

ORAL PRESENTATION

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The immune biology of microsatellite unstable cancer

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Colorectal cancers (CRC) develop through 2 major pathways of genetic instability. In contrast to the majority of CRCs, which are characterized by chromosomal instability, high-level microsatellite unstable (MSI-H) CRCs arise as a consequence of the loss of DNA mismatch repair (MMR) functions and show accumulation of insertion and deletion mutations particularly in microsatellite sequences. MSI-H occurs in about 15% of CRCs, and virtually all CRCs occurring in the context of the hereditary cancer-predisposing Lynch syndrome. These tumors are characterized by a comparably good prognosis and a low frequency of distant metastases. Because of the expression of a defined set of tumor-specific antigens, MSI-H CRCs elicit a strong local and systemic antitumoral immune response of the host and therefore use different strategies to evade the control of the immune system. At the conference we will summarize novel molecular mechanisms that at the same time drive pathogenesis, immunogenicity and immune evasion during the development and progression of MSI-H CRCs. We will focus on the current knowledge about alterations in human leukocyte antigen (HLA) antigen presentation and discuss how immune evasion-while offering protection against local antitumoral immune responses-paradoxically might interfere with the ability of the tumor to form distant organ metastases.

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