Abstract

Infiltrative tumor growth into adjacent soft tissues is a major cause of the frequent recurrence and tumor-related death of myxofibrosarcoma (MFS), but no useful biomarkers reflecting tumor burden and infiltrative growth are available. While emerging evidence suggests a diagnostic and functional role of extracellular/circulating microRNA (miRNA) in various malignant diseases, their significance in MFS patients remains unknown. Global miRNA profiling identified four upregulated miRNAs in MFS patient sera and culture media of MFS cells. Among these, serum *miR-1260b* level was significantly upregulated in patient serum discriminating from healthy individuals and closely correlated with clinical status and tumor dynamics in MFS-bearing mice. In addition, high *miR-1260b* expression in serum was correlated with radiological tail-like patterns, characteristic of the infiltrative MFS. The extracellular *miR-1260b* was embedded in tumor-derived extracellular vesicles (EVs) and promoted cellular invasion of MFS through the downregulation of *PCDH9* in the adjacent normal fibroblasts. Collectively, circulating *miR-1260b* expression may represent a novel diagnostic target for tumor monitoring of this highly aggressive sarcoma. Moreover, EV-*miR-1260b* could act as a transfer messenger to adjacent cells and mediate the infiltrative growth of MFS, providing new insights into the mechanism of infiltrative nature via crosstalk between tumor cells and their microenvironment.