Press release

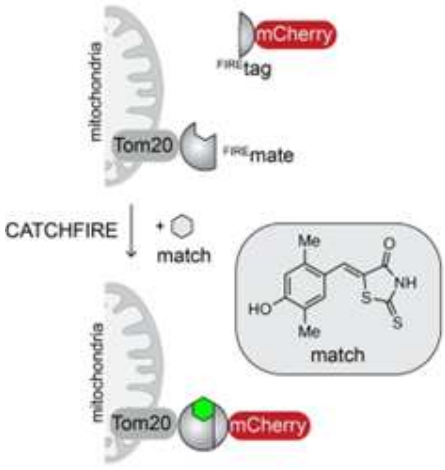
29 August, 2023

CATCHFIRE: An innovative tool to control the private lives of cells and view them via fluorescence

Researchers from Institut Curie, the CNRS, Sorbonne University and ENS-PSL have just developed an innovative molecular tool. Known as CATCHFIRE, it lets you not only control the closeness of two proteins, but also view their proximity. These multi-disciplinary efforts offer a number of applications for study of basic biological processes, but also in biomedicine, for genetic and metabolic diseases for example, or in the field of cell therapy for cancer treatment. These results are published on August 28, 2023, in *Nature Methods*.

Gene expression, protein transport, activation of signaling pathways, immune response, inter- and intra-cellular communication... All basic processes in biology are governed by complex mechanisms regulated by the physical proximity of molecules. How can we control and view these proximities to better understand and decipher the phenomena occurring in the cell? How can we exploit this proximity in a variety of applications?

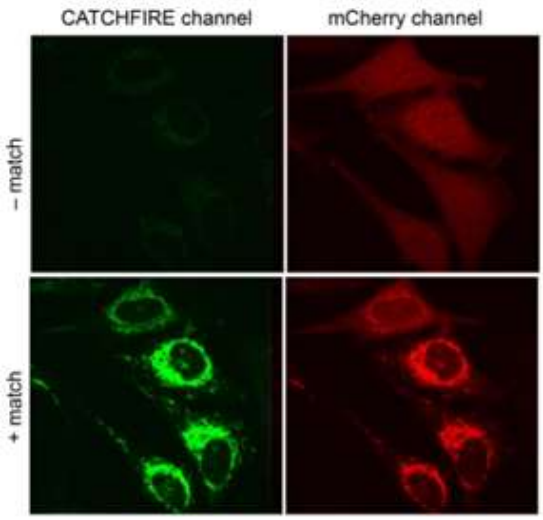
The teams of Prof. Arnaud Gautier, researcher at the Laboratory of Biomolecules (Sorbonne University, ENS-PSL University, CNRS) and Dr. Franck Perez, CNRS researcher director at Institut Curie (Cell Biology and Cancer unit/Institut Curie/CNRS) have designed an **original and unique molecular tool capable of artificially controlling the proximity of two proteins in cells, but also of viewing their interactions in order to dissect the various molecular events involved.**



This new method has been named CATCHFIRE for *Chemically Assisted Tethering of Chimera by Fluorogenic Induced Recognition*.

How does CATCHFIRE work? The two molecules in question (for example mCherry and Tom20 in the diagram opposite) are merged to two small protein domains (Firemate et Firetag), which are capable of interacting together in the presence of a small synthetic molecule, called "match", acting as molecular adhesive.

When the two domains interact, the match molecule sees its fluorescence increase by a factor of 100. Researchers can then observe the newly-induced interaction via fluorescence microscopy. Another advantage of the system is that it's reversible.



CATCHFIRE in action in mammal cells that jointly express the protein of the external membrane of Tom20 mitochondria merged with FIREmate and the red fluorescent protein mCherry merged with FIREtag. The addition of "match" induces the interaction of the two proteins (visible due to activation of its green fluorescence) leading to recruitment of mCherry at the surface of the mitochondria.

The advantage of CATCHFIRE is that this tool can reproduce itself and can be applied over and over with a number of proteins. This objective and quantitative approach has enabled researchers to **control and track various interactions involved in the transport and location of proteins, secretory protein traffic, transport of organelles such as lysosomes and cellular mechanisms such as mitophagy.**

In addition, they exploited the fluorogenic nature of CATCHFIRE to **design new sensors - "biosensors" - that can quantify the activation of certain signaling pathways or trigger cellular processes such as apoptosis (programmed cell death).**

"Our approach elegantly illustrates how the combination of concepts and principles from two disciplines - chemistry and biology - enables us to design new and innovative molecular tools for the study and control of cell functions" proclaim the authors, **Dr. Franck Perez, biologist and CNRS researcher at Institut Curie and Prof. Arnaud Gautier, Professor of Chemistry at Sorbonne University**. The application potential of CATCHFIRE is immense: the possibilities for studying basic biological processes are numerous, and the developments in biomedicine are promising, in particular in cellular therapy, which represents enormous hope for treatment of cancer and genetic and metabolic diseases, for example."

Reference: A fluorogenic chemically induced dimerization technology for controlling, imaging and sensing protein proximity. Sara Bottone, Octave Joliot, Zeyneb Vildan Cakil, Lina El Hajji, Louise-Marie Rakotoarison, Gaelle Boncompain, Franck Perez, Arnaud Gautier.
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About Institut Curie

Institut Curie, France's leading cancer center, combines an internationally-renowned research center with a cutting-edge hospital group, treating all types of cancer, including the rarest. Founded in 1909 by Marie Curie, Institut Curie has 3 sites (Paris, Saint-Cloud and Orsay) with over 3,700 researchers, physicians and health professionals working on its 3 missions: treatment, research and teaching. A foundation with public utility status, Institut Curie is authorized to accept donations and bequests, and thanks to the support of its donors, is able to accelerate discoveries and improve patient treatment and quality of life. Find out more: www.curie.fr / **See Institut Curie's new press area dedicated to journalists**

About the CNRS

The CNRS (Centre national de la recherche scientifique) is one of the world's most renowned and reputed public research institutions. For over 80 years it has achieved excellence in terms of its recruitment and develops multi- and inter-disciplinary research throughout the country, Europe and the world. An entity focused on the common good, it contributes to scientific, economic and social progress in France. The CNRS is all about its 33,000 women and men and its 200 professions. Its 1,000 laboratories, most of them shared with universities, schools and other research bodies, represent over 120,000 people, working to further knowledge through exploration of living organisms, matter, the universe and the way human societies function. The close tie that it forms between its research activity and transfer of this activity to society has made it a crucial player in innovation. Partnership with companies is the bedrock of its development policy. It is deployed through over 200 structures shared with industrial players and through the creation of some hundred start-ups each year, testifying to the economic potential of its research work. The CNRS makes its research work and data available, and this knowledge is shared with various audiences including scientific communities, media, decision-makers, economic players and the general public. *For more information:* www.cnrs.fr

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The École normale supérieure - PSL is a world-class institute of higher education and research that trains over 2,000 students, including 600 PhD students and 200 post-doctoral fellows, in careers covering scientific research, higher and secondary education, State administrative services, regional authorities, public institutions and private companies. With a firmly international reach, 15 departments, 31 research units and over one hundred research teams covering most disciplines, including the humanities, social sciences and life sciences, the École Normale Supérieure receives regular awards and today boasts 15 Nobel Prize winners, 10 Fields medal winners, and 28 CNRS gold medal winners. ENS-PSL is looking to develop partnerships with foundations that work for equal opportunity and is a founding member and component of PSL University. *Find out more*: www.ens.fr

About Sorbonne University

Sorbonne University is a world-class multidisciplinary intensive research university covering the arts and the humanities, medicine, science and engineering. Based in the heart of Paris and present in other regions of France, Sorbonne University has 52,000 students, 6,400 members of teaching and research staff, and over one hundred laboratories. Alongside its partners from the Sorbonne University Alliance, and via its multidisciplinary initiatives and institutes, it conducts and programs research and training to shore up its collective contribution to the challenges of three major transitions: the global health approach (One Health), resources for a sustainable planet (One Earth), societies, languages and cultures in mutation (One Humanity). Sorbonne University is also a member of the 4EU+ Alliance, an innovative European university model that develops strategic international partnerships and promotes its community's engagement with the rest of the world. https://www.sorbonne-universite.fr / @ServicePresseSU