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Marquette University: Chemistry professor receives $1.8 million grant to modernize processes in medicine synthesis

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MILWAUKEE — Dr. Joseph Clark, associate professor of chemistry in Marquette University's Klingler College of Arts and Sciences, has received a $1.8 million Maximizing Investigators' Research Award from the National Institutes of Health for his research to modernize the synthesis of selectively deuterated small molecules. Recently, deuterated small molecules have emerged as novel drug leads, creating a demand for new techniques for precision deuteration in drug synthesis.

Deuterium is a naturally occurring isotope of hydrogen and contains an additional neutron which makes it twice as heavy. When deuterium is precisely installed into a drug molecule, the metabolic profile of the drug can be changed. Significantly, this modification can lead to safer drug candidates with improved metabolic properties without sacrificing drug potency.

"Despite the tremendous promise that novel deuterated small molecules have in the development of new medicines, methods to incorporate deuterium into molecular scaffolds are significantly underdeveloped," Clark said. "We are launching a holistic research program to not only develop highly selective reactions for deuterium incorporation but pioneer the expansion of analytical techniques required to support the development and use of these reactions among the broader scientific community."

Through established collaboration with leaders in the spectroscopy field, Clark and his team have started to develop analytical techniques that provide the foundation

for accurate characterization and quantification of deuterated small molecules. Preliminary studies indicate that deuterium can be installed precisely into small molecules and the team's research is now positioned for expansion into broader classes of organic molecules.

"This award is an outstanding and well-deserved honor for Dr. Clark and demonstrates the innovate research happening at Marquette," said Dr. Heidi Bostic, dean of the Klingler College of Arts and Sciences. "The NIH has recognized the importance of this project and its potential for an important contribution to the safety of new medicines. This research will drastically expand the development of new therapeutics to address many of the safety and tolerability problems plaguing modern medicine."

The processes being utilized for this grant were the basis of a paper from the Clark Lab at Marquette and Pate Lab at University of Virginia, "Enantioselective Synthesis of Enantioisotopomers with Quantitative Chiral Analysis by Chiral Tag Rotational Spectroscopy," which appeared in the July 25, 2022, edition of "Angewandte Chemie," a journal of the German Chemical Society and one of the prime chemistry journals in the world. The paper received "Very Important Paper' status, which is reserved for the top 5% of all papers submitted.

The MIRA is spread out over five years and is worth $1,848,854. It is intended to provide support for the research in an investigator's laboratory that falls within the mission of the National Institute of General Medicine Sciences. The goal is to increase the efficiency of NIGMS funding by providing investigators with greater stability and flexibility, thereby enhancing scientific productivity and the chances for important breakthroughs.