# Full-length p53 mRNA is a frequent source of Δ133p53 and Δ160p53 protein isoforms

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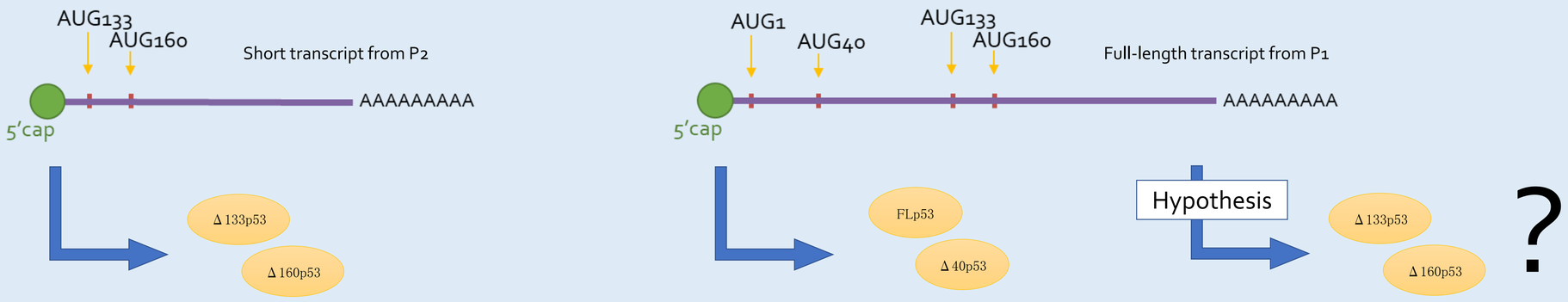
## Background

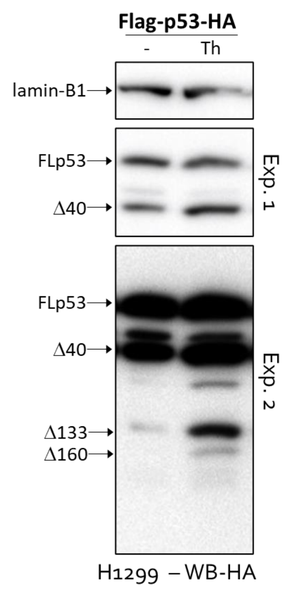
**Tumor suppressor p53**, considered the most extensively studied gene in the medical field, still keeps some secrets. Up to the present, human short isoforms **Δ133p53** and **Δ160p53** have been thought to be **translated** exclusively from the **short mRNA transcript**, which originates from an internal promoter at intron 4.




## Results & conclusions

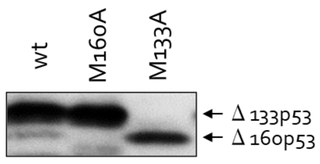
### Q1. Can short isoforms **Δ133p53** and **Δ160p53** be translated from the full-length p53 mRNA?


p53 **full-length** (FL) **coding sequence** was cloned adding **tags** at both N-terminal (**Flag**) and C-terminal (**HA**) ends. Bands corresponding to **Δ133p53** and **Δ160p53** protein isoforms were visualized in immunoblotting using anti-tag antibodies.



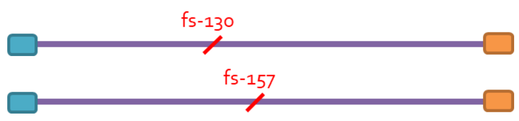
H1299 – WB-HA

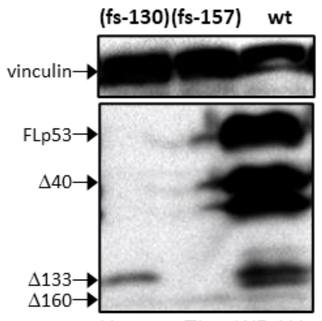
The identities of the bands were then confirmed with **mutations** on the respective **start codons**…



H1299 - WB


… as well as with **frameshift** mutations (single-nucleotide deletions) **upstream** of these.

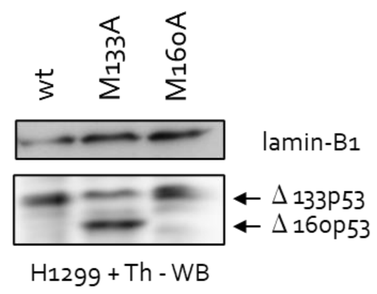


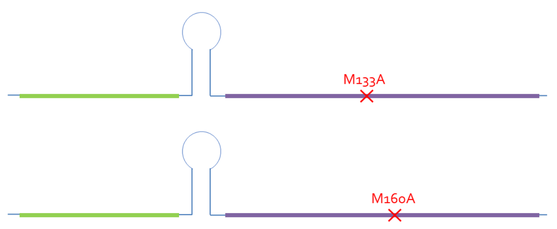
H1299 + Th – WB-HA

### Q2. Is the **translation** of these short isoforms dependent on the 5'-cap?


The presence of an **Internal Ribosome Entry Site** (IRES) and its 5'cap-independent nature were validated using **bicistronic** constructs harboring the FL coding sequence, which could produce both short isoforms.

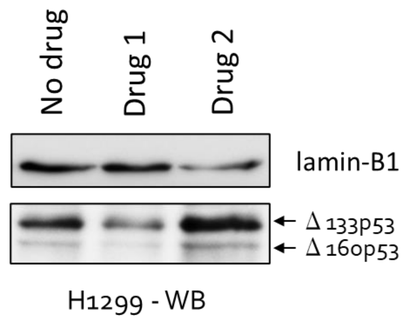


H1299 + Th - WB



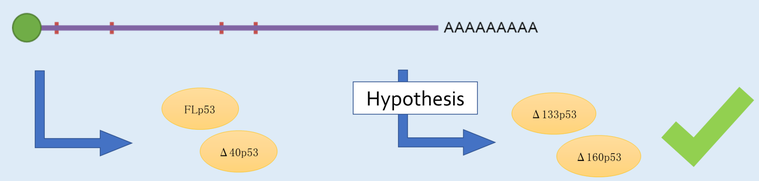

### Q3. Does the **expression** of the short isoforms **vary** depending on **drug usage**?

There is **differential expression** among the isoforms **Δ133p53** and **Δ160p53** translated 5'cap-independently, depending on **drug usage**.



H1299 - WB

## Remarks




With this study we have proved that short **p53** isoforms **Δ133p53** and **Δ160p53** can be translated from the **FL transcript**.

Translation of **Δ133p53** and **Δ160p53** from FL mRNA is IRES-mediated, **5'cap-independent**.

**Drug usage** changes the **expression** levels of these **isoforms**.

Understanding the expression patterns and differential regulation of **shorter p53 isoforms** is crucial as they may contribute differently to p53 associated **functions** and to the development of diseases.

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Shrutee Parkaar

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