MASTER'S THESIS

Exploring alternative cytotoxic strategies for cancer treatment

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Abstract

Triggering direct cytotoxicity has been the most common strategy for developing cancer treatments. The cytotoxic regimens currently used in the clinic mainly include radiation therapy, classic chemotherapeutic drugs (e.g. DNA damaging drugs and anti-mitotic drugs) and selected new targeted drugs. Although these therapies are the standard of care for most cancer patients, they suffer significant limitations: responses to these therapies vary significantly between cancer types and patients; sensitive cancers tend to acquire resistance; and they cause serious toxicity, particularly to dividing cells in the bone marrow and gut, and to neurons. It is not clear whether major improvements in cytotoxic anticancer therapies are possible; if they are, progress is likely to come from either new methods for identifying sub-populations of patients that respond well to current drugs, or developing new therapies with novel cytotoxic mechanisms. To pursue the above two avenues towards potential improvement of cytotoxic therapies, this thesis investigates: biomarkers that determine the sensitivity of distinct cancer cell types to common anti-mitotic chemotherapeutics; and the mechanistic basis to employ alternating electric field and Natural Killer cells as alternative methods to trigger cancer cell death. The study uses time-lapse microscopy as the major technique to characterize and quantify response dynamics to the different cytotoxic treatments, and the results provide important new insight not only for understanding existing cytotoxic anticancer drugs but also for developing novel cytotoxic regimens.

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