

The Royal Swedish Academy of Sciences has decided to award the Nobel Prize in Chemistry 2022 "for the development of click chemistry and bioorthogonal chemistry" to Carolyn R. Bertozzi, Morten Meldal and **K. Barry Sharpless**.

Their functional chemistry works wonders

The Nobel Prize in Chemistry 2022 is about making difficult processes easier. Barry Sharpless and Morten Meldal laid the foundation for a functional form of chemistry – *click chemistry* in which molecular building blocks snap together quickly and efficiently. Carolyn Bertozzi has taken click chemistry to a new dimension and implemented it in living organisms.

Chemists have long been driven by the desire to build increasingly complicated molecules. In pharmaceutical research, this has often involved artificially recreating natural molecules with medicinal properties. This has led to many admirable molecular constructions, but unfortunately these are generally time consuming and very expensive to produce.

The Nobel Prize in Chemistry 2022 deals with rethinking and renewing; not overcomplicating matters and instead working with what is easy and simple. Advanced and functional molecules can be built even by taking a straightforward

route. The chemical reactions being recognised are so unique they can be used in living organisms; they are *bioorthogonal*, which means they do not disturb the other chemistry in the cell.

Barry Sharpless – who was also awarded the Nobel Prize in Chemistry in 2001 – set the ball rolling. In 2001, he encouraged chemists to leave difficult reactions behind and to stop trying to imitate nature's most complex molecules. He coined the concept of click chemistry for a simple and reliable form of chemistry in which reactions occur quickly and unwanted by-products are minimised.



The crown jewel of click chemistry

In 2002, Morten Meldal and Barry Sharpless – independently of each other – presented what has become the crown jewel of click chemistry: the copper catalysed azide-alkyne cycloaddition. This is an elegant chemical reaction between two chemical groups: an alkyne and an azide. They react efficiently with each other when copper ions are added. This reaction is now used around the world to link molecules in a simple manner.

Click chemistry illuminates cells

Carolyn Bertozzi took click chemistry to a new level. To map important but elusive biomolecules on the surface of cells – glycans – she developed click reactions that work inside living organisms. Her bioorthogonal reactions take place without disrupting other chemistry in the cell and are now used globally to explore cells and track biological processes.



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More information about the Nobel Prize in Chemistry 2022 is available at www.kva.se/nobelchemistry2022 and www.nobelprize.org, with video and detailed information about the prize and the laureates.

The Nobel Prize 2022 in Chemistry



For the greatest benefit to humankind Click chemistry is used in many different ways, including the development of new pharmaceuticals, mapping DNA and the creation of more fit-for-purpose materials.

Bertozzi's bioorthogonal reactions have been developed and are now not only involved in the study of glycans, but also proteins, DNA and RNA. They are often used to track disease processes, and researchers are also investigating whether bioorthogonal chemistry can be utilised in the creation of new types of pharmaceuticals.

1. To study glycans – special carbohydrates that sit on the surface of cells – Bertozzi fed cells a modified sugar with an azide on it. The azide functioned as a type of molecular handle.

2. The modified sugar was incorporated into the glycans on the cell's surface.

3. In the next step, Bertozzi used an alkyne that was forced into a ringshaped molecule. The alkyne clicked with the azide.

4. A fluorescent green molecule sat on the ring-shaped molecule. This allowed Bertozzi to track the glycans on the cell's surface.

Carolyn R. Bertozzi

Triazole

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Printing and distribution made possible by VOLVO

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