CAMTA1 is a novel tumour suppressor regulated by miR-9/9* in glioblastoma stem cells.

Abstract:
Cancer stem cells or cancer initiating cells are believed to contribute to cancer recurrence after therapy. MicroRNAs (miRNAs) are short RNA molecules with fundamental roles in gene regulation. The role of miRNAs in cancer stem cells is only poorly understood. Here, we report miRNA expression profiles of glioblastoma stem cell-containing CD133(+) cell populations. We find that miR-9, miR-9(*) (referred to as miR-9/9(*)), miR-17 and miR-106b are highly abundant in CD133(+) cells. Furthermore, inhibition of miR-9/9(*) or miR-17 leads to reduced neurosphere formation and stimulates cell differentiation. Calmodulin-binding transcription activator 1 (CAMTA1) is a putative transcription factor, which induces the expression of the anti-proliferative cardiac hormone natriuretic peptide A (NPPA). We identify CAMTA1 as an miR-9/9(*) and miR-17 target. CAMTA1 expression leads to reduced neurosphere formation and tumour growth in nude mice, suggesting that CAMTA1 can function as tumour suppressor. Consistently, CAMTA1 and NPPA expression correlate with patient survival. Our findings could provide a basis for novel strategies of glioblastoma therapy.

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