Identifying potential dietary treatments for combating infant genetic disorders

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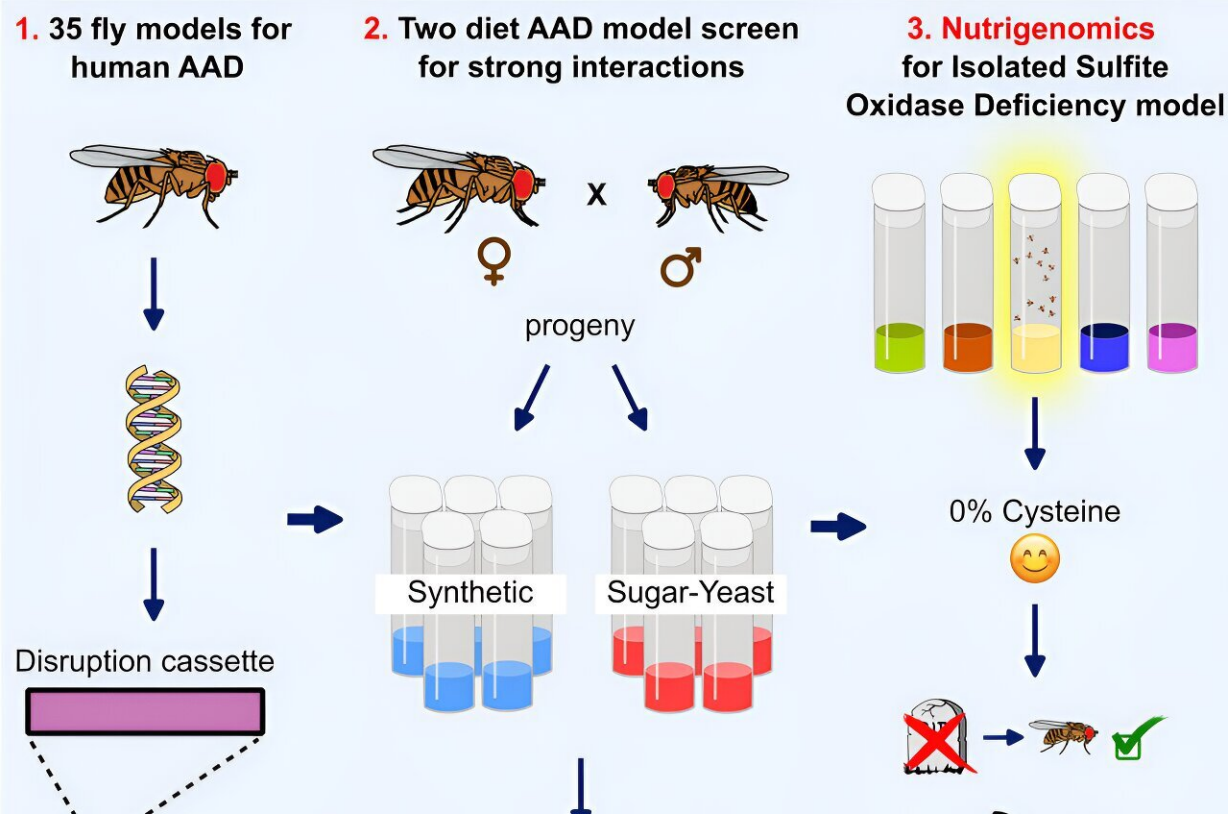

Credit: *Cell Reports* (2024). DOI: 10.1016/j.celrep.2024.113861

In world-first research led by scientists at La Trobe University and Monash University, fruit flies were used to investigate the effect diet has on babies with inherited metabolic disorders (IMDs), a group of more

than 1,400 individual genetic disorders that impact the body's ability to digest and metabolize nutrients that are crucial for brain and organ development.

Published today in *Cell Reports*, the findings suggest that the interaction between diet and IMDs has more impact on health than previously thought, with nearly three-quarters of the fruit flies used to model human IMDs in the study critically affected by what they were fed.

In addition, it shows that health could be restored by removing a single micronutrient from their diet—in this case, amino acids, which are the building blocks of protein.

Co-lead researcher Dr. Travis Johnson, from the La Trobe Institute for Molecular Science (LIMS) and the School of Agriculture, Biomedicine and Environment (SABE), said this research addresses an urgent, unmet need for the development of new precision treatments for IMDs, which on average affect 1 in 800 newborns per year and have a high death rate in children under 5.

"Although there are existing dietary treatments for some IMDs, the rarity and large number of individual disorders make it nearly impossible to develop and test new, tailored dietary treatments. As a result, many children continue to die from potentially treatable disease due to a lack of investigation into relatively simple dietary cures," Dr. Johnson said.

For decades, scientists have known that the cause of these disorders, which manifest in the early weeks of infancy, stem from genetic mutations inherited from the baby's parents.

The mutations affect the baby's metabolism—their body's ability to break down nutrients like proteins, fats and carbohydrates into simpler substances which are then converted into energy, promoting growth and

development.

Without the ability to process crucial nutrients, babies can suffer brain damage and even death, but current dietary treatments first developed in the 1950s for a limited number of these disorders show that this fate is preventable by feeding the affected babies with a medical formula that has had the relevant nutrient removed.

Traditional research methods using mice makes finding new, targeted dietary treatments for a larger variety of IMDs almost impossible. But the research team for this study hope to change this by establishing a practice of using Drosophila melanogaster—a type of fruit fly commonly used in genetic research—as a model organism to conduct large-scale investigations in this field.

"With the rarity of these disorders, and given that most patients are babies or young children, clinicians cannot easily trial a range of different diets to see what works. With flies, we can do that," Dr. Felipe Martelli, co-first author of the work said.

Drosophila melanogaster share 75% of disease-causing genes with humans, have a short life span, are easily grown in large amounts, and their DNA can be altered to be consistent with the needs of research—a combination which allows for quick and efficient research for a variety of human disorders.

"We can grow thousands, if not millions, of flies and test a large variety of different treatments to see what works and what doesn't," Jiayi Lin, Monash University Ph.D. candidate and co-first author of the paper, said.

Associate Professor Matthew Piper, co-lead researcher and Head of the Nutrition and Aging Lab at Monash University's School of Biological

Sciences, hopes that in the future the use of fruit flies in IMD research can improve the health and save the lives of more children affected by these disorders.

"Our findings suggest disease-diet interactions are the rule, rather than the exception. We expect that our work with Drosophila will provide a foundation from which interactions between nutrition and disease can be unraveled for the benefit of human health," Associate Professor Piper said.

More information: Felipe Martelli et al, Identifying potential dietary treatments for inherited metabolic disorders using Drosophila nutrigenomics, *Cell Reports* (2024). DOI: 10.1016/j.celrep.2024.113861

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