

SMELL GONE WRONG

One suspect mechanism for the smell dysfunction associated with a number of neurodegenerative diseases is damage to the basal forebrain cholinergic system. This system, whose cell bodies are located at the base of the forebrain **1**, sends cholinergic neural projections to the olfactory bulb **2** and other brain structures critical for the perception of smell, memory, and cognition. Importantly, neurons in this system keep in check the activity of immune cells, such as microglia and astrocytes **3**. Damage to neural cells projecting to the olfactory bulb can result in the activation of these resident immune cells, which, in turn, can wreak inflammatory havoc, releasing factors such as cytokine tumor necrosis factor-alpha (TNF- α) **4**. Low levels of TNF- α can be neuroprotective, but high levels risk cell damage and even death, possibly resulting in neurodegenerative disease and olfactory impairment.

