

Myc-driven murine prostate cancer shares molecular features with human prostate tumors

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During further characterization of the Hi-Myc and Lo-Myc prostate cancer transgenic mice, we discovered that 34 amino acids of additional sequence (derived from the Bluescript multiple cloning site) were inadvertently added to the C terminus of the human c-Myc protein during subcloning, creating an unintended C-terminal tag. Consequently, the transgenic Myc protein (Myc-Tg) runs with higher mobility than endogenous Myc (85–90 kDa versus 65 kDa). It is unlikely that the additional C-terminal sequences alter Myc function because the transforming activity of Myc-Tg was comparable to that of Myc in NIH3T3 fibroblast transformation assays (Table 1). Furthermore, proliferation of Myc-CaP cells, a new line derived from Hi-Myc prostate tumors, is restored by ectopic Myc expression when Myc-Tg levels are lowered by androgen withdrawal (Watson et al., 2005). Since untagged human Myc can compensate for loss of Myc-Tg function, we consider the Myc-Tg protein that is expressed in Hi-Myc and Lo-Myc to be an epitope-tagged Myc protein. Since the publication of our findings in mice, others have reported that overexpression of wild-type c-Myc is sufficient to induce tumor formation of normal human prostatic epithelial cells in a tissue recombination assay (Williams et al., 2005), confirming the oncogenic potential of Myc in prostate cancer.

Table 1. Soft agar transformation assay

Cell type	Number of foci
3T3	1
3T3 Myc-wt	8
3T3 Myc-Tg	9
3T3 c-term 34 AA	2
3T3 Ras(KV12)	136
3T3 Myc-wt + Ras(KV12)	202
3T3 Myc-Tg + Ras(KV12)	224
3T3 c-term 34 aa + Ras(KV12)	168

NIH3T3 cells were transfected with a plasmid expressing Myc-wt, Myc-Tg, or the 34 amino acid tail added to the Myc-Tg alone or together with a plasmid expressing activated Ras(KV12) as indicated then grown in soft agar. The number of foci obtained after growth in soft agar is averaged in the column on the right.

References

- Watson, P., Ellwood-Yen, K., King, J., Wongvipat, J., LeBeau, M., and Sawyers, C.L. (2005). Context dependent hormone-refractory progression revealed through characterization of a novel murine prostate cancer cell line. *Cancer Res.*, in press.
- Williams, K., Fernandez, S., Stien, X., Ishii, K., Love, H.D., Lau, Y.F., Roberts, R.L., and Hayward, S.W. (2005). Unopposed c-MYC expression in benign prostatic epithelium causes a cancer phenotype. *Prostate* 63, 369–384.

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