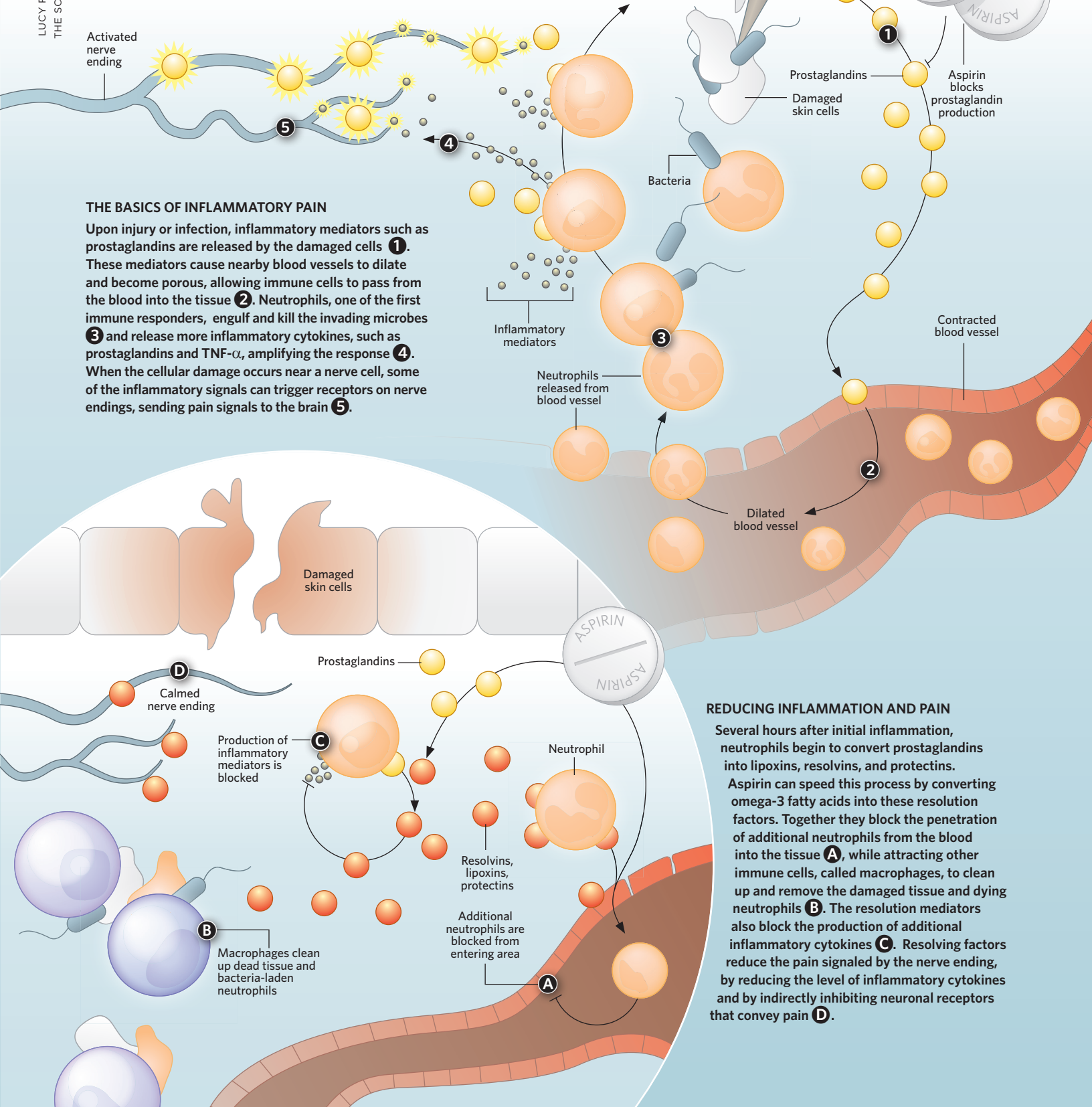


## INFLAMMATION, PAIN, AND RESOLVINS

Not all inflammation leads to pain. Despite widespread infection followed by fever, colds rarely cause pain. But when some cytokines and certain immune cells are active near pain-sensing nerves, they trigger receptors that convey pain sensations to the brain. Resolvins are naturally produced part-way into an inflammatory reaction, and help diminish inflammation as well as pain.



### THE BASICS OF INFLAMMATORY PAIN

Upon injury or infection, inflammatory mediators such as prostaglandins are released by the damaged cells **1**. These mediators cause nearby blood vessels to dilate and become porous, allowing immune cells to pass from the blood into the tissue **2**. Neutrophils, one of the first immune responders, engulf and kill the invading microbes **3** and release more inflammatory cytokines, such as prostaglandins and  $\text{TNF-}\alpha$ , amplifying the response **4**. When the cellular damage occurs near a nerve cell, some of the inflammatory signals can trigger receptors on nerve endings, sending pain signals to the brain **5**.

### REDUCING INFLAMMATION AND PAIN

Several hours after initial inflammation, neutrophils begin to convert prostaglandins into lipoxins, resolvins, and protectins. Aspirin can speed this process by converting omega-3 fatty acids into these resolution factors. Together they block the penetration of additional neutrophils from the blood into the tissue **A**, while attracting other immune cells, called macrophages, to clean up and remove the damaged tissue and dying neutrophils **B**. The resolution mediators also block the production of additional inflammatory cytokines **C**. Resolving factors reduce the pain signaled by the nerve ending, by reducing the level of inflammatory cytokines and by indirectly inhibiting neuronal receptors that convey pain **D**.