

## Letter to the Editor

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### SV40 Tag/p53 complexes actively promote malignant cell growth of human mesothelial cells [1] \*

To the Editor,

SV40 is a DNA tumor virus that causes malignant transformation of human cells in tissue culture. SV40-transformed human cells contain a large number of chromosomal alterations that may be sufficient to sustain tumor growth even in the absence of viral protein expression. Different types of human cells show different susceptibility to SV40-mediated transformation and mesothelial cells are the most susceptible [2]. SV40 preferentially induces mesothelioma in animals [2], SV40 has been detected in human mesotheliomas [2], and synergize with asbestos in carcinogenesis *in vitro* and *in vivo* [3]. We previously demonstrated that the unusual high levels of wild-type p53 normally present in mesothelial cells are a critical factor in determining the susceptibility of these cells to SV40-mediated transformation [4]. In cells infected with DNA tumor viruses, p53 is bound to the viral Tumor antigens (Tags). The current “dogma” views the Tag-p53 complexes as a way of sequestering and inactivating p53. Using primary human mesothelial cells and SV40-transformed human cells, we now show that in addition of inactivating p53 tumor suppressor activities, the Tag-p53 complex has growth stimulatory activities that are required for the initial stages of malignant cell growth. We found that in human cells, Tag/p53 complexes regulate transcription of the Insulin-like growth factor 1 (IGF-1) gene by binding to the IGF-1 promoter together with pRb and p300. Depletion of p53 leads to structural rearrangements of this multi-protein complex, resulting in IGF-1 pro-

motor transcriptional repression and growth arrest. Our data provide a novel mechanistic and biological interpretation of the p53/Tags complexes and of DNA tumor virus transformation in general. In the model we uncovered, p53 is not a passive inactive partner of Tag. Instead the p53/Tag complex promotes malignant cell growth through its ability to activate the IGF-1 signaling pathway.

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### References

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