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HLA-G-specific microRNAs a novel approach for targeting tumors

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Immune inhibitory molecules on immune cells as well as on tumor cells appear to play a key role in modulating the immunogenicity of tumors and the efficacy of immunotherapies. One mediator is represented by the non-classical HLA-G antigen, which is often overexpressed in human tumors when compared to corresponding normal tissues thereby inhibiting both innate as well as adaptive immune responses. Since discordant HLA-G transcript and protein expression levels were often found in tumors of distinct origin posttranscriptional control mechanisms have been recently suggested. Indeed, different HLA-G-specific miRs have been identified, which were able to downregulate HLA-G surface expression. The miR-mediated inhibition of HLA-G enhanced the NK cell recognition. These miRs were also differentially expressed in renal cell carcinoma (RCC) versus normal kidney epithelium. Immunohistochemical analysis demonstrated of a high frequency HLA-G expression in RCC lesions, which was associated with disease progression and inversely correlated with the expression of HLA-G-specific miRs. These data postulate that HLA-G-specific miRs might be used as prognostic markers as well as potential therapeutics for targeting HLA-G expressing RCC.

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