

Targeting tumor stroma to destroy cancer variants

Hans Schreiber*, Michael T. Spiotto, and Donald A. Rowley

The University of Chicago, Chicago, Illinois

**Presenting author*

Cancers express antigens that are targets for specific cytotoxic T lymphocytes (CTLs). However, cancer cells are genetically unstable. Consequently, sub-populations that no longer express the target antigen may escape destruction by CTLs and grow progressively. In a model system, we show that cytotoxic T cells indirectly eliminate these antigen-loss variants (ALVs) when the parental cancer cells express sufficient antigen to be effectively cross-presented by the tumor stroma. When the parental tumor expressed lower levels of antigen, cytotoxic T cells eradicated the antigen-positive parental cancer cells but the ALVs escaped, grew and killed the host. By contrast, when the parental tumor expressed higher levels of antigen, cytotoxic T cells eradicated not only the parental cancer cells but also the ALVs. This “bystander” elimination of ALVs required stromal cells expressing MHC molecules capable of presenting the antigen and occurred in tumors showing evidence of stromal destruction. Apparently, ALVs were eliminated indirectly when tumor-specific CTLs killed stromal cells cross-presenting antigen produced by and released from antigen-positive cancer cells. These results highlight the general importance of targeting the tumor stroma to prevent the escape of variant cancer cells.

References

1. Spiotto MT, Rowley DA, Schreiber H. Bystander elimination of antigen loss variants in established tumors. *Nat Med* 2004; 10: 294-8. (PMID: 14981514) [PubMed]

© 2005 by Hans Schreiber