

# Jeremy M. Berg: Life-saving medicines begin in the basic research DOGE wants to stop funding

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We should not lose sight of how wonderfully productive the biomedical research enterprise — now under threat — can be. The interplay between curiosity-driven fundamental research, more targeted academic research, and both targeted research and risk-taking drug development campaigns in industry drives a powerful engine of discovery and progress.

But now, the public sector component is under attack through DOGE's efforts to "improve the efficiency" of the system through ill-considered modification of a rigorous method for covering all research costs, blocking normal grant-making processes, and terminating dedicated scientists and other workers at the NIH and other agencies, or coercing them into retirement.

Let me give one example of how research works and what it accomplishes. Discoveries begin in research that has no obvious application, doing work that others will build on in their own research and eventually yet others will find a way to apply it.

#### How research works

Many patients experience pain after minor surgery. In many cases, doctors prescribe opioids. However, studies have shown that more than 5% of patients are still taking opioids three to six months after surgery and are likely addicted.

Two months ago, the Food and Drug Administration approved suzetrigine (trade name Journavx), the first representative of a new drug class that has great potential both to help patients and to aid our nation in the fight against opioid addiction. It works by blocking proteins that allows sodium ions to pass through nerve cell membranes.

The journey to this drug began just before World War II when two British scientists discovered that nerve impulses involve the one-way flow of sodium ions across the nerve cell membrane, followed by the flow of potassium ions in the other direction. The scientists shared a Nobel prize for this seminal work.

Other scientists figured out more details of how nerve transmission works. A young pharmacologist in training at the National Institutes of Health (NIH) studied toxins from scorpions and salamanders that blocked the flow of sodium ions. After a few years, he set up his own federally funded laboratory and, in 1980, used the scorpion toxin to mark the sodium channel protein itself.

Over the next two decades, scientists discovered nine distinct sodium channels in humans and revealed further details of how sodium channels work throughout the body. Some studies revealed a role in pain sensation, and scientists started thinking about these proteins as targets for novel

pain killers. The motivation for this pursuit was enhanced by the discovery that some rare individuals who could not sense physical pain had mutations in genes for one specific type of sodium channel.

#### A major challenge

However, the fact that we have nine closely related types of sodium channels represents a major challenge. A good drug must target only those involved in peripheral pain sensation.

Effectively inhibiting a sodium channel in our central nervous systems or muscles would be devastating, as this is how the animal toxins work. The challenge of finding a drug candidate that targets only the pain sensing channels is akin to finding someone with an affinity for flat-coated retrievers, but who has no interest at all in goldens, Labradors, or other retrievers.

Many pharmaceutical companies launched programs to find pain killers based on these observations. However, these all failed, either in the laboratory or in clinical trials. It seemed to be an enticing puzzle that was just too hard to crack.

Scientists at one company first worked on the channel from the painresistant individuals, but these trials failed as well. But they persisted and discovered a molecule and refined it. The refined molecule showed remarkable specificity for only one type of sodium channel, one that had been implicated in pain sensation.

The company tested this molecule in clinical trials with patients undergoing relatively non-serious but still painful procedures: a tummy tuck or bunion-removal. It worked quite well, significantly better than placebo controls.

Because it does not act in the central nervous system, there is essentially no risk of addiction. This drug, and its likely successors, are huge steps in confronting the intertwined public health challenges of pain management and opioid addiction.

### An amazing feat

The drug discovery team, many of whom were trained initially at academic centers and at NIH, pulled off an amazing feat: They placed the crucial last piece into a 10,000-piece puzzle. But without pioneers finding the edge pieces, and many others filling in the middle, they would never have discovered that last piece.

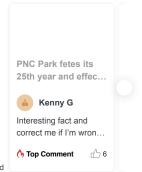
If the goal is to fix public sector research, this approach is akin to performing open heart surgery on this system using a blunt axe. Is our system perfect? No, good faith reforms are welcome.

But, if the government persists in this thoughtless approach, America will pay a very dear price, reducing the chances of future advances, and relinquishing our international leadership position in this important sector.

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