

## Letter

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### Adaptive immunity maintains occult cancer in an equilibrium state

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**The capacity of immunity to control and shape cancer, that is, cancer immunoediting, is the result of three processes<sup>1, 2, 3, 4, 5, 6, 7, 8</sup> that function either independently or in sequence<sup>9</sup>: elimination (cancer immunosurveillance, in which immunity functions as an extrinsic tumour suppressor in naive hosts); equilibrium (expansion of transformed cells is held in check by immunity); and escape (tumour cell variants with dampened immunogenicity or the capacity to attenuate immune responses grow into clinically apparent cancers). Extensive experimental support now exists for the elimination and escape processes because immunodeficient mice develop more carcinogen-induced and spontaneous cancers than wild-type mice, and tumour cells from immunodeficient mice are more immunogenic than those from immunocompetent mice. In contrast, the equilibrium process was inferred largely from clinical observations, including reports of transplantation of undetected (occult) cancer from organ donor into immunosuppressed recipients<sup>10</sup>. Herein we use a mouse model of primary chemical carcinogenesis and demonstrate that equilibrium occurs, is mechanistically distinguishable from elimination and escape, and that neoplastic cells in equilibrium are transformed but proliferate poorly *in vivo*. We also show that tumour cells in equilibrium are unedited but become edited when they spontaneously escape immune control and grow into clinically apparent tumours. These results reveal that, in addition to destroying tumour cells and sculpting tumour immunogenicity, the immune system of a naive mouse can also restrain cancer growth for extended time periods.**

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