2018 YOUNG INVESTIGATOR GRANT
Targeting Glutamine Metabolism in MYC Driven Atypical Teratoid Rhabdoid Tumors

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Dr. Rubens’ project aims to target changes in tumor metabolism (how tumor cells generate energy) in an effort to improve survival rates in children with brain tumors. Cancer cells are more dependent on glutamine to generate energy to support their rapid growth while normal cells are more dependent on glucose for these metabolic needs. This difference in metabolism allows his lab to specifically target tumor cells with a medication called DON that blocks this glutamine metabolism. This medication has previously been used in humans and has been shown to be safe and well tolerated but has never been used to treat childhood brain tumors. The project aims to prove the preclinical efficacy of DON therapy with a plan to develop a new clinical trial at the completion of this research that will improve treatment for children suffering from brain tumors.

UPDATE 1: “We continue to be very excited about the progress we have made in our SebastianStrong Foundation funded research. We continue to develop the pre-clinical data that will support a future clinical trial aimed at improving survival in atypical teratoid rhabdoid tumors (AT/RT). We have found that the glutamine metabolic inhibitor, 6-diazo-5-oxo-L-norleucine (DON) combines synergistically with carboplatin to extend survival in orthotopic mouse models of AT/RT. We aim to submit our findings for publication this month, & continue to work toward developing the first clinical trial utilizing DON therapy to target aggressive, MYC- expressing tumors.”

UPDATE 2: “We continue to be excited by the progress we have made. We submitted our findings that the glutamine metabolic inhibitor 6-diazo-5-oxo-L-norleucine (DON) combines synergistically with chemotherapy to extend survival in AT/RT for publication in the journal Clinical Cancer Research. Our manuscript was reviewed favorably and we are currently working on revisions before sending the manuscript back for publication. We are also working toward translating these findings into a new clinical trial to treat AT/RT. Finally, we have teamed up with the Drug Discovery Program at Johns Hopkins...
University to test the efficacy of novel DON pro-drugs that are able to better cross the blood-brain-barrier and achieve higher concentrations in brain tumors. These pro-drugs hold great promise to further improve therapies in AT/RT while reducing side effects associated with the medications.”