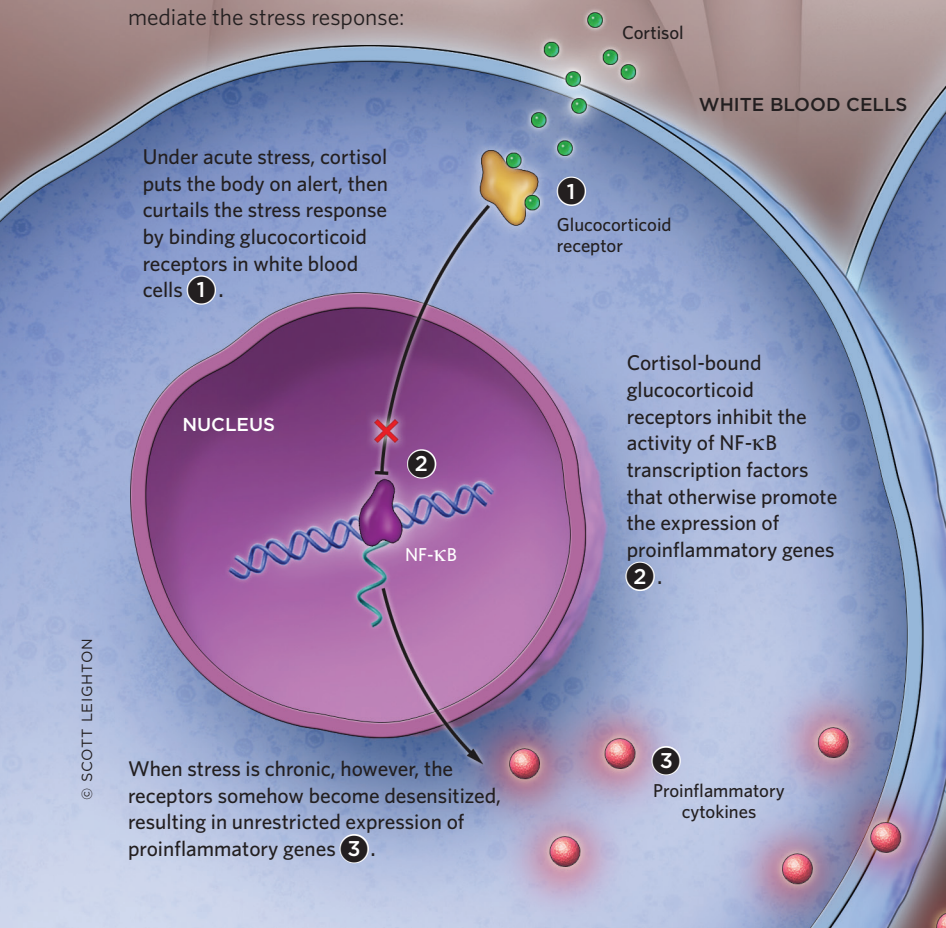


## STRESS IN THE BODY

Psychological stress resulting from our social environment causes the same physiological reaction that occurs in response to the threat of physical attack. Signals processed in the brain trigger the release of stress hormones such as cortisol and epinephrine to put the body on high alert. When stress is chronic, changes in the expression of large groups of immune-related genes in circulating white blood cells can cause ramped-up inflammation that influences susceptibility to disease.

Social stress causes the sympathetic nervous system to release the neurotransmitter norepinephrine directly from nerve fibers and the hormone epinephrine via the adrenal gland. Both neurotransmitters bind beta-adrenergic receptors, leading to increased inflammation and reduced viral defenses:

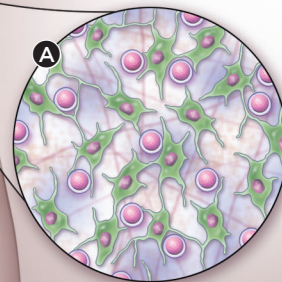
In response to social stress, the endocrine system, governed by the hypothalamus-pituitary-adrenal (HPA) axis, releases cortisol, which binds glucocorticoid receptors in white blood cells to mediate the stress response:



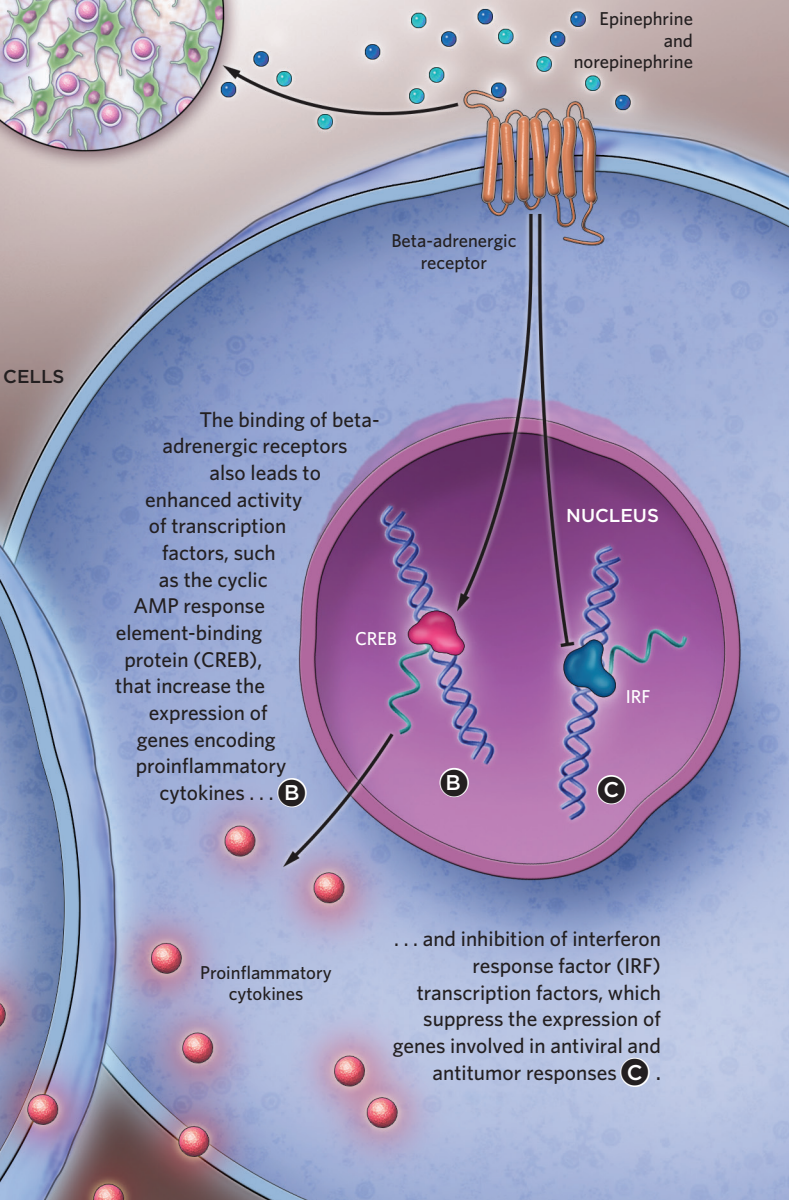
Under acute stress, cortisol puts the body on alert, then curtails the stress response by binding glucocorticoid receptors in white blood cells **1**.

Cortisol-bound glucocorticoid receptors inhibit the activity of NF-κB transcription factors that otherwise promote the expression of proinflammatory genes **2**.

When stress is chronic, however, the receptors somehow become desensitized, resulting in unrestricted expression of proinflammatory genes **3**.



Beta-adrenergic binding during chronic stress leads to increased production of a particular type of white blood cell, an immature proinflammatory monocyte **A**.



The binding of beta-adrenergic receptors also leads to enhanced activity of transcription factors, such as the cyclic AMP response element-binding protein (CREB), that increase the expression of genes encoding proinflammatory cytokines ... **B**

... and inhibition of interferon response factor (IRF) transcription factors, which suppress the expression of genes involved in antiviral and antitumor responses **C**.