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BB9 ACEs the HSC compartment

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In an effort to discover specific markers to isolate human hematopoietic stem cells, Jokubaitis and colleagues report that the monoclonal antibody BB9 reacts with hematopoietic cells displaying morphologic, phenotypic, and/or functional properties of stem and progenitor cells throughout human ontogeny.

Why the continued search for a stem-cell marker? In the murine system, hematopoietic stem cells (HSCs) can be isolated to near homogeneity, permitting detailed comparative analysis throughout ontogeny, and recent data suggest that there may be distinct differences in clonal HSC behavior in vivo.1 In contrast, the human HSC is less well defined; although several cell-surface molecules have previously been identified on bone marrow and peripheral-blood subpopulation of CD34+ cells,3 the present data suggest that BB9 marks a subpopulation of CD34+ hematopoietic cells throughout human ontogeny and may serve as a reagent to further interrogate the human HSC compartment.

But what is the antigen recognized by BB9? Jokubaitis and colleagues report that BB9 binds to the somatic form of angiotensin-converting enzyme (ACE/CD143), a key regulator in the renin-angiotensin system (RAS). This well-recognized system that plays important roles in blood pressure regulation, renal physiology, and reproduction is now known to participate in the pathophysiology of diabetes, cancer, and cardiovascular dysfunction. ACE and other members of the RAS have previously been reported to play a role in avian yolk sac erythropoiesis,3 and the notion of a local RAS functioning within the bone marrow compartment was proposed a decade ago.4 Although a role for ACE in HSC physiology was not delineated in the present study, Jokubaitis and colleagues speculate that the potential substrates for ACE may be broader than those typically restricted to the RAS system, as ACE is known to target numerous non-RAS molecules. These exciting possibilities add to the increasing recognition that HSCs play an active role in niche homeostasis, and suggest that some systems, such as the RAS, may need to be further explored as possible common regulatory pathways that transcend the multiple sites of hematopoiesis throughout ontogeny and function to maintain HSC biological properties required at each stage of development.

Conflict-of-interest disclosure: The author is a cofounder and consultant for EndGenitor Technologies (Indianapolis, IN), whose potential product was not described in this commentary.

REFERENCES

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