p53 isoforms combinatorics: is there a p53 code?

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The human *TP53* gene encodes at least 12 different p53 protein isoforms. Altering expression of a few p53 protein isoforms, *in vivo,* is sufficient to trigger different or opposite cell responses to a same cell signal, suggesting that the balance between p53 isoforms define cell responses.
However, because of its apparent high expression level, it is currently understood that the p53-mediated responses are exclusively dependent of canonical full-length p53 protein (p53α).

Here we investigated by manipulating endogenous expression of a few p53 isoforms using siRNAs whether endogenous p53 isoforms regulate cell response to treatment in cells devoid of p53α expression. In addition, we explored the molecular mechanisms of p53 isoforms in presence and in absence of p53α in cells treated or not treated with UV.
The data leads us to realise that a p53-mediated cell response, which involved coordination of numerous complex biological pathways, is not orchestrated by only one p53 protein isoform but by all p53 protein isoforms. None of the p53 isoforms, including canonical p53α, is able to abolish the activity of the other co-expressed p53 isoforms. Thus, a p53-mediated cell response is the sum of the activities of co-expressed p53 isoforms, which can be controlled by manipulating p53 isoform expression and/or post-translational modifications. It suggests that p53 isoforms work in combination and would compose a cellular code.