An immature B cell population from peripheral blood serves as surrogate marker for monitoring tumor angiogenesis and anti-angiogenic therapy in mouse models

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Tumor growth depends on the formation of new blood vessels (tumor angiogenesis) either from preexisting vessels or by the recruitment of bone marrow-derived cells. Despite encouraging results obtained with preclinical cancer models, the therapeutic targeting of tumor angiogenesis has thus far failed to deliver an enduring clinical response in cancer patients. One major obstacle for improving anti-angiogenic therapy is the lack of validated biomarkers, which allow patient stratification for suitable treatment and a rapid assessment of therapy response. Toward these goals, we have employed several mouse models of tumor angiogenesis to identify cell populations circulating in their blood that correlated with the extent of tumor angiogenesis and therapy response. Flow cytometry analyses of different combinations of cell surface markers that define subsets of bone marrow-derived cells were performed on peripheral blood mononuclear cells from tumor-bearing and healthy mice. We identified one cell population, CD45(dim)VEGFR1(-)CD31(low), that was increased in levels during active tumor angiogenesis in a variety of transgenic and syngeneic transplantation mouse models of cancer. Treatment with various anti-angiogenic drugs did not affect CD45(dim)VEGFR1(-)CD31(low) cells in healthy mice, whereas in tumor-bearing mice, a consistent reduction in their levels was observed. Gene expression profiling of CD45(dim)VEGFR1(-)CD31(low) cells characterized these cells as an immature B cell population. These immature B cells were then directly validated as surrogate marker for tumor angiogenesis and of pharmacologic responses to anti-angiogenic therapies in various mouse models of cancer.

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