Researchers develop new chemical method to enhance drug discovery

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Credit: Edward Jenner from Pexels

Moffitt Cancer Center researchers have developed a novel reagent that enhances the precision of drug synthesis. This innovative method, published in *Nature Communications*, introduces a new sulfur fluoride

exchange (SuFEx) reagent that allows for highly controlled production of crucial sulfur-based molecules, including sulfinamides, sulfonimidamides and sulfoximines.

These compounds are essential in the pharmaceutical industry but have been challenging to synthesize with the required stereochemical accuracy. The innovative reagent t-BuSF uses strain-release reactivity to achieve a level of efficiency and selectivity previously unattainable, paving the way for more effective drug development and broader applications in medical research.

"Sulfur-based compounds, including those developed using the new methods, are known to have favorable physiochemical properties that make them ideal candidates for drug development," said Justin M. Lopchuk, Ph.D., lead author and associate member of the Drug Discovery Department at Moffitt. "The ability to synthesize these compounds rapidly and stereochemical control open new possibilities for designing targeted therapies that combat cancer cells more effectively while minimizing side effects."

By leveraging the unique properties of the t-BuSF reagent, researchers were able to explore previously inaccessible chemical space within the sulfur family, particularly in the S(IV) and S(VI) oxidation states. This advancement has resulted in the creation of over 70 new chemical compounds, many of which have immediate applications in medicinal chemistry and the development of new pharmaceutical agents.

Lopchuk adds that this research has already been used to significantly improve the scalable synthesis of DFV890, an investigational compound from Novartis currently in clinical trials at Moffitt and other locations for myeloid diseases.

More information: Paresh R. Athawale et al, Strain-release driven

reactivity of a chiral SuFEx reagent provides stereocontrolled access to sulfinamides, sulfonimidamides, and sulfoximines, *Nature Communications* (2024). DOI: 10.1038/s41467-024-51224-w

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