THE COLD SHOULDER OF CANCER UNDERSTANDING RESISTANCE TO TREATMENT

THE BARRIER TO TREATING CANCER

There are now more cancer treatment options than ever before. However, almost all of them face the same major challenge: eventually, they stop working. There are several unique ways in which cancer cells evade death. Now, scientists are inventing new technologies to target these mechanisms and overcome resistance.



Resistance to chemotherapy typically occurs due to host factors or genetic mutations in the cancer cells. Host factors that influence how well a drug is absorbed by the body limit a drug's ability to reach cancer cells effectively (1). Genetic mutations, such as those that cause increased activity of ABC transporters, proteins that pump drugs out of the cell, also affect drug efficacy (1). Scientists hope to overcome this major hurdle by developing drugs that inhibit ABC transporters for administration alongside chemotherapy (2).

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Immunotherapy increases the immune systems ability to fight cancer cells. Cancer cells down-regulate specific antigens on their surfaces to evade the immune system, rendering them invisible to important immune response cells, including T cells (7). A promising new therapy involves the combination of immunotherapy and targeted therapy to improve patient outcomes (8).

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Radiotherapy relies on high doses of radiation to kill cancer cells by destroying their genetic material. However, many tumors have sub-populations of radiation-resistant stem cells (3). These cells rapidly repair their DNA and proliferate to become new cancer cells. Radiotherapy is combined with other therapies to treat various types of cancer (4).

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Targeted therapy precisely attacks the mechanisms that support cancer cells, such as survival signals in the cell (apoptosis-inducing drugs) or growth of new blood vessels (angiogenesis inhibitors). Much like chemotherapy resistance, cancer cells can adapt to targeted therapies by altering their internal mechanisms to prolong survival (5). Scientists are now exploring precision medicine techniques to further target cancer treatment strategies to the individual (6).



Breast and prostate cancers are examples of steroid hormone-dependent cancers that may be treated with anti-hormone therapies. Tumors develop resistance by compensating for the drug-induced low hormone levels, either by increasing the number of steroid hormone-detecting receptors or the sensitivity of these receptors. To counteract hormone therapy resistance, scientists are developing nonsteroidal chemicals that specifically target cancerous tissue and inhibit the action of their hormone receptors (9).

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Cell Signaling

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