Antigen expression profile in circulating endothelial progenitor cells

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The clinical applications of discoveries in angiogenesis and vasculogenesis research necessitate the development and validation of surrogate markers of tumour neovascularization and anti-angiogenic drug efficacy. Candidate biomarkers include circulating endothelial cells (CECs) shed by the tumour vasculature and circulating endothelial progenitors (CEPs) derived from the bone marrow, both measured by multiparametric flow cytometry. In their remarkable Review[1], Bertolini and colleagues define CEPs as expressing low levels of the pan-haematopoietic antigen CD45 ($CD45^{dim}$) (Figure 1). However, in the same article their flow cytometry approach consists of excluding all haematopoietic cells by sequential gating, thereby only selecting CD45-negative cells for further analyses (page 837 and Figure 2). Although the exact identity and function of CEPs is the subject of debate, these seemingly contradictory statements merit clarification. CEPs, defined as $CD34^{+}CD133^{+}CD45^{dim}$, $CD34^{+}VEGFR2^{+}CD45^{dim}$ or $CD34^{+}CD133^{+}VEGFR2^{+}CD45^{dim}$ cells, have been reported to be present in the peripheral blood of cancer patients[2,3], cardiac patients[4] and smokers[5] as well as in umbilical cord blood[2]. Nevertheless, the lack of haematopoietic antigen expression, such as CD45, has also been used to show the endothelial nature of CEPs and CECs[6,7]. In addition, studies in murine models have documented the existence of bone-marrow-derived $SCA1^{+}FLK1^{+}CD45^{+}$ and $SCA1^{+}TIE2^{+}CD31^{+}CD45^{+}$ endothelial precursor cell populations[8,9]. These differences might reflect, in part, our limited understanding of the potential origin and steps of differentiation of CEPs toward the endothelial lineage in postnatal vasculogenesis[10,11]. In light of the growing interest in vasculogenesis and anti-angiogenic therapy trials, we encourage the authors to clarify the issue.

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