

The Use of Hypomethylating Agents as a Therapeutic Against DNA Hypermethylation in ccRCC

Mock NIH Grant Proposal by
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In reference to: [NIH Mock Grant Proposal on The Use of Hypomethylating Agents as a Therapeutic Against DNA Hypermethylation in ccRCC](#)

Introduction

Background

Numerous research studies have shown that DNA hypermethylation is linked to the development of ccRCC.

- Activates many oncogenes in renal cells
- Inactivates VHL tumor suppressor genes
- This contributes heavily to the development and progression of the disease

Hypothesis

I hypothesize that with the use of hypomethylating agents, clear cell renal cell carcinomas (ccRCC) could be cured or prevented.

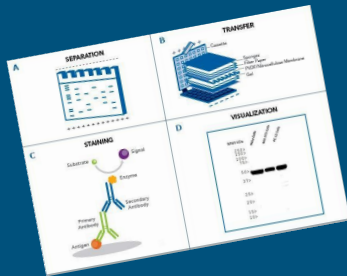


APPROACH

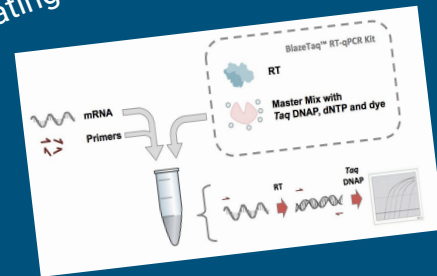
Specific Aim 1

Investigate the precise epigenetic mechanisms by which hypomethylating agents counteract the effects of hypermethylation in ccRCC.

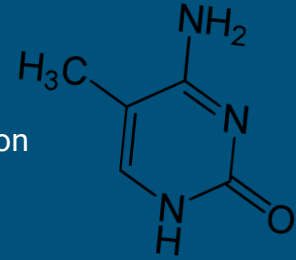
1d: Use Western Blotting to assess the difference in the quantity of proteins produced between tumor suppressor genes and oncogenes



1c: Use of RT-qPCR to analyze the efficacy of HMA in downregulating Wnt pathways



1a: Investigate the demethylation and reactivation of VHL tumour suppressor genes by HMA using MeDIP



1b: Explore the demethylation and reactivation of WIF-1 to downregulate overactive Wnt pathways



Specific Aim 2

Investigate the effects of hypomethylating agents on kidney physiology.



2b: Compare and contrast the differences in symptoms between patients receiving a placebo and patients receiving hypomethylating agents as therapy for ccRCC

2a: Assess the change in renal cell and overall kidney function after the administration of hypomethylating agents

