INTRODUCTION

- Melanoma is an aggressive form of skin cancer
- Approximately 106,000 new melanomas will be diagnosed in the United States in 2021 alongside an estimated 7,180 deaths
- Despite the increasing incidence and notably high mortality rates, current cancer therapies are hindered by innate drug resistance
- Epigenetics unveils a new perspective to combat melanoma given the reversible nature of gene-targeting approaches

HYPOTHESIS

- We hypothesize that cluster specific enhancers may regulate key oncogenes that are associated with drug response

BACKGROUND

- MITF, the master regulator of melanocyte development, is a frequently amplified oncogene in human melanoma
- H3K27ac is an epigenetic modification which can distinguish between active and 'poised' enhancer regions

METHODOLOGY

- ChIP-seq for H3K27ac was performed on 18 CCLE (Cancer Cell Line Encyclopedia) human melanoma cell lines
- To gain insight on how enhancer changes may impact gene expression, ChIP-seq data was integrated with RNA-seq data
- Response to drug treatment was assessed by standardizing the treatment group to the untreated control
- AVANA dataset, large-scale genome-wide CRISPR screen for cancer cell lines, was used to confirm the functional capability of MITF melanoma cells
- In vitro inhibitor treatment was performed to validate the drug response

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CONCLUSION

- MITF enhancers correlate with BRAFi response in melanoma
- BRAF inhibitor can slow the growth of metastatic melanoma in patients whose tumors have a BRAF mutation
- Understanding molecular mechanisms of MITF will pave ways to improve therapeutic approaches for melanoma

FUTURE DIRECTION

- Silencing the MITF enhancer with CRISPR dCas9-KRAB to validate its functionality

REFERENCES