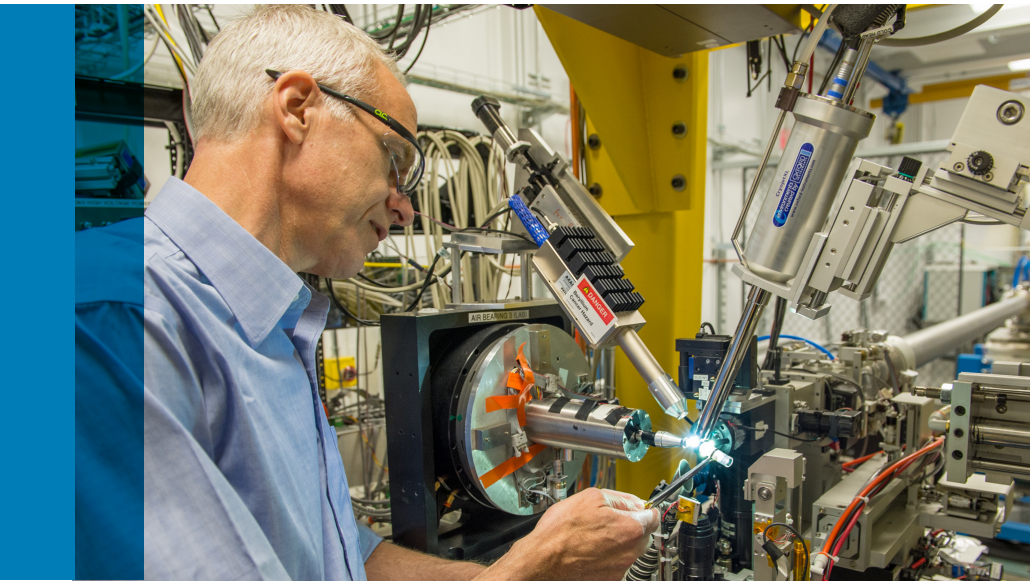
Argonne NATIONAL LABORATORY

ADVANCED PHOTON SOURCE TECHNOLOGY REMOVES BARRIER TO DRUG DESIGN



Stanford University Professor Brian Kobilka is shown using the micro-x-ray beam developed at the APS. This technology was used to conduct nearly all of the x-ray research that earned Kobilka and Duke University Professor Robert Lefkowitz a 2012 Nobel Prize. The beam enables the study of previously unusable protein crystals, which opens the door to new pharmaceutical research.

The advent of the first micro x-ray beam for structural biology at the Advanced Photon Source (APS) at Argonne National Laboratory enabled the research that earned the 2012 Nobel Prize in Chemistry and lays the groundwork for countless new pharmaceuticals.

Nearly half of today's pharmaceuticals work by connecting with many of the 800 or so human G-protein-coupled receptors (GPCRs). GPCRs are a large set of proteins embedded in a cell's membrane that sense molecules outside the cell and activate a cascade of different cellular processes in response, including breathing and dilating of arteries.

But to do this well, a drug needs to connect to the protein like a key opens a lock. Improving drugs requires knowing exactly how these proteins work and are structured, which is difficult because the long, slender protein chains are folded in an intricate pattern that threads in and out of the cell's membrane.

Nearly all of the Nobel Prize -ray research done to unravel and identify how GPCRs work was done at the National Institute of General Medical Sciences and National Cancer Institute (GM/CA-XSD) x-ray beamline at the APS because the scientists needed an x-ray beam that was very stable, intense, and focused to a small spot. This work included discovering the first structure of a human GPCR and later the first study of a GPCR in the process of sending signals to activate a cellular response.

IMPACT

These studies represent a huge leap forward in understanding how cells work at the molecular level, lay the groundwork for new therapies and open up new frontiers in biology.

PARTNERS

The National Institute of General Medical Sciences (NIGMS), the National Cancer Institute (NCI), and the National Institutes of Health (NIH) operate the GM/CA-XSD beamline where the work was done. The technology was developed by scientists from Argonne, NIGMS, NCI, NIH, and the University of Michigan.

FUNDING

The U.S. Department of Energy Office of Science funds the APS. The micro-x-ray beam was funded by NIH, NIGMS, and NCI.

AWARD

Micro-x-ray beam technology won a 2010 R&D 100 award and enabled the research that was awarded the 2012 Nobel Prize in Chemistry.

MORE INFO

http://www.anl.gov/articles/advanced-photon-source-lights-way-2012-chemistry-nobel

http://www.aps.anl.gov/News/APS_News/Content/APS_NEWS_20121015.php

TIMELINE

1947: synchrotron x-radiation is first observed
1962: first protein sequence determined
1994: first G-protein determined
2007-2009: GM/CA-XSD staff developed the micro x-ray beam

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