DRUG RESISTANCE IN *D. DISCOIDEUM*: ISOLATION OF 4-NITROQUINOLINE 1-OXIDE RESISTANT MUTANTS

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The drug 4-nitroquinoline 1-oxide (4NQO) displays both carcinogenic and anti-tumor effects, a well known characteristic of many chemotherapeutic drugs. In addition 4NQO shares a similar operating mechanism with the commonly used chemotherapeutic drug cisplatin. Previously, using the model organism *Dictyostelium discoideum,* we have shown that we can alter sensitivity to cisplatin by deleting or overexpressing enzymes in the sphingolipid metabolic pathway. Similarly, this work analyzed the cellular response to 4NQO in *Dictyostelium discoideum*.

To study the molecular basis of 4NQO resistance in *Dictyostelium*, I used restriction enzyme mediated integration (REMI), a direct insertional mutagenesis approach, to isolate 4NQO resistant mutants. This study lead to the isolation of two *Dictyostelium* mutants showing about 1.5 to 4.5 fold more resistance than the wild-type. Using inverse PCR and DA sequencing one mutant disruption was found to be in a retrotransposon and in the second mutant the disruption was fond to be in an intergenic region between a S-adenosylmethionine-dependent methyltransferase gene and a retrotransposon.

This study confirmed that *Dictyostelium discoideum* can be used as a model system to study the molecular basis of resistance to anticancer drugs.