REACTIVATION OF p53 TO PREVENT ORAL CANCER

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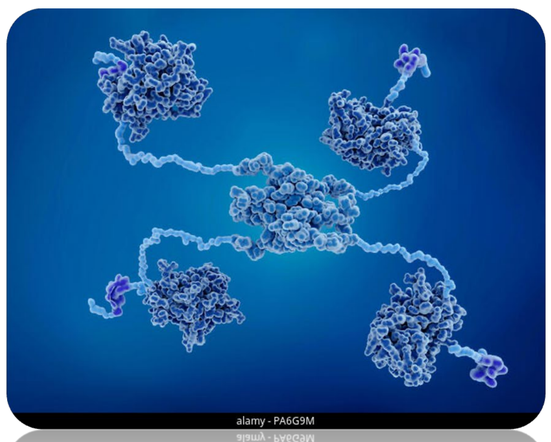
ABSTRACT

In vitro experiments when concentration of 4-Hexylresorcinol or 4HR was increased and p53 was acetylated (Ac-p53) and phosphorylated (p-p53) and administered to a xenograft model, it showed tumor expantion rate was supressed compared with the control and the mice exhibited a higher survival rate.

Findings reveal that 4HR is a potential agent that restores loss of function in mutant p53 cancer cells via acetylation and phosphorylation of p53 as well of inhibition of Histone deacetylase or HDAC. But can 4HR help to prevent oral cancer?



p53

METHODS & MATERIAL

YD-15 cells from tongues of patients diagnosed with mucoepidermoid carcinoma. YD-15 cell has mutant p53.

YD-9 cells from squamous cell carcinoma derived from buccal cheek. YD-9 cell has wild-type p53.

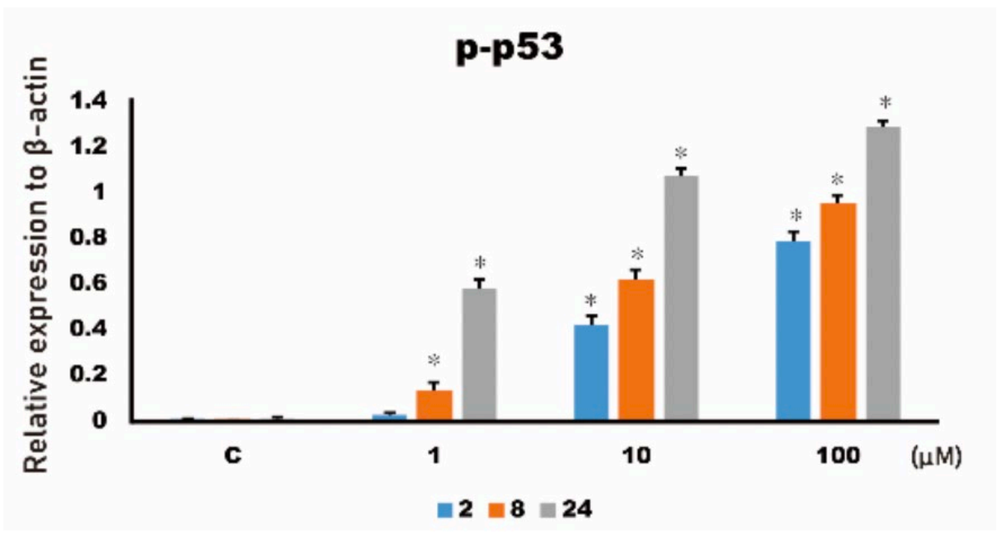
Cells were grown in six-well culture plates in a himudified CO_2 incubator at 37°C, supplemented with 40% foetal bovine serum (FBS) and 7.5% dimethyl sulfoxide, L-glutamine (300mg/L), 2.5mM HEPES and 2.5mM $NaHCO_3$.

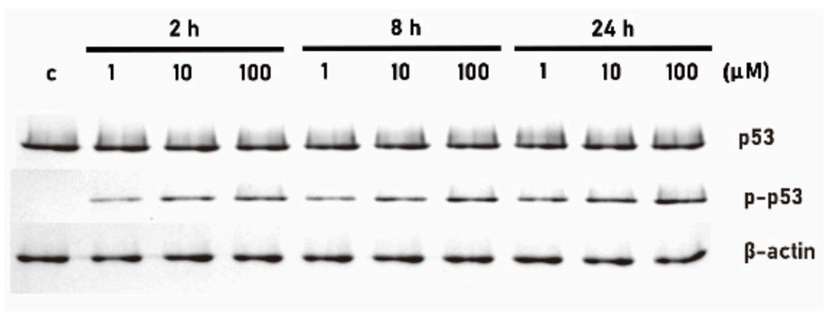
Once grown to approximately 70%, they were treated with 1, 10 and 100 µm 4HR for 2, 8 and 24h.

The lysates were subjected to western blotting to detect the expression levels of p53, p-p53 and Ac-p53 and it was collected after 2, 8 and 24h, than, centrifuged at 10,000x g for 1min. The extracted protein was diluted with 50 µL of celular lysis buffer, the result was incubated at 37°C for 2H. Fluorescence intensity was measured with a plate reader.

RESULTS

Treatment of YD-15 and YD-9 cells with 4HR resulted in a significantly increased expression of p-p53 (Ser 315).



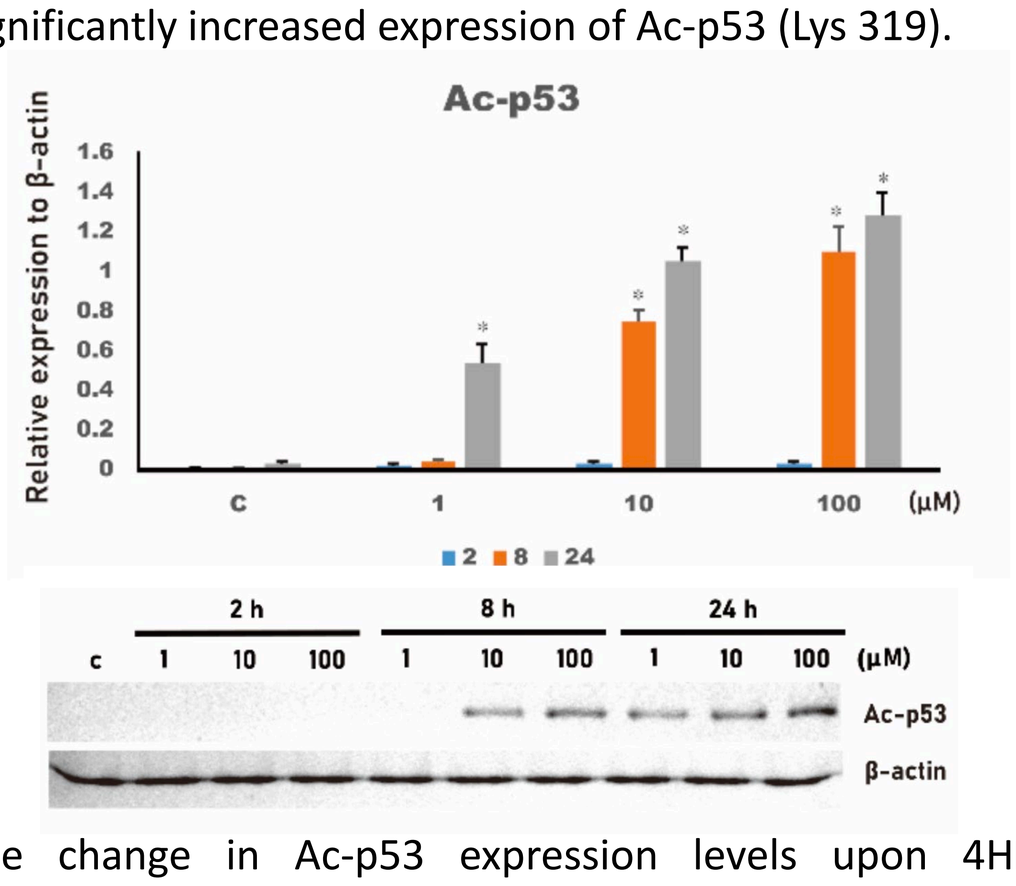


The change in p-p53 expression levels upon 4HR treatment in YD-15 and YD-9 cells. When compared to the untreated control.

INTRODUCTION

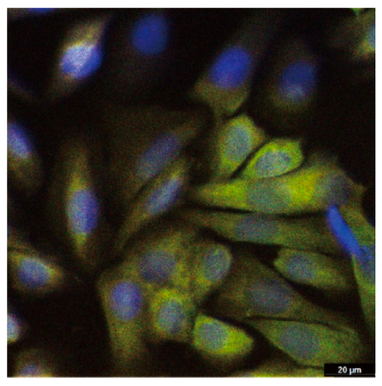
4-Hexylresorcinol or **4HR** induces celular apoptosis in cancer cells, it increases phosphorylation and acetylation which is key to evaluating the function recovery of p53. **Oral carcinomas** have a much higher index of p53 mutations, mutant may hide the aminoacids not allowing to start apoptosis, here is when chemical chaperone induces conformational changes that may expose these aminoacids so they can get phosphorylated and acetylated. This is important because it's how it can induce apoptosis. 4HR has been recognised as a Class I **HDAC inhibitor**, this ones have shown anticancer effects by increasing acetylation.

Treatment of YD-15 and YD-9 cells with 4HR resulted in a significantly increased expression of Ac-p53 (Lys 319).



The change in Ac-p53 expression levels upon 4HR treatment in YD-15 and YD-9 cells. When compared to the untreated control.

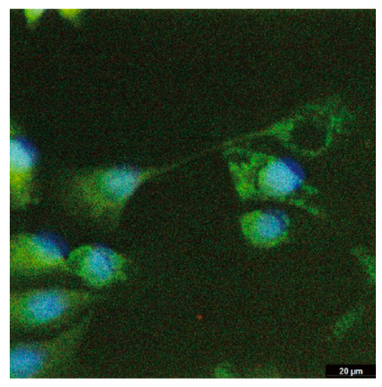
(A)



Control

- Cytochrome C and ATPsynthase in Green
- Cytoplasm in bright yellow

(B)



YD-15

- Green cytoplasm due to Cytochrome C release from mitochondria

CONCLUSION

4HR is a potential agent for recovering loss of function in mutant p53 and acts as a pharmacological chaperone which induces phosphorylation of p53 and acetylation of p53. Therefore, it can be taken as a posible option on oral carcinoma preventive treatment. When applied on mice with sublingual tumors showed a higher survival rate and much smaller tumor lesions compared to control.

Recognition to;
Kang, Y.-J.; Kim, D.-W.; Che, X.; Choi, J.-Y.; Kim, S.-G. Inhibition of *TP53* Mutant Oral Cancer by Reactivating p53. *Appl. Sci.* **2022**, *12*, 5921. Published: 10 June 2022