Vesicular Stomatitis Virus Infection Promotes Immune Evasion by Preventing NKG2D-Ligand Surface Expression

Vesicular stomatitis virus (VSV) has recently gained attention for its oncolytic ability in cancer treatment. Initially, we hypothesized that VSV infection could increase immune recognition of cancer cells through induction of the immune stimulatory NKG2D-ligands. Here we show that VSV infection leads to a robust induction of MICA mRNA expression, however the subsequent surface expression is potently hindered. Thus, VSV lines up with human cytomegalovirus (HCMV) and adenovirus, which actively subvert the immune system by negatively affecting NKG2D-ligand surface expression. VSV infection caused an active suppression of NKG2D-ligand surface expression, affecting both endogenous and histone deacetylase (HDAC)-inhibitor induced MICA, MICB and ULBP-2 expression. The classical immune escape mechanism of VSV (i.e., the M protein blockade of nucleocytoplasmic mRNA transport) was not involved, as the VSV mutant strain, VSV DM51, which possess a defective M protein, prevented MICA surface expression similarly to wild-type VSV. The VSV mediated down modulation of NKG2D-ligand expression did not involve apoptosis. Constitutive expression of MICA bypassed the escape mechanism, suggesting that VSV affect NKG2D-ligand expression at an early post-transcriptional level. Our results show that VSV possess an escape mechanism, which could affect the immune recognition of VSV infected cancer cells. This may also have implications for immune recognition of cancer cells after combined treatment with VSV and chemotherapeutic drugs.

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