Interaction between tumour-infiltrating B cells and T cells controls the progression of hepatocellular carcinoma.

The nature of the tumour-infiltrating leucocytes (TILs) is known to impact clinical outcome in carcinomas, including hepatocellular carcinoma (HCC). However, the role of tumour-infiltrating B cells (TIBs) remains controversial. Here, we investigate the impact of TIBs and their interaction with T cells on HCC patient prognosis. Tissue samples were obtained from 112 patients with HCC from Singapore, Hong Kong and Zurich and analysed using immunohistochemistry and immunofluorescence. RNA expression of CD19, CD8A, IFNG was analysed using quantitative PCR. The phenotype of freshly isolated TILs was analysed using flow cytometry. A mouse model depleted of mature B cells was used for functional study. Tumour-infiltrating T cells and B cells were observed in close contact with each other and their densities are correlated with superior survival in patients with HCC. Furthermore, the density of TIBs was correlated with an enhanced expression of granzyme B and IFN-γ, as well as with reduced tumour viability defined by low expression of Ki-67, and an enhanced expression of activated caspase-3 on tumour cells. CD27 and CD40
costimulatory molecules and TILs expressing activation marker CD38 in the tumour were also correlated with patient survival. Mice depleted of mature B cells and transplanted with murine hepatoma cells showed reduced tumour control and decreased local T cell activation, further indicating the important role of B cells. The close proximity of tumour-infiltrating T cells and B cells indicates a functional interaction between them that is linked to an enhanced local immune activation and contributes to better prognosis for patients with HCC.