Prostate-specific Antigen Expression in Normal Human Bone Marrow Cells

To the Editor:

Improved procedures for measuring prostate-specific antigen (PSA) protein and mRNA have demonstrated that this kallikrein-like serine protease is present in many nonprostatic sources, indicating that PSA production/secretion is not tissue- or sex-specific, but rather is a steroid hormone-dependent phenomenon (1). Reports on PSA-positive cells in bone marrow (BM) and peripheral blood mononuclear cells are contradictory (2–6). The elucidation of this controversy might be of clinical utility to establish the nonspecificity of PSA as an indicator of micrometastases (7, 8).

Belonging to a large study project on the extraprostatic expression of PSA, we undertook the present study to evaluate the presence of PSA in human BM hematopoietic stem/progenitor cells from a healthy adult donor, who gave written informed consent. He was without clinical findings referable to the prostate and did not take any medication during the preceding 6 months. The BM sample was enriched in mononuclear cells, and the CD-34+ or CD-34− subpopulations were purified by immunomagnetic separation (9). The BM cells were then lysed immediately, and the supernates were assayed for PSA content and analyzed by Western blot (10). The ultrastructural immunolocalization of PSA in BM cells was performed as described previously (10). The results, reported as the mean ± SE of at least three independent experiments performed in triplicate, were analyzed statistically with the Stat-View, Ver. 4, package (Abacus Concepts) on a Macintosh Power PC (Apple). Significance was established as \( P < 0.05 \).

The total-PSA content in extracts from CD-34+ cells was significantly higher than that found in CD-34− cells (0.208 ± 0.024 ng/10^7 cells and 0.072 ± 0.006 ng/10^7 cells, respectively; \( n = 9; P < 0.0001 \), paired \( t \)-test). The subpopulations of BM cells also showed a marked difference for free PSA (77% vs 18% for CD-34+ and CD-34− cells, respectively). The linear correlation between PSA concentration and dilution \( (r^2 = 0.96) \) demonstrated that the cell matrix did not affect PSA analysis.

Western-blot analysis confirmed the quantitative results. The electron microscopic examination of immunolabeled CD-34+ cells displayed a specific cytoplasmic PSA distribution, localized mainly on small vesicles, whereas CD-34+ cells showed only a negligible signal.

The different patterns of PSA expression in CD-34+ or CD-34− cells may reflect different characteristics of these cell subpopulations; in fact, BM cells represent a quite heterogeneous cell population (9).

Our present findings are in agreement with the previously reported PSA detection in BM and peripheral blood mononuclear cells from healthy subjects (2–4), confirming that these cells can express PSA and that PSA in BM may not represent hemogenous micrometastases (3, 6). Similarly, human leukemic cell lines have been demonstrated to produce/secrete PSA (2, 11).

Although the biological and physiological roles of PSA in BM progenitor/stem cells remain unknown, the presence of PSA in these cells of nonprostatic origin further supports the hypothesis about possible extraprostatic functions of this protease in nonpathologic conditions and should be taken into consideration when using methods to detect hematogenous micrometastases (7, 8).

References
