Self-assembling molecules could help in cancer therapy

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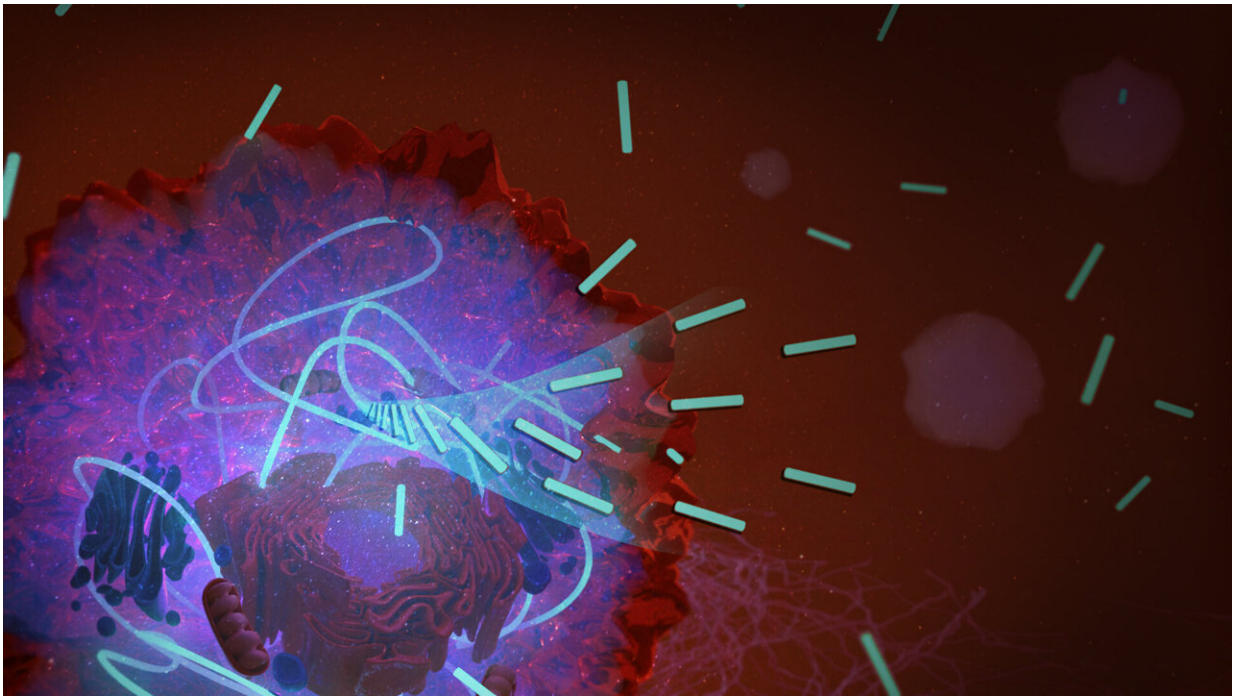

Artistic illustration of a new method of cancer therapy: due to the conditions in a cancer cell, molecules—drawn here in light green—can join together to form long hairs. These then stop the conversion of oxygen into energy, which the cell needs to grow. The result: the cancer cell dies. Credit: Max Planck Institute for Polymer Research

Treatment of cancer is a long-term process because remnants of living cancer cells often evolve into aggressive forms and become untreatable.

Hence, treatment plans often involve multiple drug combinations and/or radiation therapy in order to prevent cancer relapse. To combat the variety of cancer cell types, modern drugs have been developed to target specific biochemical processes that are unique within each cell type.

However, cancer cells are highly adaptive and able to develop mechanisms to avoid the effects of the treatment. "We want to prevent such adaptation by invading the main pillar of cellular life—how cells breathe—that means take up oxygen—and thus produce chemical energy for growth," says David Ng, group leader at the MPI-P.

The research team produced a synthetic drug that travels into cells where it reacts to conditions found inside and triggers a chemical process. This allows the drug's molecules to bind together and form tiny hairs that are a thousand times thinner than human hair. "These hairs are fluorescent, so you can look at them directly with a microscope as they form," says Zhixuan Zhou, an Alexander-von-Humboldt-fellow and first author of the paper.

The scientists monitored the oxygen consumption in different cell types and found that the hairs stop all of them from converting oxygen into ATP, a molecule that is responsible for energy delivery in cells. The process worked even for those cells derived from untreatable metastatic cancer. As a result, the cells die rapidly within four hours. After some more years of research, the scientists hope that they can develop a new method to treat up-to-now untreatable cancer.

Weil, Ng and colleagues have shown an exciting outcome under controlled laboratory culture and will continue to unravel deeper insights on the basis of how these tiny hairs prevent the conversion of oxygen to chemical energy. With further development, these objects could in the future possibly also be manipulated to control other cellular processes to address other important diseases.

They have published their results in the *Journal of the American Chemical Society.*

More information: Zhixuan Zhou et al, In Situ Assembly of Platinum(II)-Metallopeptide Nanostructures Disrupts Energy Homeostasis and Cellular Metabolism, *Journal of the American Chemical Society* (2022). DOI: 10.1021/jacs.2c03215