

# Action of drug compounds in tissue revealed by new technique

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A new technique that can analyze how drug molecules bind to proteins in tissue samples could offer an improved route to drug discovery and development.

Researchers at the University of Birmingham developed the technique in

collaboration with global biopharmaceutical company AstraZeneca. It uses mass spectrometry, an [analytical tool](#) commonly used for identifying the properties of molecules within a sample.

Part of the early stages of [drug discovery](#) takes place in [cell cultures](#), clusters of cells that are grown in the laboratory, outside of their natural environment. Cell cultures enable the effects of different compounds to be tested on specific biological targets involved in various diseases. Although this allows researchers to assess how the compounds act against the target, it does not capture the full effects of the physiological environment.

This new technique, described in a paper published in *Angewandte Chemie*, enables researchers to use real [tissue samples](#) to assess which proteins the drug will bind to in the body and therefore how effective it is likely to be against the target.

Being able to pinpoint the interaction between the drug and the protein can provide valuable insight to guide drug discovery.

Lead researcher Professor Helen Cooper says that "usually in early-stage drug discovery, measurements are taken outside of the physiological environment, so when researchers move onto testing drugs in tissue, they can fail because they have interactions that were not expected."

"Identifying the drug protein interaction at this early stage, however, is incredibly hard. Using mass spectrometry on proteins is often compared to making an elephant fly. What we've done is add an unsecured hat—the drug molecule—to the elephant, and measured the whole process. It's exciting because it opens up the possibility of being able to follow the route of a drug through the body. By identifying which proteins it interacts with scientists will be able to predict at an earlier stage whether or not it will have the desired therapeutic effect."

In the study, the researchers used tissue taken from the livers of rats dosed with bezafibrate, a drug commonly used to treat high cholesterol. They used [mass spectrometry](#) on thin sections of tissue to detect the drug molecule and the specific fatty acid binding [protein](#) to which it attaches to form a complex.

The researchers were also able to measure both the varying amounts of this complex in the liver over time, and how it spreads through the tissue.

AstraZeneca lead Professor Richard Goodwin, Senior Director, Imaging Sciences says that "what is key to delivering such innovative science is sustained collaboration between academic leaders and industry partners. This research builds on a long-standing collaboration between AstraZeneca and the University of Birmingham, and exemplifies what can be done when we combine complementary skills to address significant unmet need. This research will continue to support drug discovery and help accelerate us bringing new medicines to patients."

Next steps for the research will include improving the sensitivity of the technique, and extending it to other types of [drug](#) compounds. Looking further ahead, the team hopes it can be developed for use in [human tissue](#), taken from biopsies. This would yield a greater understanding of why drugs work differently in different patients.

**More information:** Eva Illes-Toth et al, Mass Spectrometry Detection and Imaging of a Non-Covalent Protein–Drug Complex in Tissue from Orally Dosed Rats, *Angewandte Chemie* (2022). [DOI: 10.1002/ange.202202075](#)

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