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Title: “MicroRNA genes and Lymphoma Biology”

Abstract: Lymphomas are common, heterogeneous and often fatal cancers. In recent years, significant progress has been made in understanding the molecular pathogenesis of these tumors. However, these data derive almost exclusively from studies in classical mRNA genes, whereas the role of microRNAs in lymphoma biology remains to be fully explored. MicroRNAs belong to a novel class of small non-protein coding RNAs, that regulate gene expression by binding to the 3'UTR of target transcripts. MicroRNAs play critical role in various physiologic processes, and their dysfunction has emerged as an important component in cancer development and progression. To address the contribution of microRNAs to lymphomagenesis we used global and focused approaches. In the former, we created the first integrative map of the microRNA genome in lymphomas, and identified a novel, clinically relevant, microRNA-driven molecular substructure in these tumors. Furthermore, we examined the mechanism by which overexpression of microRNA-155 contributes to lymphoma aggressiveness. Starting from an unbiased genome-wide approach, we found that microRNA-155 directly targets the transcription factor SMAD5, and thus blocks the cytostatic effects of the TGF β pathway in lymphomas.