MyD88^{L265P} participates in the extracellular vesicles and enables the transfer of the proinflammatory signaling complex to the neighboring cells

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MyD88 is the central signaling adapter of innate immunity, mediating signaling through Toll-like receptors and IL-1R. MyD88L265P constitutively triggers myddosome assembly and activates the signaling pathway thus providing a survival signal to WM cells. In addition to the cytosol of cancer B-cells mutated MyD88 was also detected in the extracellular vesicles (EVs) shed by WM cells. The mechanism of localization and trafficking of mutated MyD88 through EVs was investigated in different cell types, where we detected that MyD88 can be internalized and that it can recruit the endogenous MyD88, triggering inflammatory pathway. MyD88 transferred via EVs into the cytoplasm of the recipient mast cells and macrophages, affecting cells in the tumor`s microenvironment. Internalization of the EVs containing MyD88 was observed *in vivo* with modification of the bone marrow microenvironment. MyD88-loaded EVs were also detected in the bone marrow aspirates of WM patients which suggests the physiological role of the EVs for shaping the proinflammatory microenvironment. This study identified a mechanism for the transmission of signaling components via EV to propagate inflammation as a new paradigm of intercellular communication.