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Existing cancer drugs can be regenerated to fight certain aggressive cancers: Study

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Singapore, July 20 (ANI): A group of researchers led by Nanyang Technological University, Singapore (NTU Singapore) discovered that a cancer medicine that is currently on the market might be modified to target a subgroup of malignancies that are frequently linked with poor outcomes and lack focused therapy choices.

This category of malignancies, which accounts for 15% of all cancers, is particularly common in malignant tumors such aggressive osteosarcomas and glioblastomas in the brain.

These cancerous cells 'stay immortal' using a mechanism called the alternative lengthening of telomeres (ALT), but the team has demonstrated that ponatinib, a cancer drug approved by the US Food and Drug Administration, blocks key steps in the ALT mechanism that leads it to fail.

Reporting their findings based on laboratory experiments and preclinical animal studies, the scientists found that ponatinib helped to shrink bone tumours (a type of ALT cancer) without causing weight loss, a common side effect associated with cancer drugs. In mice with tumours treated with ponatinib, they found a reduction in a biomarker for ALT cancer as compared to untreated mice. The findings are published in the scientific journal Nature Communications.

The researchers say that the findings move them a step closer to developing a targeted therapeutic option for ALT cancers, which lack clinically approved targeted treatments to date.

Dr Maya Jeitany and a team of researchers from the NTU School of Biological Sciences, together with collaborators from the Cancer Science Institute of Singapore and the Yong Loo Lin School of Medicine, both at the National University of Singapore (NUS), and the Genome Institute of Singapore at the Agency for Science, Technology and Research (A*STAR), are seeking to address this unmet need.

Dr Jeitany, study lead and senior research fellow at NTU's School of Biological Sciences, said: "A prominent feature of cancer is its ability to evade cell death and acquire indefinite replication -- to stay immortal, in other words -- which it can do through the alternative lengthening of telomeres (ALT) mechanism. While a sizeable portion of cancer cells depend on this mechanism, there is no clinically approved targeted therapy available.

"Through our study, we identified a novel signalling pathway in the ALT mechanism and showed that the FDA-approved drug ponatinib inhibits this pathway and holds exceptional promise in stopping the growth of ALT cancer cells (/topic/alt-cancer-cells). Our findings may provide a new direction for the treatment of ALT cancers by repurposing an FDA-approved drug for these types of tumours."

Commenting as an independent expert, Assistant Professor Valerie Yang, medical oncologist with the Department of Lymphoma and Sarcoma at the National Cancer Centre Singapore, said: "Sarcomas and glioblastomas are both highly complex cancers that are more prevalent in young people and currently have limited treatment options. The identification of a drug that is FDA-approved which can be repurposed to target ALT, an Achilles heel in these cancers, is very exciting."

The study aligns with NTU 2025, the University's five-year strategic plan, which aims to address humanity's grand challenges by responding to the needs and challenges of healthy living.

Telomeres are protective "caps" at the tips of every chromosome, which carries our DNA. With each cell division, a bit of the telomeres is naturally snipped off, until they become too short, leading to cell death.

Most cancer cells bypass this process by activating an enzyme called telomerase, which lengthens the telomeres so that the cells can replicate indefinitely. However, about 15 per cent of cancers lengthen their telomeres through alternative pathways, rather than activating telomerase. This mechanism is known as the alternative lengthening of telomeres (ALT).

To date, there is no clinically approved targeted treatment for ALT cancers. Furthermore, many ALT cancers, such as osteosarcoma and glioblastoma, show resistance to chemotherapy, highlighting the need for a more targeted form of treatment.

Through high-throughput drug screening -- a process of screening large numbers of relevant biological or pharmacological compounds -- and subsequent testing of shortlisted compounds, the scientists discovered that ponatinib, a drug approved by the US Food and Drug Administration for a type of bone marrow cancer (/topic/type-of-bone-marrow-cancer), can kill ALT cancer cells (/topic/alt-cancer-cells) effectively.

When osteosarcoma and liposarcoma (a tumour that grows in fatty tissues) cells were treated with ponatinib, the scientists found that the drug led to DNA damage, dysfunctional telomeres, and triggered senescence, a process in which the cell stops dividing. Importantly, the synthesis of telomeres in the cells also dropped after 18 to 20 hours of treatment with the drug.

Pre-clinical studies conducted on mice that had received transplants of human bone cancer cells further validated the potential of ponatinib. The drug reduced the tumour sizes without affecting the mice's body weight, a common side effect associated with cancer treatments. (ANI)