



Transforming BIOLOGICAL SCIENCE and BIOMEDICAL PRACTICE

Opioid overdoses killed more than 50,000 people in the U.S. in 2016, reaching epidemic proportions. New opioid drugs that suppress pain but are neither addictive nor likely to cause overdose deaths are now in the pharmaceutical pipeline, the result of decades of research into how medicines attach to and communicate with the body's cells. Critical to that research was a new method of determining the structure of large biological molecules, using extremely powerful beams of X-rays developed and supported at shared research facilities by the Basic Energy Sciences (BES) office of DOE. Such X-ray studies are now central to new drug development: the BES facilities are used by the pharmaceutical industry to screen most new drug candidates.

▶ The Breakthrough

The discovery that intense X-ray sources developed to study the structure of materials could also unlock the structure of large biological molecules.

- As biomedical research has increasingly focused at the molecular level, biological scientists from universities and from the pharmaceutical industry have become the largest user group at the five BES X-ray facilities spread across the country.
- Repeated X-ray studies by university researchers led to determining the structure of the family of proteins to which most drugs attach, research that enabled more rational drug design and that was awarded a Nobel Prize.

▶ The Impact

- Pharma companies now operate (and pay for) dedicated X-ray beamlines at two separate BES shared research facilities, enabling rapid screening of more than 20,000 new drug candidates a year to optimize their structure before clinical trials.
- Knowledge of how opioid drugs attach to multiple targets in the body—those that relieve pain, and others that cause addiction or suppress breathing—has led to the development of drug candidates which only relieve pain.

▶ The Takeaway

Access to shared research facilities such as the BES X-ray sources has transformed understanding of the structure of biological materials, which in turn has transformed both biological science and drug development, speeding the availability of new medicines.

ABOUT THE IMAGES

The epidemic of opioid overuse—both prescription medicines and illegal drugs—has become a national public health crisis.
(KAREN FOLEY PHOTOGRAPHY / SHUTTERSTOCK.COM)

X-ray analysis showed how drugs attach to and interact with a family of large, complex protein molecules. That knowledge enabled pharma companies to fine tune new drug candidates.
(BRIAN KOBILKA / STANFORD UNIVERSITY)

Two scientists discuss how to adjust the BES X-ray beamline they used to determine the structure shown above.
(MARK LOPEZ / ARGONNE NATIONAL LABORATORY)