# CALIFORNIA SCIENCE & ENGINEERING FAIR
# 2018 PROJECT SUMMARY

**Name(s)**

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**Project Number**

38154

**Project Title**

## Combination Therapy Using Drug Repurposing and Drug Mapping: A Method to Find Synergistic Treatments for Leishmaniasis

**Abstract**

**Objectives/Goals**

Neglected tropical disease, Leishmaniasis, is a deadly disease that is most prevalent in poverty stricken countries. The purpose of this project is to create a drug therapy that will address the problems of the current treatments used for Leishmaniasis: inefficacy, adverse effects, and high cost of treatment. The hypothesis is that the combination of 2 FDA approved compounds with associated mechanisms of action will result in synergy, leading to lower dosage, decreased resistance, and shortened treatment time.

**Methods/Materials**

Compounds to repurpose were chosen based on the following criteria: target of the compound must exist in the parasite and the compounds selected to be used in a combination must have different mechanisms of action in the parasite. A computer generated drug map taking into account compound toxicity and compound mechanism of action was created. Human macrophages were infected with Leishmania donovani to replicate the host environment. 34 single compounds and 35 drug combinations were screened in a cell-based assay against Leishmania donovani parasites. Set ratios were used for the combination concentrations, and a software called Compusyn was used to measure synergy. Compusyn generated a combination index (CI value), and a CI value less than one indicates that the combination is synergistic.

**Results**

Compusyn generated 4 synergistic combinations from our set of 35 drug combinations: Afatinib and Rolipram, Afatinib and Mefloquine, Afatinib and Metformin, and Tacrolimus and Reserpine. All combinations were replicated in both plates and were only considered as hits when both of their CI values were under 1. The synergistic combinations that were found are extremely promising candidates for the treatment of leishmaniasis.

**Conclusions/Discussion**

Our research confirmed the advantageous use of combination therapy in discovering synergistic combinations while repurposing FDA approved drugs. Combination therapy combined with drug repurposing allowed us to answer our question on how to find a more efficient method to to identify synergistic combinations, while drug repurposing addressed our concern with lowering the cost and time of the drug development process. In addition, synergistic combinations allows for a lower concentration of compounds to be used in treatment, which greatly lowers side effects and toxicity.

**Summary Statement**

We combined drug repurposing and combination therapy along with drug mapping in order to find synergistic combinations to treat the neglected tropical disease, leishmaniasis.

**Help Received**

We conducted our research at the University of California, San Diego and mainly received help from Dr. Jair Lage who was our mentor, and additional help from Dr. Julia Souza, Dr. Jean Bernatchez, and Dr. Ruben Abagyan.