Study shows how different people respond to aspirin—an important cardioprotective drug

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Researchers have learned new information about how different people respond to aspirin, a globally prescribed drug in cardioprotection. The research team, led by scientists at Cardiff University in the United Kingdom and including representatives from the University of Alabama at Birmingham and the University of Colorado, identified more than 5,600 lipids—or fats—in blood platelets and gained new insights into how these cells respond to aspirin.

"Aspirin is a widely used cardiovascular preventive drug and also has an emerging role in cancer treatment and prevention," said Valerie O'Donnell, Ph.D., Division of Infection and Immunity, Cardiff University, and the study's lead author. "Understanding how people respond to aspirin is key in terms of knowing who will benefit from it."

The findings, published April 28 in *Cell Metabolism*, are the first comprehensive lipidomic profile of human platelets in response to stimulation and aspirin treatment.

"Our research shows a new link between energy metabolism and inflammation, as well as giving early insights into the fundamentals of precision medicine regarding the variation of the lipidome among individuals," said Victor Darley-Usmar, Ph.D., Endowed Professor of Mitochondrial Medicine and Pathology at UAB and a co-investigator on the study.

Lipids play essential structural roles, act as nutrients, and control a broad

range of physiological and pathophysiological events in cells, according to the researchers.

"While several lipid families are well-characterized at the molecular level, the total diversity and number of unique lipids in cells, how they change during cellular activation, and how they differ in individuals is unknown," said Darley-Usmar. "This hampers integration of lipidomics into systems biology, and addressing it will improve our fundamental understanding of lipid biology, help identify new drug targets for therapy and discover lipid biomarkers from disease cohorts."

"This work led by Professor O'Donnell is a technical tour de force, providing a wonderful resource for other biomedical researchers," said Mike Murphy, Ph.D., programme leader, Mitochondrial Biology Unit at Cambridge University, U.K. "A particularly important aspect is the focus on platelets, which are readily available from patients' blood in diagnosis, prognosis or as a biomarker in assessing therapies. In addition to its future use, this work also demonstrated an unexpected link between mitochondrial fat metabolism and platelet activation during inflammation."

"Given the importance of aspirin as both a cardioprotective and possible cancer therapeutic, a full understanding of how it regulates platelet lipids will be the focus of a follow-on study with a larger number of volunteers," said Robert Murphy, Ph.D., professor in the Department of Pharmacology, University of Colorado, and a study co-investigator. "The stability of the global lipidome with age, diet and over time is unknown, and the influence of external factors such as epigenetic control of lipid metabolizing enzymes could be considerable."

More information: David A. Slatter et al. Mapping the Human Platelet Lipidome Reveals Cytosolic Phospholipase A2 as a Regulator of Mitochondrial Bioenergetics during Activation, *Cell Metabolism* (2016).

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