Humans have two immune systems, explains Randolph Noelle, Ph.D. So it makes sense to take advantage of both when developing vaccines. In a recent article in the journal *Blood*, Noelle described an experimental cancer vaccine that triggers the innate and acquired immune responses, resulting in a vast improvement over treatments that activate only one or the other.

Innate immunity provides the first defense against pathogens, responding almost immediately when a viral or bacterial invader enters the body. This response is prompted by toll-like receptors (TLRs), which are present in several types of cells involved in immunity. When they recognize a pathogen, they bind to bits of it, leading to swelling at the site of the infection and a low fever—signs the body is trying to fight off a threat.

Critical: This initial response is a critical part of fighting disease. "You've got to be able to initiate the immune response within minutes to hours," says Noelle. "You'd be dead without your innate immune system."

Acquired immunity, the next layer of protection, is activated in large part by the receptor CD40. Once stimulated, this molecule fires up an all-out defense against a pathogen. Noelle calls it "the on-off switch for acquired immunity. Without CD40, you don't make antibodies, you don't make cytotoxic T cells, you don't make inflammatory T cells."

Cells: Together, innate and acquired immunity shield humans from a world full of potentially harmful viruses and bacteria. But they often have trouble reacting to tumor cells, because those cells can appear similar to normal human cells, so the immune system doesn't mount a response. Cancer vaccines succeed by mimicking a natural pathogen, causing the immune system to respond to tumor cells that it might otherwise leave alone.

Noelle's lab has developed a way to stimulate both TLRs and CD40 with a single treatment—with impressive results. "The magnitude of the immune response that you get is spectacular," he says. In experiments with mice, he found that this approach is far more effective than activating either TLRs or CD40 alone.

To conduct the experiment, mice were injected with tumor cells. Then some of the mice were administered a vaccine that trig-