directly modify the behavior of healthy immunocompetent cells, particularly by promoting changes in IL-6. Finally, we identified cross-reactivity between EBNA1 and Ro60, supporting the hypothesis of molecular mimicry as one of the mechanisms underlying the loss of immune tolerance.
Taken together, this study provides an integrated view of the role of EBV, endogenous retroviruses, and immune dysregulation in the pathogenesis of SLE. Beyond expanding the biological understanding of the disease, these findings suggest potential biomarkers and therapeutic pathways that may contribute to more precise and personalized management of lupus in the future.

KeyWords: Systemic lupus erythematosus (SLE); Epstein-Barr virus (EBV); Molecular mimicry; Cytokines (TNF-α, IFN-γ, IL-10, IL-6); Endogenous retroviruses (HERV-E).

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