CARD9 Promotes Sex-Biased Colon Tumors in the APCmin Mouse Model.

Caspase recruitment domain-containing protein 9 (CARD9) functions in different inflammation pathways to elicit responses to microbial signals and is known to affect intestinal inflammation. Examining the APC(min) mouse model of intestinal tumorigenesis and using stringently controlled, sex- and age-matched pairs of CARD9-competent and CARD9-deficient mice, we have found that CARD9 has a restricted but strong effect on tumorigenesis in the large intestine. We have found that CARD9 reduces viability specifically in males and promotes tumorigenesis specifically in the large intestines of these male mice. To our knowledge, this is the first gene ablation in APC(min) mice that solely affects colon tumors in male subjects and, as such, may have significant clinical implications. Additional data suggest correlative disruption of plasma cytokine expression and immune infiltration of the tumors. We speculate that known sex-specific differences in human colorectal cancer may involve inflammation, particularly CARD9-dependent inflammation.