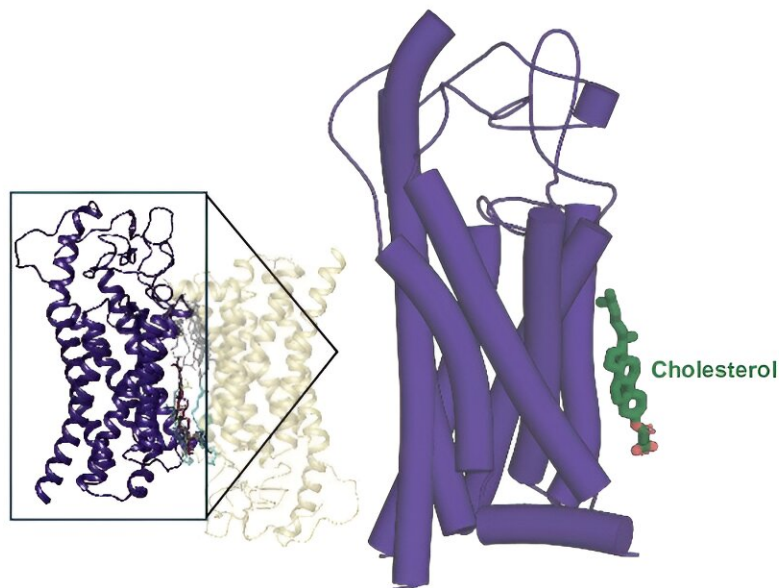


# New knowledge about cell receptors paves the way for future drugs against intestinal tumors

August 29 2024, by Anne Hammarskjöld

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High-resolution cryo-EM structure of FZD<sub>7</sub> reveals a functional cholesterol important in transmitting signals into the cell. Credit: Adapted from *Nature Communications* (2024). DOI: 10.1038/s41467-024-51664-4

A new study from Karolinska Institutet [published](#) in *Nature Communications* provides valuable insights into the activation of

receptors on the cell surface. The knowledge could lead to new targeted therapies and drugs against intestinal tumors, among other cancers.

Receptors on the surface of the cell are a kind of signal receiver that conveys information to the cell's interior. In a new study, researchers have focused on FZD<sub>7</sub>, a G-protein-coupled receptor that is involved in several important biological functions in the body. It is also linked to various cancers, including [colorectal cancer](#).

"Receptor activation is an important step in how the cells receive and send out signals. When receptors such as FZD<sub>7</sub> are activated, they trigger a series of events inside the cell that control cell growth, differentiation and movement," explains the study's last author Gunnar Schulte, professor at the Department of Physiology and Pharmacology, Karolinska Institutet.

Using [cryo-electron microscopy](#), the researchers have been able to create a clear image of the structure of FZD<sub>7</sub> with a resolution of 1.9 Angstrom. It is one of the best resolutions that has been reported when this type of protein has been studied with cryo-electron microscopy.

"This outstanding [resolution](#) allows us to understand in detail the receptor's activation mechanism. Understanding these processes can help us develop targeted therapies for diseases where these pathways are disrupted, such as colorectal cancer," says Schulte.

## **Cholesterol plays an important role**

The researchers discovered that the presence of cholesterol seems to facilitate the interaction between the FZD<sub>7</sub> receptor and another protein called "Dishevelled."

This interaction is the basis for the receptor to be able to transmit signals

to the cell, and it is also crucial for driving various biological processes such as intestinal epithelium renewal and homeostasis.

## Enabling targeted therapies

The results from the study not only increase the understanding of how receptors work, but also pave the way for the development of targeted medical therapies.

"In colorectal cancer, FZD<sub>7</sub> is overactive. The activation mechanism is now revealed in great detail, which makes it easier to find therapeutic approaches to block the overactivity," says Schulte.

The study lays the foundation for future research that will be complemented by pharmacological analyses with the ultimate goal of developing drugs.

**More information:** Julien Bous et al, Structural basis of frizzled 7 activation and allosteric regulation, *Nature Communications* (2024). [DOI: 10.1038/s41467-024-51664-4](https://doi.org/10.1038/s41467-024-51664-4)

Provided by Karolinska Institutet

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