



## 2018 ACS-IRG Pilot Grant

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**PROJECT TITLE: DETERMINATION OF CANCER PERSISTER CELL MUTATIONAL RATE**

**ABSTRACT:**

ACQUIRED RESISTANCE TO CANCER DRUGS OCCURS IN THREE STAGES DURING DRUG TREATMENT. IN THE FIRST STAGE, DRUG SENSITIVE TUMORS RESPOND TO DRUG TREATMENT AND SHRINK. IN THE MIDDLE STAGE, A RESIDUAL TUMOR CELL POPULATION REMAINS ALIVE WHICH ULTIMATELY SEEDS, IN THE THIRD STAGE, OVERTLY DRUG RESISTANT TUMORS. THESE FINAL DRUG RESISTANT TUMORS OFTEN HARBOR GENETIC MUTATIONS, WHICH ARE LIKELY TO EXPLAIN THEIR DRUG RESISTANCE, THOUGH THE TIMING AND ORIGIN OF THESE RESISTANCE CONFERRING MUTATIONS IS NOT KNOWN. CANCER PERSISTER CELLS ARE A RECENTLY DISCOVERED SUBPOPULATION OF DRUG TOLERANT CANCER CELLS THAT HAVE BEEN OBSERVED WITHIN A WIDE RANGE OF TUMOR TYPES. THESE CELLS REVERSIBLY ENTER A QUIESCENT, PROSURVIVAL CELL STATE CHARACTERIZED BY DISTINCT CHROMATIN MARKS, CANCER STEM CELL MARKERS, AND A MESENCHYMAL GENE EXPRESSION PATTERN. PERSISTER CELLS FORM A SURVIVING CELL RESERVOIR WITH THE POTENTIAL TO SEED OVERTLY DRUG RESISTANT TUMORS DURING ACQUIRED DRUG RESISTANCE. HOWEVER, THE PRECISE ROLE OF PERSISTER CELLS IN ACQUIRED DRUG RESISTANCE HAS NOT BEEN DETERMINED.