LONG NON-CODING RNAs REGULATED BY SUPER ENHANCERS IN CUTANEOUS SQUAMOUS CELL CARCINOMA

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MOLECULAR BIOSCIENCES, CELL BIOLOGY

INTRODUCTION

Cutaneous squamous cell carcinoma (cSCC) is a cancer which originates from keratinocytes. It is mainly caused by prolonged exposure of UV radiation. Studies of different cSCC cell lines have shown that **long non-coding RNA molecules** (lncRNAs) are expressed in cSCC and they play a role in the development of this cancer – lncRNAs LINC7, LINC9, PICSAR and PRECSIT are upregulated in cSCC and they are known to affect the growth and invasion of cSCC. In general, lncRNAs affect for example modification of chromatin, gene transcription and functions of transcription factors in cell nucleus. **Super enhancers (SEs)** in turn are regions of genom including clusters of enhancers which are bound by transcription factors, and in addition they take part to the transcriptional mechanisms, they are also proven to be responsible of regulation of lncRNAs.

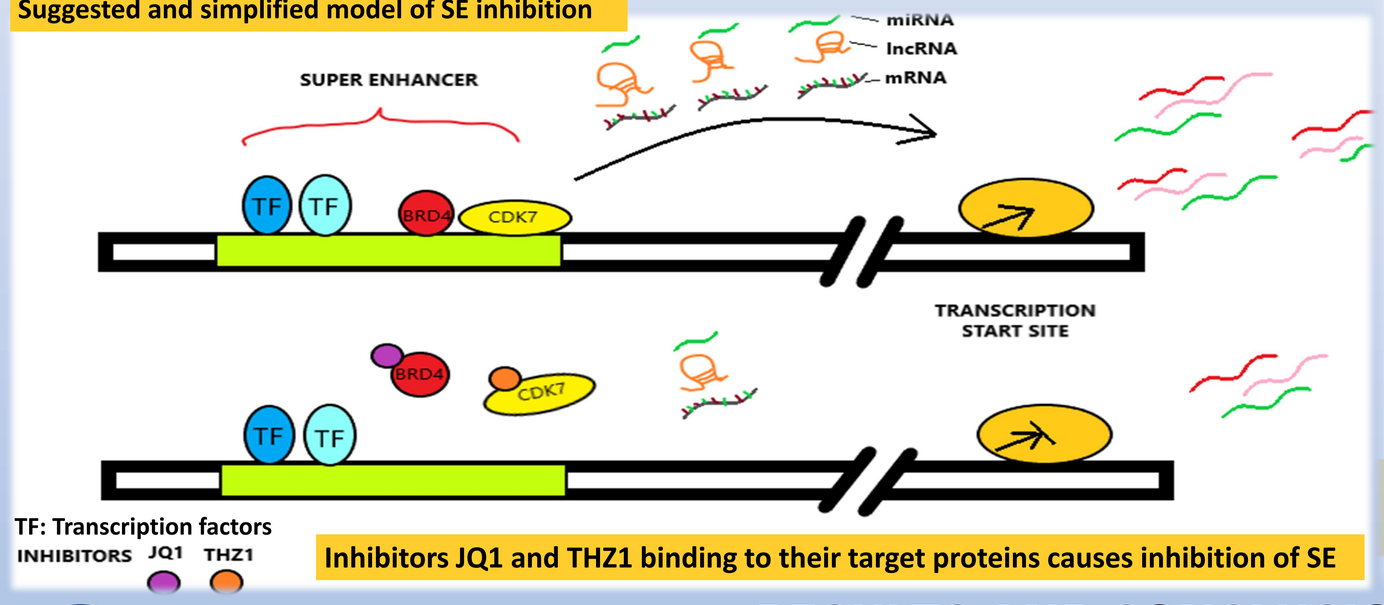
AIMS

The incidence of cSCC is increasing and there is no existing specific treatment for it. The main aim is **to find new potential therapeutic targets** to treat the patients.

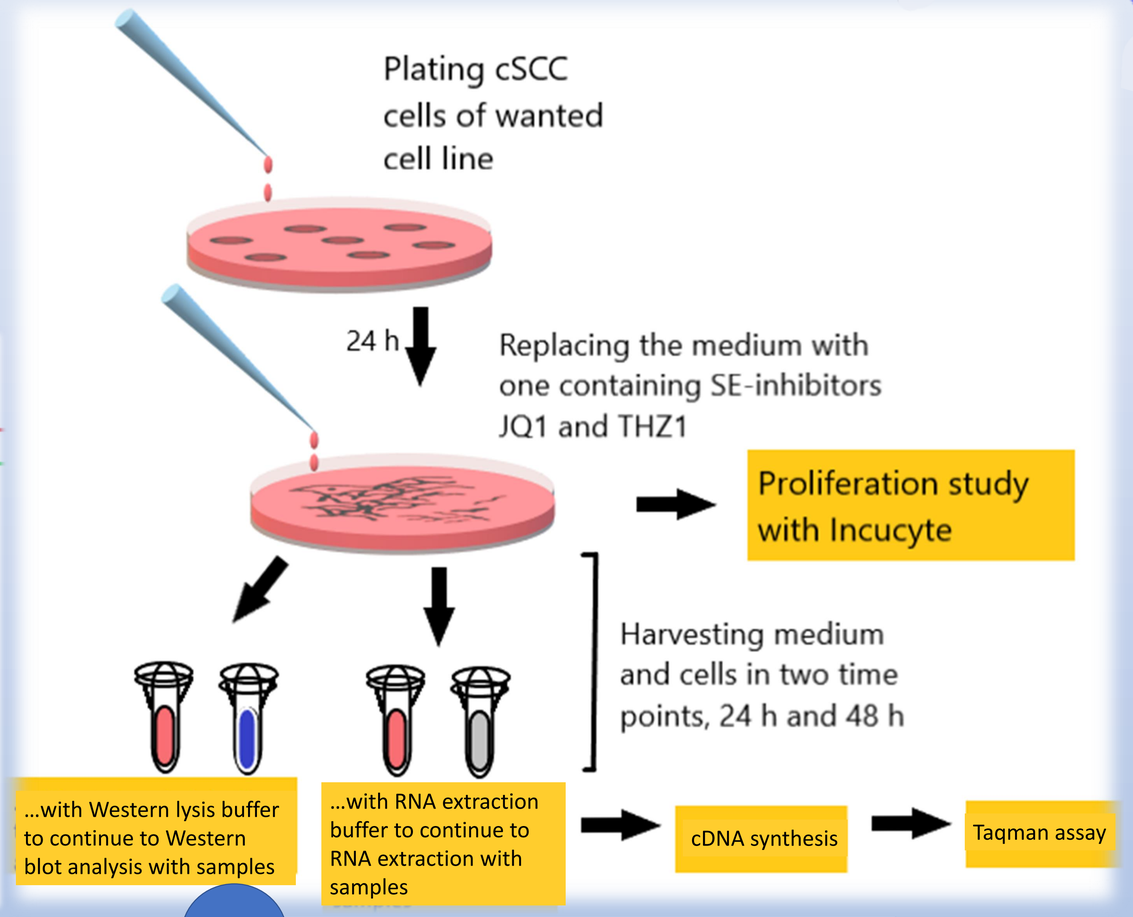
1 Ensuring that the cSCC cells have specific target proteins for SE-inhibitors to bind
2 To see how SE-inhibitors affect the proliferation of cSCC cells
3 To see how SE-inhibitors in different concentrations inhibit the expression of different lncRNAs, and if the regulation of the expression of lncRNAs differ between cSCC cell lines

MATERIALS AND METHODS

Suggested and simplified model of SE inhibition



Inhibitors JQ1 and THZ1 binding to their target proteins causes inhibition of SE



RESULTS AND CONCLUSIONS

1. UT-SCC12A Western blot

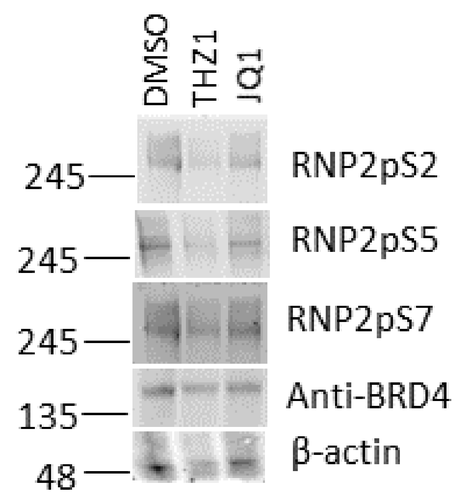
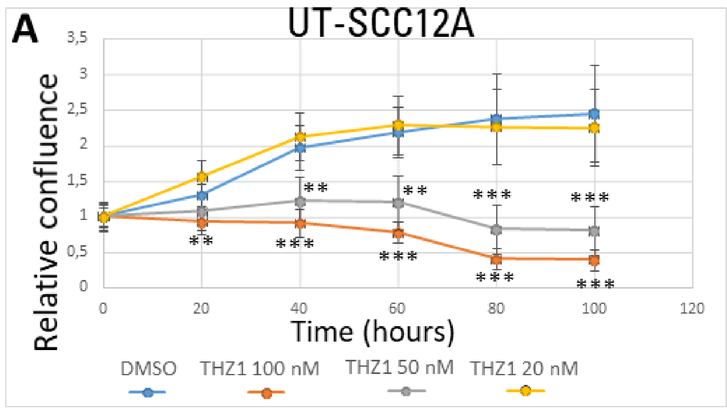
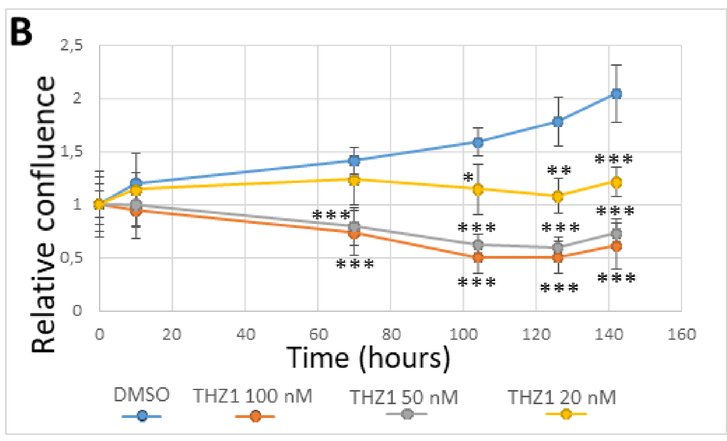


Figure 1. Western blot with UT-SCC12A cells when incubated 24 hours. BRD4 is produced by cSCC cells. THZ1 inhibits the phosphorylation of RNA polymerase II.

2. INHIBITORY EFFECT ON PROLIFERATION





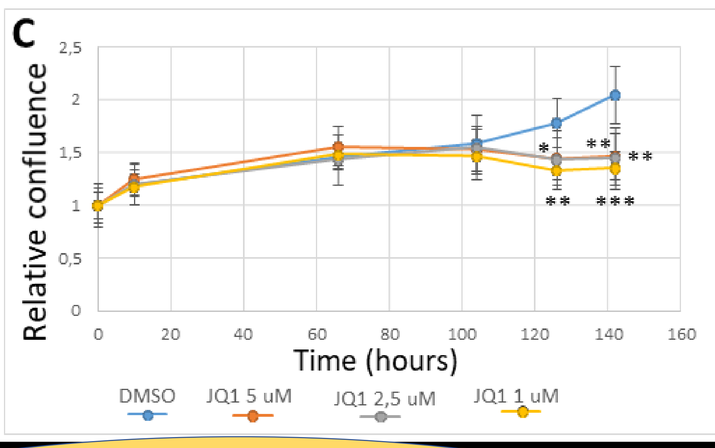


Figure 2 A. THZ1 inhibits the proliferation of UT-SCC12A cells in different concentrations. Inhibition effect of JQ1 was no detectable. **Figures 2 B-C.** THZ1 and JQ1 inhibit the proliferation of UT-SCC91 cells in different concentrations. DMSO was used as sample control. Mean±SD is shown, *p<0,05; **p<0,01; ***p<0,001. Student's T-test.

3.

Figure 3. Taqman assay results. THZ1 and JQ1 inhibit the expression of lncRNAs in cSCC cells in 24 h and 48 h incubation time points. DMSO was used as sample control. Mean±SD is shown, *p<0,05; **p<0,01; ***p<0,001. Student's T-test.

Preliminary results show that super enhancers could be good potential therapeutic targets in the treatment of cutaneous squamous cell carcinoma.