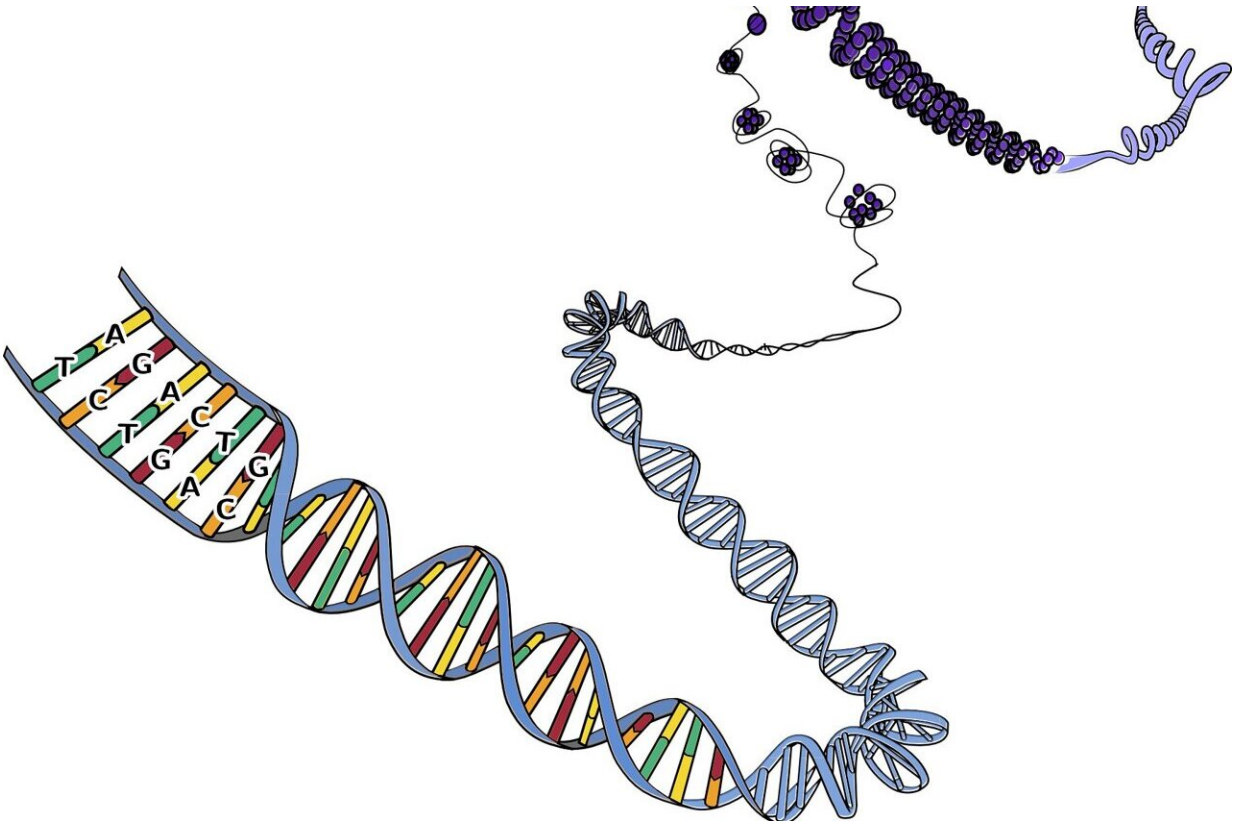
Biological mechanism discovered that could lead to new treatments for neurological disorders and cancers

April 5 2024



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The lab of Yongchao C. Ma, Ph.D., at Stanley Manne Children's Research Institute at Ann & Robert H. Lurie Children's Hospital of

Chicago has discovered a fundamental biological mechanism that could lead to new treatments for neurological diseases, such as spinal muscular atrophy (SMA) and autism, as well as different cancers.

The study was published in the journal *Human Molecular Genetics*.

Dr. Ma's team found that chemical modification of RNA (called RNA methylation) regulates mitochondrial function. Mitochondria is best known for generating energy in the cell. However, Dr. Ma explains, mitochondria does much more. It also acts as a signaling center that regulates broad biological processes within the cell. Dr. Ma's lab had previously linked mitochondrial dysfunction to the development of SMA and autism, while other labs have implicated it in cancer pathogenesis.

"Our finding establishes a critical link between RNA methylation, mitochondria and diseases that relate to mitochondrial dysfunction, which means that now we have potential for new treatments for many different disorders," said Dr. Ma, who is the senior author on the study. He holds the Children's Research Fund Endowed Professorship in Neurobiology at Lurie Children's and is Associate Professor of Pediatrics, Neurology, and Neuroscience at Northwestern University Feinberg School of Medicine.

Dr. Ma's lab found that RNA methylation regulates mitochondrial function by controlling production of key enzymes that are components of mitochondria. They demonstrated in a neural stem cell model and a mouse model that loss of RNA methylation significantly changed mitochondrial function in stem cells and neurons.

"We are very excited about this discovery and the promise of innovative treatments, which could involve developing modifiers of RNA methylation to rectify the mitochondrial defect," said Dr. Ma. "We are also honored to contribute significantly to the study of RNA

methylation. There is exponential growth in this field, and we hope that our ongoing research on RNA methylation in the nervous system will bring new insights on brain development and neurological disorders."

More information: Michael Kahl et al, m6A RNA methylation regulates mitochondrial function, *Human Molecular Genetics* (2024). DOI: 10.1093/hmg/ddae029

Provided by Ann & Robert H. Lurie Children's Hospital of Chicago