To the Editor: In the review of tumor angiogenesis by Kerbel (May 8 issue),\(^1\) endothelial progenitors are described as negative for CD45, positive for vascular endothelial growth factor receptor 2 (VEGFR-2), and positive for CD133, and the review by Bertolini et al.\(^2\) is cited as the source for this definition. This assertion is incorrect; in the article by Bertolini et al., endothelial progenitors are actually defined as CD45\textsuperscript{dim}-CD34\textsuperscript{+}-VEGFR-2\textsuperscript{+}-CD133\textsuperscript{+} cells.

Flow cytometric analyses that we performed on blood from normal subjects showed that, among CD34\textsuperscript{+} cells, a discrete population of CD45\textsuperscript{dim}-CD34\textsuperscript{+}-VEGFR-2\textsuperscript{+}-CD133\textsuperscript{+} cells could be discerned. Back-gating on VEGFR-2\textsuperscript{+}-CD133\textsuperscript{+} cells showed that all these cells expressed CD34. CD34\textsuperscript{+}-CD45\textsuperscript{−} cells were virtually absent, with the exception of possible debris or endothelial-cell microparticles, as demonstrated by their forward and orthogonal light-scatter properties (Fig. 1). Our results confirm Bertolini and colleagues’ definition of endothelial progenitors as CD45\textsuperscript{dim}CD34\textsuperscript{+}VEGFR-2\textsuperscript{+}CD133\textsuperscript{+}.

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Figure 1. Analysis of Peripheral-Blood Mononuclear Cells Stained with CD45-PE-Cy7, CD34-PE, and VEGFR-2-APC.

Electronic back-gating on CD34\textsuperscript{+}-VEGFR-2\textsuperscript{+} cells shows three cell clusters with varying intensities of CD45 (Panel A). The light-scatter properties of the back-gated cluster for CD45\textsuperscript{−} cells are consistent with those of dead cells and cellular debris (red dots in Panel B). The CD45\textsuperscript{dim} population has light-scatter properties that are consistent with small viable cells (green dots in Panel B). The CD45 bright population has light-scatter properties that are consistent with monocytes. As a point of reference, ungated light scatter of peripheral-blood mononuclear cells (Panel C) shows the three major cell subgroups: lymphocytes, monocytes, and granulocytes. VEGFR-2 denotes vascular endothelial growth factor receptor 2. The numbers on the axes in all three panels are arbitrary units.
THE AUTHOR REPLIES: Zerbini and colleagues are correct about the discrepancy in referring to endothelial progenitor cells as “CD45−” versus “CD45dim.” It is not uncommon for some investigators to use these terms interchangeably, as I have, and to sometimes describe these cells as CD45− (e.g., in a report by Alvarez et al.) and sometimes as CD45dim (e.g., in a report by Duda et al.). However, partly on the basis of data in the figure presented by Zerbini and colleagues, the point is made that these cells are phenotypically distinct, thus calling for a more precise definition when referring to endothelial progenitor cells. I agree. Whether endothelial progenitor cells are CD45dim in all cases cannot be said with certainty at present, which highlights the problem of an accepted standard definition of endothelial progenitor cells based especially on expression of cell-surface markers but also on functional criteria. An international consensus workshop is needed to make recommendations regarding such a standard definition, given the importance of endothelial progenitor cells in cancer and cardiovascular disease. It is also reassuring that the data of Bertolini and colleagues showing that human endothelial progenitor cells have a CD45dim-CD34+VEGFR-2+CD133+ phenotype were confirmed.

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Pursuit of an Expanded Physician Supply

TO THE EDITOR: In his Health Policy Report on physician supply, Iglehart (April 17 issue) focuses on a result of the Medicare Payment Advisory Commission (MedPAC) 2006 survey of Medicare beneficiaries: among a small percentage of beneficiaries who were seeking a new specialist, more of them had a problem finding one in 2006 than in 2004. This finding must be considered in context. Each year, beneficiaries who respond to our survey report having better access to specialists than to primary care physicians. That was the result again in 2007, when 85% of those seeking a new specialist reported having no problem, as compared with 70% of those seeking a new primary care physician. Moreover, MedPAC is concerned that primary care services are undervalued in Medicare’s physician fee schedule and are at risk of being underprovided relative to procedurally based services. In response, MedPAC recently recommended increases in fee-schedule payments for primary care services that are “furnished by practitioners focused on delivering primary care” and a medical home pilot program in Medicare. These recommendations are in addition to reforms MedPAC recommended previously to better address overvalued services in the fee schedule.

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TO THE EDITOR: Iglehart leaves out one factor that impinges on physician supply: the number of applicants to medical school. The number relative to positions has gradually fallen over the years. When I applied to medical school in 1942, some schools received as many as 10 applications for every position. The current ratio of applicants to acceptance is approximately 2.1:1. If this trend continues, quality will eventually decrease, and it is possible that later there won’t be enough qual-