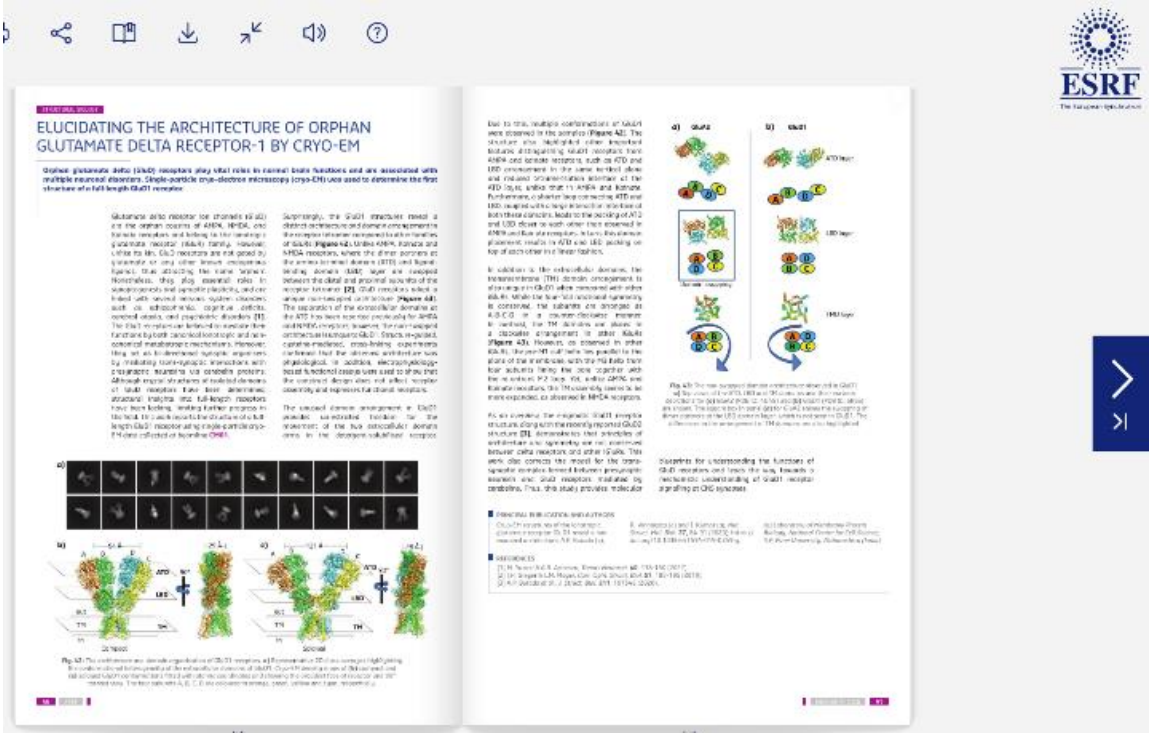
Synchrotron Radiation Facility highlights work of DBT-NCCS scientists

New Delhi, Feb 18: The European Synchrotron Radiation Facility (ESRF) is an international research centre located in Grenoble, France. It has extremely sophisticated, cutting-edge research tools, such as the world's brightest X-ray source and a cryo electron microscope (cryo-EM), which are used to determine the structure of different materials at very high resolutions.



It is a product of international cooperation between 22 partner nations, including 13 Member Countries and 9 Scientific Associates. It is an example of countries coming together to work towards research goals that would be challenging for countries to achieve individually. India joined it in 2017 as a Scientific Associate, making it the 22nd partner nation, when the Department of Biotechnology (DBT) of the Government of India and the ESRF Council signed an agreement to provide access to it for Indian scientists, especially for research in structural biology.

Structural biology deals with determining the three-dimensional molecular structure of biological macromolecules like proteins, which helps understand what these molecules do and how. These insights are valuable for various biotechnological applications, such as for development of drugs and vaccines.

Dr. Janesh Kumar, scientist at the National Centre for Cell Science (DBT-NCCS) in Pune, is a structural biologist who studies the structures of protein molecules called ‘receptors’ present in the brain. Cutting-edge research carried out by Dr. Janesh & his team has led to

key brain receptors being decoded at the molecular level. This team has captured the first three dimensional views of a class of receptors, called GluD1-subtype glutamate receptor, using a technique called cryo electron microscopy (cryo-EM) available at the ESRF. These special receptors play crucial roles in motor coordination and motor learning, and high-frequency hearing, and are also key to many other brain functions. They are also linked to social and cognitive deficits, and to neuronal disorders like schizophrenia and cocaine addiction.

This discovery could therefore lead to novel insights into the mechanism behind a wide range of nervous system disorders and diseases. The outcomes of this research resulted in a paper published in the prestigious scientific journal, Nature Structural and Molecular Biology, which was selected as one of the most exciting subjects investigated at the European Synchrotron Radiation Facility (ESRF) last year. Subsequently, this paper was featured in 'ESRF Highlights 2020'. This is an annual booklet published by the ESRF to highlight the exciting scientific work carried out at ESRF, and it presents information on major scientific results and important contributions made by users of this facility from different countries.

The findings of Dr. Janesh Kumar and his team have revealed an unprecedented novel molecular architecture of GluD1 receptors, which is distinct from that observed in other members of the glutamate receptor family. This highlights the fact that glutamate receptor ion channels are not built the same, and provides valuable insights into the molecular underpinnings of receptor functions. The majority of excitatory brain signalling is carried out by glutamate receptor ion channels that are present on the synaptic junctions of neurons. These receptors form cornerstones of a multitude of high cognitive functions, including learning and memory. However, unlike other members of this family of receptors, the orphan delta receptors are not activated by neurotransmitter glutamate binding. This has been puzzling researchers in the field for decades.

The current discovery made by this group offers clues into the structural differences that might be responsible for this inactivity, and the unique functions of orphan delta receptors. The GluD1 structure deciphered by these scientists corrects the decade-old model of the receptor that was built on other members of the glutamate receptor family. These scientists also propose a new model for the way this receptor interacts with other proteins at the synapse. Thus, this study creates a robust platform for understanding the functions of these receptors, and for developing therapeutics to treat neurological disorders that are associated with GluD1 dysfunction. Cryo-EM, the tool used for this research, is a revolutionary technique that images several thousand molecules in the frozen state, and combines the 2D images generated to build a three-dimensional view. Joachim Frank, Jacques Dubochet and Richard Henderson were awarded the Nobel Prize for Chemistry in 2017, for the development of this technique.

Contact details: Dr. Janesh Kumar, janesh@nccs.res.in

Communication coordinator: Jyoti Rao jyoti@nccs.res.in

Link: https://www.nccs.res.in/