Abstract

The physiological role of the reduced expression of immortalized cells (REIC)/Dickkopf-3 (Dkk-3) protein in patients with hepatocellular carcinoma (HCC) remains unclear. In this study, we evaluated the effect of the REIC/Dkk-3 protein on HCC cell proliferation and assessed the relationship between the serum REIC/Dkk-3 protein level and the prognosis in patients with HCC. We evaluated the REIC/Dkk-3 protein-induced anticancer effects on Huh7 and Hep3B cells (HCC cell lines) in the presence of peripheral blood mononuclear cells (PBMCs), and found that combination treatment with REIC/Dkk-3 protein and PBMCs reduced the proliferation of HCC cells (Hep3B: 82.0% ± 16.3%; Huh7: 72.6% ± 9.1%). We also studied 194 HCC patients who underwent primary liver resection or primary radiofrequency ablation from 2008 to 2017. Serum REIC/Dkk-3 protein levels were measured by an enzyme-linked immunosorbent assay and compared to the prognostic data. The 3-year disease-free survival of the REIC/Dkk-3 high group was significantly higher than that in the REIC/Dkk-3 low group. In conclusion, this is the first study investigating the relationship between HCC patient survival and serum REIC/Dkk-3 protein levels in a large population. Based on the results, the serum REIC/Dkk-3 protein level should be considered a new prognostic marker for patients with HCC.