

Amino acids play a key role in how cells respond to drugs

- *These molecules act as small building blocks that regulate the cellular response by switching certain internal signals on or off*
- *This is the conclusion of an international study led by the Hospital del Mar Research Institute, published in the journal Nature Communications*
- *The findings may help develop more precise drugs to treat various diseases more effectively, while avoiding side effects*

Barcelona, July 16, 2025. – Amino acids play a fundamental role in **regulating how cells respond to drugs**. These molecules, which form proteins, act like **bricks that communicate with each other within a structure**. In this way, they work together to regulate the cellular response, which could help develop more effective and safer treatments, according to an international study led by the Hospital del Mar Research Institute and published in *Nature Communications*.

The study focused on a specific cellular receptor, the **cannabinoid receptor type 2 (CB2)**, a key protein in the human immune system. It belongs to a family of proteins known as **G protein-coupled receptors (GPCRs)**, which are responsible for transmitting information into cells. Remarkably, these receptors are the target of one in three approved drugs, covering treatments for cardiovascular diseases, cancer, asthma, and mental health disorders.

The researchers used **computer simulations**, lab experiments, and machine learning tools to analyze every amino acid in the receptor one by one and observe how each change affected its behavior. As Dr. Jana Selent, coordinator of the GPCR Drug Discovery Research Group within the Biomedical Informatics Research Program at the Hospital del Mar Research Institute, and associate researcher at Pompeu Fabra University, explains:

"The most exciting part is that we've learned how these small building blocks work within a huge network to activate specific cellular responses". This could make it possible that, ***"by targeting key points in this network, we can now design drugs that guide the receptor precisely toward the desired response"***, adds Dr. Selent, who led the study.

A networked mechanism influencing cells

The study showed that amino acids do not act in isolation; instead, they constantly communicate through a dynamic network that modulates how cells respond to different stimuli — whether cellular signals, medications, or environmental changes. In the case of the cannabinoid receptor type 2, they steer the cellular response toward beneficial pathways, avoiding others that could cause unwanted effects.

With this knowledge, researchers can move toward more accurate and targeted treatments — a particularly important benefit in diseases where current drugs can trigger undesirable side effects.

"It's like giving a drug exact instruction to reach only the specific place we want, and nowhere else", explains Miguel Diéguez, co-author of the study and a research trainee at the Hospital del Mar Research Institute.

All results, datasets, and tools generated by this research have been made publicly available through the platform <https://gpcrmd.org/> so any researcher can access and use them.

Reference article

Morales-Pastor, A., Miljuš, T., Dieguez-Eceolaza, M. et al. Multiple intramolecular triggers converge to preferential G protein coupling in the CB2R. Nat Commun 16, 5265 (2025).

<https://doi.org/10.1038/s41467-025-60003-0>

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