**NCSOT ABSTRACT TEMPLATE**

**Title:**

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**Abstract (≤ 4000 characters, please include content for background/purpose, methods, results, and conclusions):**

***Example Abstract Submission***

**Title:**

Photodynamic Priming Overcomes Chemoresistance and Mitochondrial Enhancements Arising from Chronic PFAS Exposure

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**Abstract (≤ 4000 characters):**

In the context of ovarian cancer, mitochondrial health is critical in determining response to chemotherapy. Increases in mitochondrial membrane potential (MMP), reactive oxygen species, mitochondrial number, and bioenergetics are associated with resistance to first-line platinum-based chemotherapeutics, such as carboplatin. Environmental stressors such as perfluoroalkyl substances (PFAS) are reported to alter mitochondrial health, but effects of PFAS on chemotherapy resistance remain poorly studied. Recently, we demonstrated that short-term (48-hour) PFAS exposures induce resistance to carboplatin, but not cisplatin or doxorubicin, in ovarian cancer cell lines. MMP was increased in ovarian cancer cells with PFAS-induced carboplatin resistance (via JC-1 dye), but other mitochondrial parameters, including superoxide production (via MitoSOXÔ dye) and mitochondrial DNA (mtDNA) copy number (via RT-PCR) were unchanged compared to controls. To characterize endpoints under human-relevant culture conditions, long-term (144-hour, LT) or chronic (26-35 day) PFAS exposures were examined in the present study. After LT PFAS, MMP and superoxide production (via flow cytometry) were significantly increased, compared to controls, in both OVCAR-3 and Caov-3 ovarian cancer cell lines. Larger increases in MMP and superoxide production were observed in OVCAR-3 cells which, in previous work, were impacted by PFAS exposures more than Caov-3 cells. OVCAR-3 chronically exposed cells were developed based on their sensitivity to PFAS. Cells grown in medium, 1% methanol (vehicle control), or 500 nM perfluoroheptanoic acid (PFHpA; 1% methanol) were passaged every 4-5 days for a total of 26-35 days. Compared to vehicle, chronic PFAS-exposed OVCAR-3 cells were significantly more resistant to both carboplatin and doxorubicin. Chronic PFAS-exposed OVCAR-3 cells also had significantly increased survival fraction in the absence of chemotherapy treatment, suggestive of a proliferative effect. MMP and mtDNA copy number were also evaluated in chronically-exposed OVCAR-3 cells. Interestingly, MMP was significantly elevated in chronic PFAS-exposed cells compared to controls and, although not statistically significant, mtDNA copy number slightly decreased in cells that were chronically exposed to PFHpA. Prior studies have shown that mtDNA copy number decreases in advanced-stage and/or chemoresistant ovarian cancer.  These findings suggest that, compared to 48h exposure, LT and chronic PFAS exposures increase chemotherapy resistance in ovarian cancer cells and enhance mitochondrial health parameters. Since our previous studies have shown that photodynamic priming (PDP), a light-based treatment approach, can be used to overcome short-term PFAS-induced carboplatin resistance, the ability of PDP to overcome chemoresistance in PFAS chronically exposed OVCAR-3 cells was evaluated. Using benzoporphyrin derivative (BPD) as a photosensitizer for PDP, resistance to carboplatin and doxorubicin arising from chronic PFAS exposure was successfully overcome. Decreased survival was concomitant with a decrease in MMP, suggesting BPD-PDP may diminish mitochondrial health to re-sensitize cells to chemotherapy. This research provides novel insight into the mechanisms underlying PFAS-induced effects on chemotherapy efficacy and may inform personalized treatment regimens based on PFAS exposure levels.