

International Investigative Dermatology Conference 2018

I was delighted and honoured to have been chosen as the recipient of a BAD travel award to attend the highly prestigious IID 2018 conference in Orlando, Florida in May. The conference was a great success with over 1600 abstracts presented and lectures from luminaries including a nobel laureate. The range and depth of the science presented was exceptional – from imaging to sequencing and from cancer to rare single-gene disorders. The standard of presentations was universally excellent, and the opportunities to meet and get to know researchers from across the globe interested in skin disease was amazing. In addition to the professional and networking benefits, the conference also laid on a fantastic social program including an indoor beach party for early career researchers, and a trip to visit Harry Potter World – an experience I will not soon forget! I made new friends and contacts, renewed old ones and learned plenty during the visit and I thank the BAD for helping me do so.

Fascin and Cdk2 are synthetic lethal partners with exceptional potential as joint therapeutic targets in malignant melanoma.

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1. Introduction

Objective: aim to identify gene combinations in malignant melanoma with therapeutic potential.

2. Materials and Methods

1. Meta-analysis of clinical data from the Cancer Research UK melanoma TCGA was stratified into four subgroups: melanoma (MEL), melanoma with metastasis (MEL+M), melanoma with metastasis and BRAF V600E (MEL+M+BRAF), and melanoma with metastasis and BRAF V600E and KIT (MEL+M+BRAF+KIT).

2. Gene expression combinations which showed significant associations with survival were identified using the Fagerberg webpage and the RIGT package.

3. Single gene (SG) (SG1/SG2/SG3/SG4/SG5) and two gene (TG) (TG1/TG2) combinations were identified using the RIGT package. The effect size in TG1 and TG2 was calculated.

4. Further screening of gene expression combinations identified a number of Cdk2 gene pairs which were associated with survival. Cdk2 gene pairs were identified in melanoma, and in a broader population of cancer in comparison to the most significant gene pair in melanoma.

3. Results

TCGA expression data from melanoma patients (n=485) showed no correlation between expression of Cdk2 and PCNL, implying a synthetic gene dose lethality in melanoma (Figure 1).

To assess reproducibility of the result a second data set was analyzed which showed the same result (Figure 2), but also demonstrated high correlation between melanoma samples showing more activity in the gene dose synthetic lethality gene pairs system.

A third data set which included normal skin samples reproduced the findings, and showed that normal skin was not susceptible to the gene dose synthetic lethality (Figure 3).

4. Discussion and Conclusions

Cdk2 and PCNL gene expression in these systems show lethality in melanoma patients. Synthetic lethality is a potential therapeutic target in melanoma. Normal skin does not show the gene dose lethality. Early data show that combinations of these two genes in combination with melanoma growth rate may offer alone, and also in combination with other therapies.

These findings are promising, but have not been replicated in other melanoma patients. Further data are needed to confirm the synthetic lethality of the effect on synthetic lethality and cell cycle progression.

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