# OCR 7950: Novel Small Molecule Inhibitor for Treatment of PARP inhibitor-Resistant Ovarian Cancer

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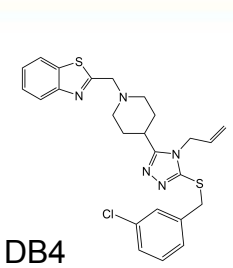
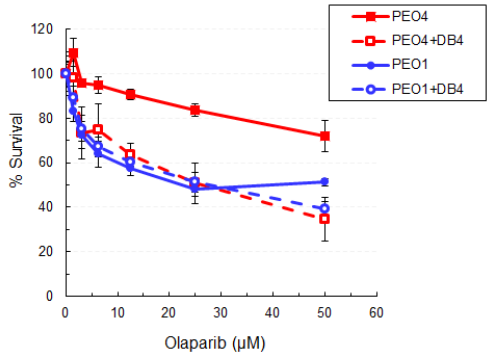
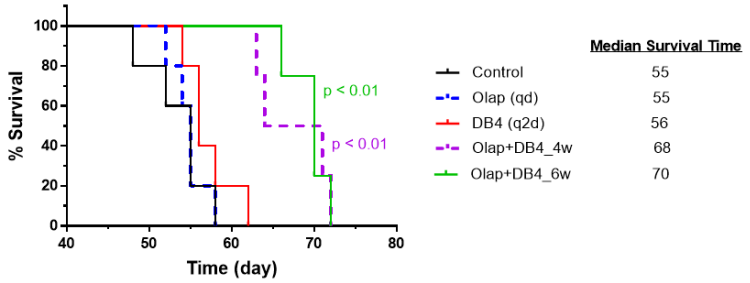
- PARP inhibitors (PARPi) are FDA-approved targeted drugs for ovarian and breast cancers with BRCA mutations or homologous recombination (HR) repair deficiency.
- However, at least 50% of ovarian cancer has no HR deficiency and is resistant to PARPi therapy. Furthermore, PARPi-sensitive cancers can potentially restore HR repair and develop resistance to PARPi in patients.
- Dr. Elena Ratner's lab at Yale performed *in silico* screening and discovered a novel small molecule inhibitor DB4 that blocks HR repair and renders PARPi-resistant cancer cells hypersensitive to PARPi, such as olaparib and niraparib.
- Combination of DB4 and olaparib efficaciously suppresses the progression of PARPi-resistant ovarian cancer xenografts and significantly prolongs the survival time of mice.

- **Intellectual Property**: Patent application pending
- **Reference:** Lin et al., *Sci Rep*. 2021 Apr 13;11(1):8042.




Figures demonstrating the efficacy of combining DB4 and the PARPi olaparib to treat PARPi-resistant ovarian cancers. **Top,** DB4 rendered PARPi-resistant PEO4 ovarian cancer hypersensitive to olaparib similar to PARPi-sensitive PEO1 ovarian cancer in culture. **Bottom,** mice were implanted with PARPi-resistant PEO4 ovarian cancer xenografts and treated with olaparib, DB4, and both concurrently. PEO4 xenografts developed ascites and the survival time of mice were determined. The combination of DB4 and olaparib significantly prolonged the survival time of mice while either drug alone had no effects compared with vehicle-treated control mice.

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