

# Unnatural fusion of API2 and MALT1 proteins leads to deregulated transcription in MALT lymphoma.

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Normal, healthy cells use specific proteins called transcription factors to regulate the activity of their genes. Importantly this is done in a tightly controlled manner. When the transcription factor NF- $\kappa$ B is functioning normally, it is capable of being turned off and on, and thus cellular function is retained. In many instances of cancer, however, NF- $\kappa$ B has lost its "off switch," which leads to unregulated gene activity (transcription).

Scientists at the University of Michigan have discovered a key factor leading to NF- $\kappa$ B deregulation in mucosa-associated lymphoid tissue (MALT) lymphoma. The proteins API2 and MALT1 are fused together to form an unnatural new protein. This fusion oncoprotein binds to NF- $\kappa$ B-inducing kinase (NIK) and cleaves it, thus removing the regulatory region of the kinase and leading to constant activity of the NF- $\kappa$ B pathway. Neither API2 nor MALT1 appear capable of cleaving NIK on their own. It is only the fusion protein that has this activity.

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