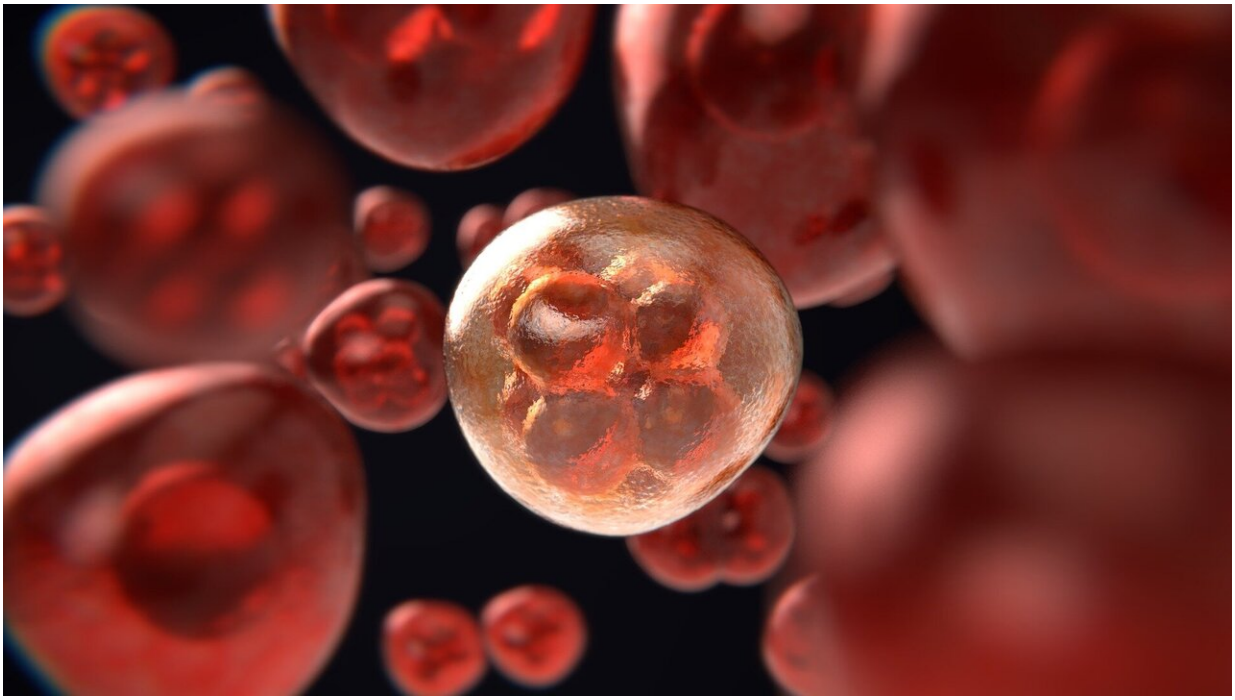
Newly synthesized fungal compound can switch on a self-destruct button for cancer

June 11 2020



Credit: Pixabay/CC0 Public Domain

Cancers cells use a special technique to propagate: They delete their "programmed death" gene through mutation, and seemingly "forget" to die when their lifetime is over, and continue to grow instead. A research team from Tokyo University of Science has developed a method through which a fungal compound capable of rearming the self-destruct gene in certain cancer cells can be artificially produced in marketable quantities,

providing a potential cancer therapeutic strategy.

All human body cells have a certain lifespan during which they perform their essential duties. At the end of this lifespan, they reach senescence and, no longer able to perform those duties, die. This suicidal death is programmed into the genes through a process called apoptosis, causing them to self-destruct in order to make way for young, healthy cells to replace them.

Mutations in a special gene called p53 can sometimes interfere with this process. Caused by aging, ultraviolet light and various mutagenic compounds, these mutations can disable the apoptosis gene, resulting in "zombie" cells that refuse to die and continue to multiply, spreading the disabled gene and replacing healthy working cells with undying, rapidly growing tumors. This is cancer, and it takes many forms depending on which body cells develop the mutations.

Previously, scientists identified an anticancer compound called FE399 in a species of filamentous fungus called Ascochyta, which is often found afflicting common food crops such as cereals. The compound is a specific group of depsipeptides, a type of amino acid group, and was shown to induce apoptosis in cancerous human cells in vitro, particularly colorectal cancer, proving its worth as an anti-cancer chemical.

Unfortunately, due to a variety of chemical complexities, the FE399 compound is not easy to purify, which hindered any plans for its widespread application in cancer treatment. It was thus clear that extracting FE399 from the fungi naturally would not be a commercially feasible method, and despite the promise of a powerful anticancer drug, research into this particular compound was stalled.

The promise of a new anticancer treatment was tempting, however, and Prof Isamu Shiina, along with Dr. Takayuki Tonoi, and his team from

the Tokyo University of Science, accepted the challenge. "We wanted to create a lead compound that could treat colon cancer, and we aimed to do this through the total synthesis of FE399," says Prof Shiina. Total synthesis is the process of the complete chemical synthesis (production) of a complex molecule using commercially available precursors, allowing mass production. The results of their extensive studies will be published in the *European Journal of Organic Chemistry*.

The team figured that first, the structure of the depsipeptide would need to be identified. This was simple and could be easily performed using commercially available and inexpensive materials. The subsequent procedures required many steps, and resulted in some small failures when isomers were unsuccessfully isolated.

However, the team was rewarded for their efforts when, in a major breakthrough, their mass spectrometry and nuclear magnetic resonance studies confirmed that a trio of spots on a plate showed identical chemical signature to the known formula of FE399, meaning that they had successfully recreated FE399 synthetically.

Their technique was found to have an overall yield of 20%, which is quite promising for future large-scale production plans. "We hope that this newly produced compound can provide an unprecedented treatment option for patients with colorectal cancer, and thus improve the overall outcomes of the disease and ultimately improve their quality of life," says Prof Shiina.

Further research is needed to test the efficiency of FE399 in the treatment of other solid and blood-based cancers, and before mass production, the biological activities and structure of the FE399 molecule will need to be evaluated. But for now, the team from Tokyo University of Science are thrilled with their findings, and are positive that their research will help to improve treatments and therapies for patients with

colorectal cancer.

More information: Takayuki Tonoi et al, Total Synthesis of the Antitumor Depsipeptide FE399 and its S-Benzyl Derivative: A Macrolactamization Approach, *European Journal of Organic Chemistry* (2020). DOI: 10.1002/ejoc.202000459

Provided by Tokyo University of Science

Citation: Newly synthesized fungal compound can switch on a self-destruct button for cancer (2020, June 11) retrieved 27 April 2024 from https://phys.org/news/2020-06-newly-fungal-compound-self-destruct-button.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.