To the editor:

**CFU-EC: how they were originally defined**

We read with interest the article “Redefining endothelial progenitor cells via clonal analysis and hematopoietic stem/progenitor cell principles” by Yoder et al.1 The authors compared 2 types of colony assays that have been shown to identify endothelial progenitor cells (EPCs)2,3 and studied the function of the cells derived from these assays. They found that a commercially available kit, which is widely used to quantify EPCs, actually detects cells of the mononuclear lineage, whereas an assay developed by the authors unequivocally measures the colony-forming potential of true EPCs. Although we agree with the authors that it is time to clearly define the term EPC and the results presented are consistent with our own experience, we have some comments regarding the nomenclature of the endothelial colonies.

In the May 15, 2000 issue of Blood, we reported the identification of human endothelial progenitor cells expressing CD133 (previously known as AC133).4 We described a suspension culture system that induces differentiation of CD133-positive (+) cells into functional endothelial cells and a methylcellulose-based colony assay for EPCs. In this assay, CD133+ progenitor cells give rise to colonies with a unique morphology, which is different from CD133-derived hematopoietic colonies grown in methylcellulose. We showed that these colonies are composed of small-sized cells that express the endothelial cell antigen von Willebrand factor. Because our colony assay for EPCs was developed in analogy to the standard colony assay for hematopoietic stem and progenitor cells, we called the EPC-derived colonies “colony-forming unit endothelial cells (CFU-EC)” and introduced this term to scientific readership for the first time.

Meanwhile, numerous studies have been published claiming that they investigated the clonogenic potential of EPCs. We are aware that some of these studies adopted the term CFU-EC, although they used different culture systems.5 However, we would like to stress that the colonies presented by Hill et al have not been referred to as CFU-EC by the authors themselves.3 With regard to the already existing confusion about the definition of EPC and their progeny, we propose to refer to the myeloid colonies occurring in the Hill assay as “CFU-Hill” according to nomenclature used by the manufacturer of this assay. The term CFU-EC should be reserved for colonies derived from CD133+ EPC as described in our study.4

In addition, we would like to note that the study by Reyes et al, cited as reference 11 in the article by Yoder and colleagues, did not use colony assays.6

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Conflict-of-interest disclosure: The authors declare no competing financial interests.

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References


To the editor:

**Associations between type of product and inhibitors in previously untreated patients (PUPs) with severe hemophilia: switches and particular products can disturb analysis**

Genetic and environmental risk factors for inhibitor development in severe hemophilia A have been reported in various observational studies. The CANAL (Concerted Action on Neutralizing Antibodies in severe hemophilia A) historical cohort studied the effect of product type by searching for differences between 1) recombinant factor VIII (rFVIII) and plasma-derived factor VIII (pdFVIII) and 2) depending on the concentration of von Willebrand factor (vWF).1 Despite a large number of patients (316 previously untreated patients [PUPs]) and a multivariate survival analysis, no difference was found. Regarding the first objective, Gouw et al observed an adjusted relative risk (aRR) rFVIII/pdFVIII of 1.4 (confidence interval [CI], 0.9 to 2.5)4 while we found an aRR of 2.4 (CI, 1.0 to 5.8),2 and a recent English study reported an adjusted odds ratio of 1.83 (CI, 0.9 to 3.72).3 The confidence intervals overlap, but 2 differences could account for the RR gradient observed. First of all, Gouw et al considered product type as a time-dependent covariate. The definition of switches was not clearly specified, but at least 54 patients, including 49 (36%) of the patients initially treated with pdFVIII, changed product early (after median of 5 cumulative exposure days [CEDs]), probably for rFVIII in most cases.1 These patients were kept in the analysis until 50 CEDs and were included in the estimation of inhibitor incidence with rFVIII. This analysis option is based on the hypothesis that product-associated risk is only determined by the product received.
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