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Public Abstract
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Biological Sciences
Drug Resistance in *D. discoideum*: Isolation of 4-nitroquinoline 1-oxide Resistant Mutants
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The drug 4-nitroquinoline 1-oxide (4NQO) is a model carcinogen that produces both DNA strand breaks (like ionizing radiation) and alkali-stable DNA lesions (like UV light.) This drug has been known to induce cancer in many organisms. However, its mechanism of action is not fully understood. In most organisms including bacteria, fungi and mammals, mutants that are sensitive to UV light and γ-irradiation are also sensitive to 4NQO. However, *D. discoideum radC* mutants that were selected for sensitivity to UV and γ-irradiation were not also sensitive to 4NQO. In contrast, *D. discoideum* mutants selected for sensitivity to 4NQO generally showed cross-sensitivity to UV and γ-irradiation, but one mutant was uniquely sensitive to 4NQO. None of the mutant genes have been identified, implying the existence of genes or pathways that specifically control the cells response to 4NQO. Furthermore, a commonly used chemotherapeutic drug cisplatin operates in a similar way as 4NQO by forming bulky DNA adducts. Understanding how 4NQO functions in the cell may in turn facilitate the understanding of the chemotherapeutic drug cisplatin and thus, how to better administer chemotherapeutic treatment to metastatic cancer patients.

For my research I used a random insertional mutagenic technique (REMI) to identify genes responsible for 4NQO resistance in *D. discoideum*. Two such mutations are discussed. The study shows the feasibility of using genome-wide screens to identify novel genes that are associated with 4NQO resistance.