A candidate HCV receptor on the surface of B cells is CD81, a member of the B-cell signaling membrane complex that includes CD19 and CD21. It is of interest that the expression of CD81 is increased in CD5+ B cells, considering that the expansion of CD5+ B cells is the hallmark of HCV-induced lymphoid stimulation.

The spectrum of HCV-related or -associated lymphoproliferative disorders is very wide. The most common form is represented by low-grade lymphomas, but intermediate to high-grade lymphomas are also positively associated with HCV, at least in the Mediterranean areas as in the case presented in this issue by Licata et al. The paper describes an interesting unusual case of an HCV-associated aggressive high-grade lymphoma that presented with skin involvement. The case reported in this issue raises the question of the relationships between HCV infection and the development of lymphoid malignancies. The close association between HCV infection and essential type II mixed cryoglobulinemia (EMC), a rather indolent lymphoproliferative disorder characterized by the production of cryoprecipitable monoclonal rheumatoid factor associated with polyclonal immunoglobulin G, has been firmly established. EMC behaves as a low-grade B-cell lymphoma. After a long follow-up, a minority of EMC cases evolve into a classical non-Hodgkin lymphoma (NHL) that retains the ability to produce cryoprecipitable rheumatoid factor. The existing data lead to the conclusion that HCV may be one of the elements involved in the multistep pathogenesis of a subgroup of indolent NHL.

The role of HCV in promoting the development of aggressive NHL is less clear. As the viral RNA sequences cannot be integrated in the host genome, a direct transforming role of HCV appears unlikely. It is also unclear...
how long the infection has to be operating in order to favor the development of HCV-related aggressive high-grade lymphomas. The lymphotropism of HCV underlines the possibility that the pathogenetic role of HCV lies in its ability to act as a chronic antigen stimulus. Among the population of HCV stimulated lymphocytes, subsequent mutational events might be triggered by the repeated stimulation and favor the emergence of a malignant clone. The result could be a B-cell NHL. Such a result may be more rapidly reached in patients with underlying immunodeficiency.

Reference