The guardians of the genome dependent tumor suppressor miRNAs network

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Questions

- **How does p63/p73 function as a tumor suppressor?**

- **What are the genes involved in the TA-p63/p73-dependent tumor suppressor pathway?**

- **Do miRNAs play a role in the TA-p73/p63-dependent tumor suppressor pathway?**

Results-1

The tumor suppressor p53 homologues, TA-p73, and TA-p63, have been shown to function as tumor suppressors. However, it is not known how they function as tumor suppressors. Here I present **models (figure 1-5) that illustrate how the TA-p73/p63 could function as tumor suppressors**. Remarkably, the **guardians—p53, p63, and p73—of the genome are in control of the**

expression of most of the known tumor suppressor miRNAs (figure 1-5).

Results-2

TA-p73/p63 and p53, by suppressing the expression of **c-Myc** through **TRIM32 and miR-145**, they could up regulate the expression of **tumor suppressor microRNAs**, such as **miR-15/16a, miR-29, miR-34, miR-26, let-7a/d/g, miR-30b/c/d/e, and miR-146a**. It appears that p53/TA-p73/p63-mediated repression of c-myc (and its repressed miRNA targets) **inhibits tumor growth.**

Thus, these findings strongly suggest that **p53, TA-p73 and TA-p63**, by **suppressing the**

expression of c-myc, they could **increase the expression of c-myc-repressed tumor suppressor miRNAs**, thereby they could function as tumor suppressors. In addition, TA-p73/p63 and p53 appears to increase the expression of miR-200b/c to inhibit EMT, invasion, and metastasis.

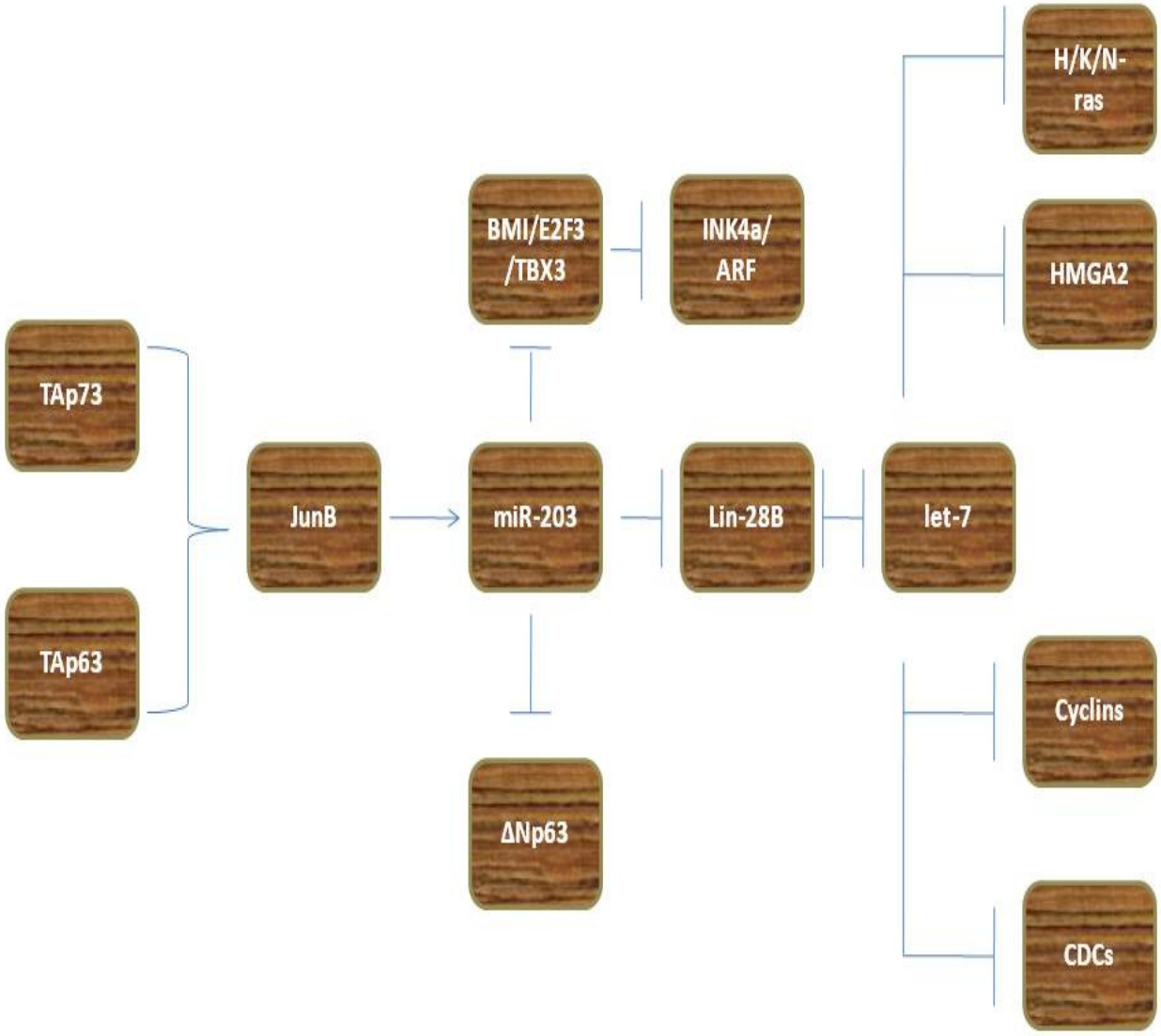

Figure 1 The TA-p63/p73 tumor suppressor pathway regulates the expression of the tumor suppressor miRNA, let-7

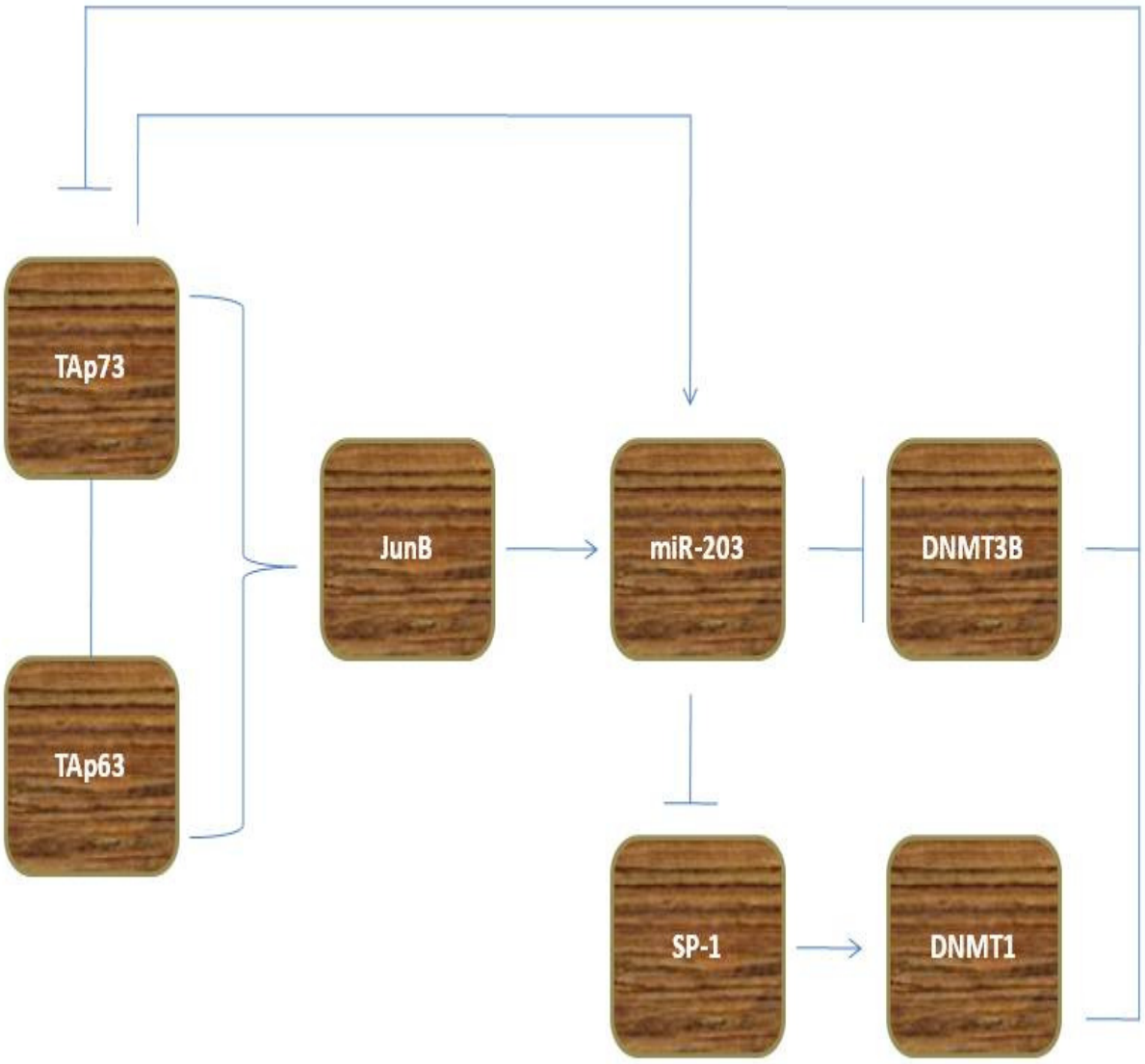

Figure 2 The TA-p63/p73 tumor suppressor pathway regulates epigenetic modifications

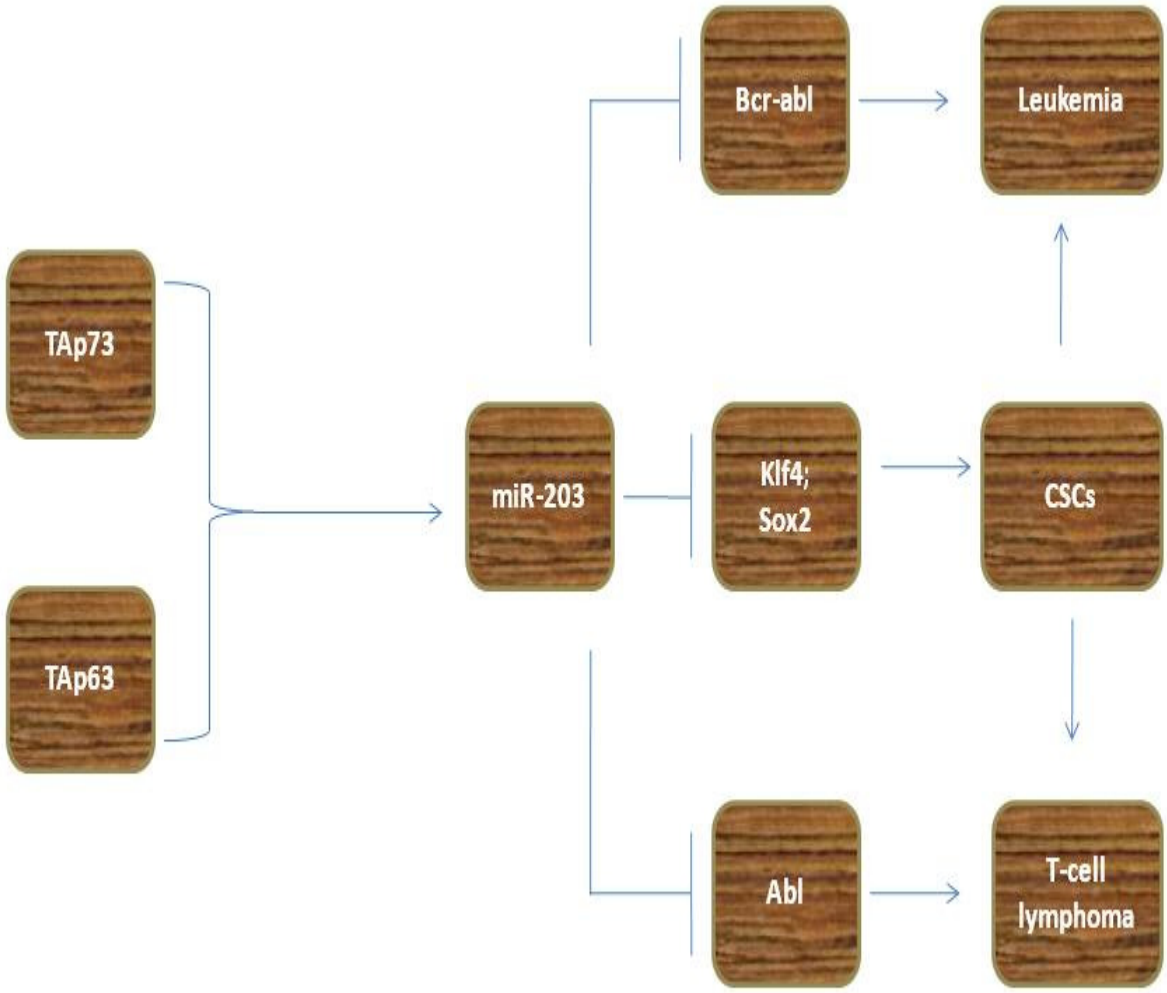

Figure 3 The TA-p63/p73 tumor suppressor pathway inhibits lymphoma and leukemia

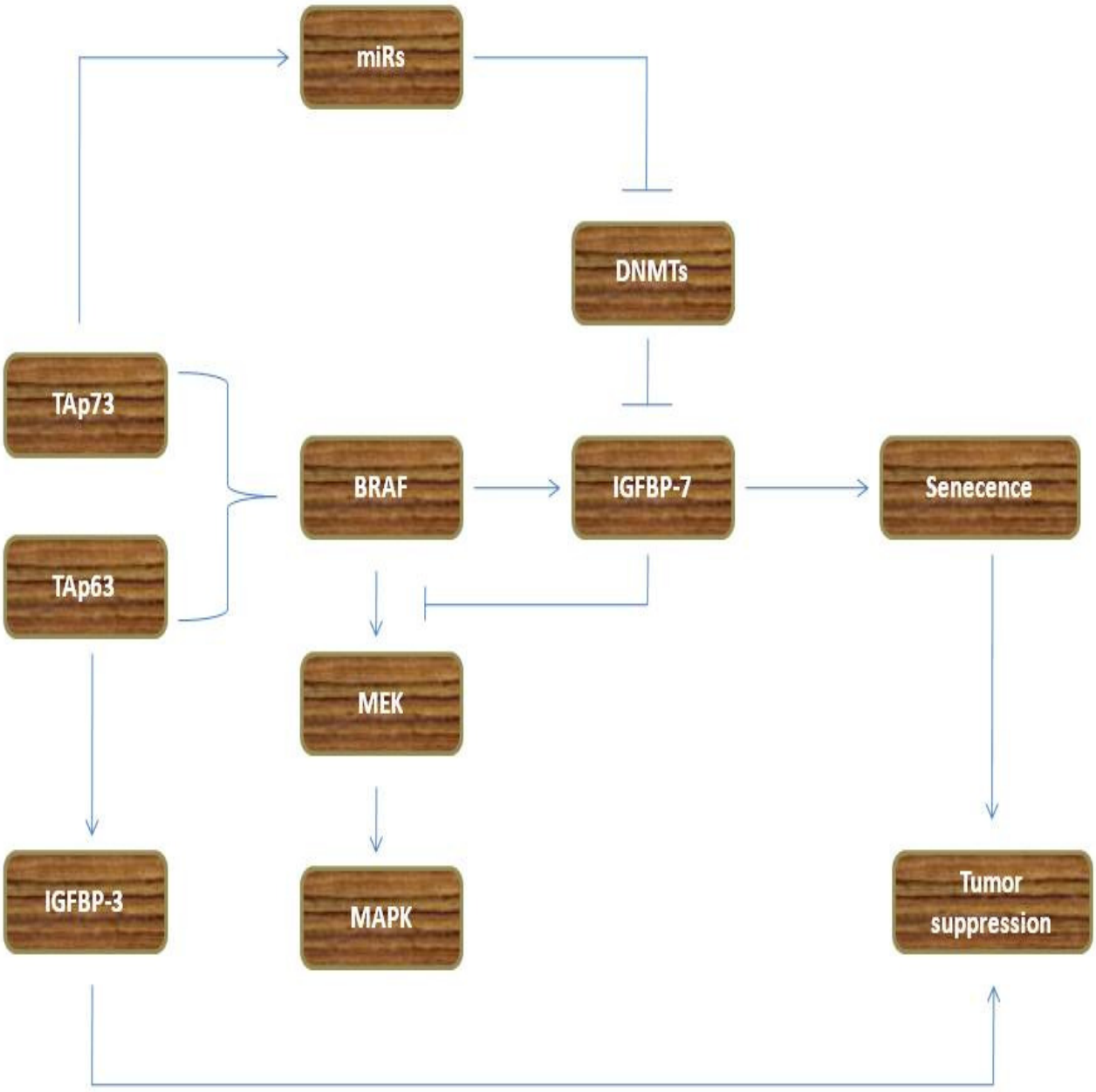

Figure 4 The TA-p63/p73 tumor suppressor pathway promotes senecence

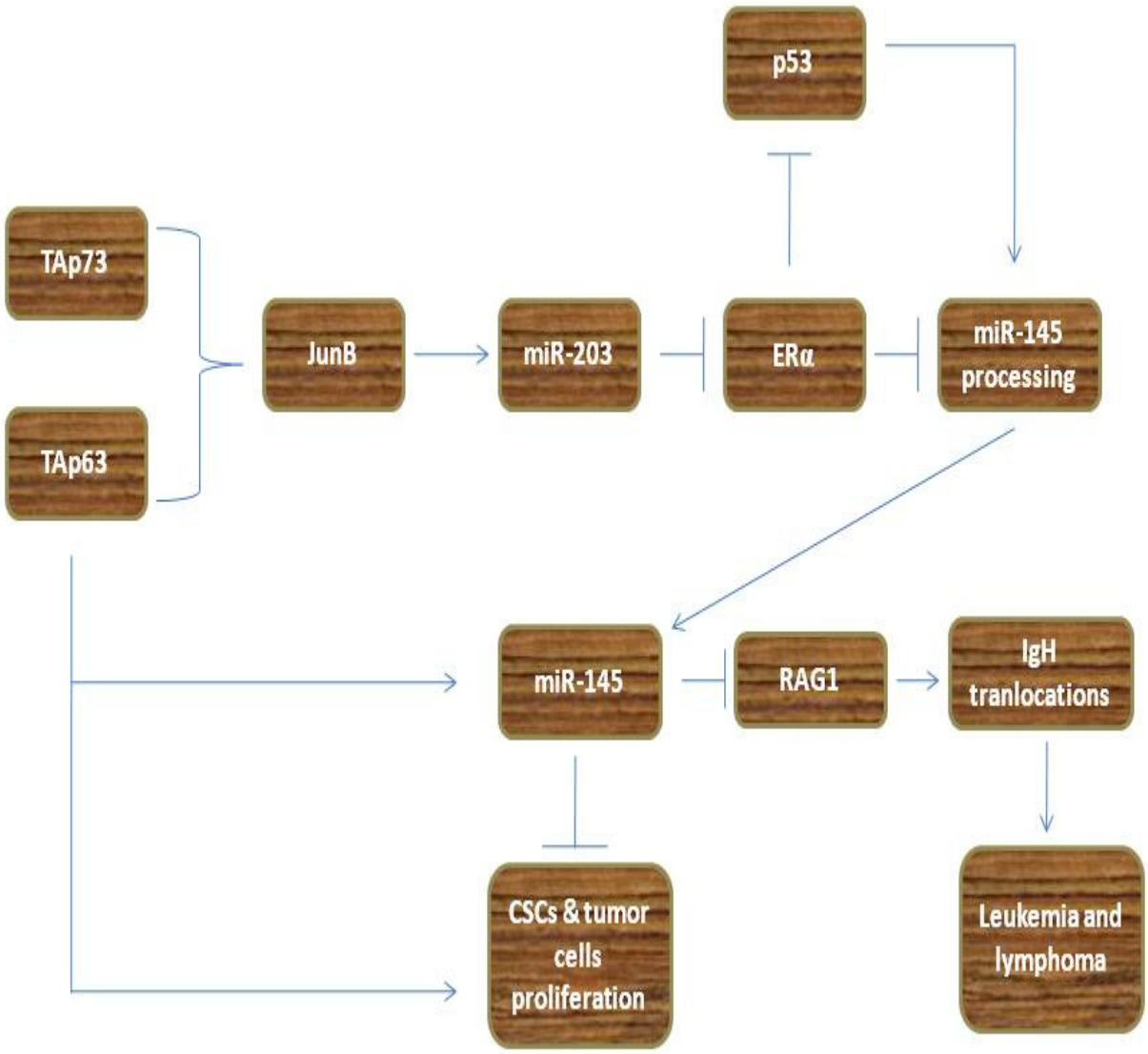

Figure 5 The TA-p63/p73 tumor suppressor pathway regulates tumor suppressor miRNA processing

Conclusion

Remarkably, microRNA processing components, such as **Dicer, P2P-R, Ago1/2, DGCR-8, are regulated by the p53, p73, and p63**. By regulating the miRNA processing components, **they could function as regulators of miRNA/siRNA biogenesis**. Therefore, this study suggests that the **guardians of the genome** p53, p73, and p63 are in **control of the biogenesis of miRNAs** as well.

Taken together, **"the guardians of the genome integrity," p53, TA-p73 and TA-p63 are not only in control of its protein coding gene targets, but also non-coding tumor suppressor microRNAs**, thereby they enlarge their tumor suppressor network to inhibit tumorigenesis.