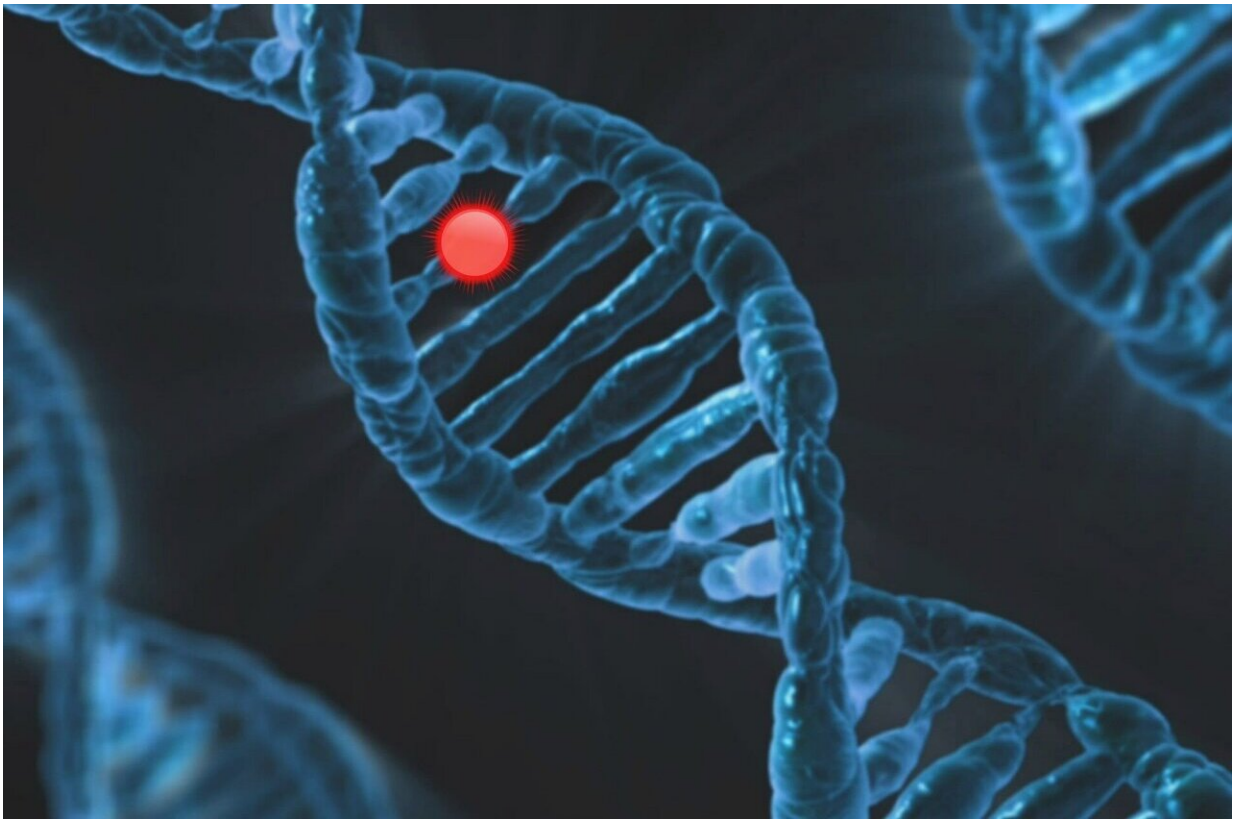


Oleic acid: A potential therapy for people with a rare genetic condition

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A mutation in a protein regulating natural killer (NK) cells' function is at the root of immune deficiency in some people with a rare genetic condition characterized by cognitive and developmental delay, seizures,

and other manifestations, new UCLA-led research suggests.

The researchers found that loss or mutations in a gene called MEF2C disrupted the ability of NK cells to take up chemical compounds called lipids that are used to fuel crucial functions such as tumor cell killing and creating inflammatory molecules. They found that people with the rare neurological syndrome called (MCHS) who have the mutation in this gene are particularly vulnerable to viral infections.

The findings, [published](#) in *Nature Immunology*, are the first to observe that these people are immune deficient and point to lipid supplementation with [oleic acid](#) as a potential therapy.

"Human NK cell deficiencies are rare but lead to a dramatic increase in vulnerability to [viral infections](#)," said first author Joey Li of the UCLA-Caltech Medical Scientist Training Program. "Clinically, we still don't know a lot of genes that can result in NK cell deficiency when mutated. Our findings identify NK cell defects associated with MEF2C haploinsufficiency syndrome that might explain the frequent infections that some of these patients experience.

"Knowing that these patients might have impaired immune systems can improve how we take care of them," he added.

Using CRISPR gene editing, the researchers screened 31 genes in human NK cells and found that MEF2C was a crucial driver for multiple functions in those cells. They also found that oleic acid enhanced the protective activity in cells from MEF2C haploinsufficient people and normal NK cells.

The findings also have broader implications for immunity and cell therapies, Li said.

"Harnessing [lipid metabolism](#) to engineer better NK cell therapies may have promise in the realm of cancer immunotherapy, as previous studies have found that tumor-infiltrating immune cells can become metabolically impaired," Li said. "In the realm of NK cell immunodeficiencies, we have noted a trend that multiple neurodevelopment disorders seem to be accompanied by NK cell defects."

But more research is needed to solidify a link between NK cell function and neurodevelopmental disorders, he added.

More information: Joey H. Li et al, MEF2C regulates NK cell effector functions through control of lipid metabolism, *Nature Immunology* (2024). [DOI: 10.1038/s41590-024-01811-2](https://doi.org/10.1038/s41590-024-01811-2)

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