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commentary Open Access

Invited Commentary on "Enrichment and Characterization of Two Subgroups of Committed Osteogenic Cells in the Mouse Endosteal Bone Marrow with Expression Levels of CD24"

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Commentary

Osteoprogenitor cells are known to reside within the Marrow Stromal Cells (MSCs) compartment. Since their first isolation in 1968 [1], MSCs have been largely studied for their cellular identity and differentiation potential, and they became an attractive source of adult stem cells useful for clinical applications. As with any stem cell type, MSCs possess self-renewal ability and the capacity to differentiate along multiple mesenchymal cell lineages, such as bone, cartilage and adipose cells, as well as along non-mesenchymal cell lineages, due to their plasticity [2]. They were initially found in bone marrow, but soon after it was found that cells with similar activity reside in many other tissues, including periosteum, skeletal muscle and adipose tissue [3-5]. Much effort during the past years has been devoted to identify markers which may specifically distinguish lineage fate among them [6,7]. Moreover, many studies compared the ability of stromal cell populations derived from different compartments to differentiate along specific lineages, i.e. bone cells, with the aim, on one hand, to identify the easiest accessible source of progenitors, and, on the other hand, to understand whether stromal cells derived from different compartments may exert preferential differentiation pathways, being enriched in specific progenitors [8,9]. However, the poor knowledge of molecular markers which may distinguish MSC subpopulations exerting different differentiation potential, limited those studies to qualitative analyses. Osteoprogenitor cells are usually isolated from the Sca1$^-$ or Sca1$^-$/CD51$^+$ cell population within MSCs non-hemopoietic and non-endothelial cell compartment, but no detailed characterization of these cells has been reported [10-12]. An elegant and reliable protocol to enrich MSCs in osteogenic progenitors is presented in the manuscript by Ching-Fang Chang et al., based on the expression level of CD24, which they identified as a novel cell surface marker of osteoprogenitor cells [13]. In this study, Ching-Fang Chang and colleagues aimed to identify specific markers useful to discriminate MSCs with osteogenic, adipogenic or other lineages potential, derived from the Endosteum. They hypothesized that the cell surface antigene CD24, may represent such a marker, as being already identified as specifically expressed in other stem/progenitor cells, including white adipose progenitors. Indeed, they found, within the Sca1$^-$ Endosteal stromal cell compartment, three subpopulations, based on the expression level of CD24: a Sca1$^-$CD24$^{-/lo}$, a Sca1$^-$ CD24^{med} and a Sca1$^-$ CD24^{hi} cell population. They also observed that, among the Sca1$^-$CD51$^+$ cells, only those CD24^{med} and CD24$^{-/lo}$ were able to commit to the osteogenic lineage. These cells were highly committed to the osteogenic lineage: they express gene signature typical of osteoprogenitor cells and give rise to osteogenic colonies (CFU-ALP) in culture, with no need of additional inducers. By contrast, they do not give rise to adipocytes, suggesting that they represent progenitors restricted to the osteogenic differentiation. The authors further characterized the obtained osteogenic progenitor sub-populations for the expression level of osteogenic markers, proliferation ability, CFU-ALP frequency, and found that those Sca1$^-$ CD24$^{-/lo}$ represent a more immature osteoprogenitors compared to those Sca1$^-$CD24^{med}.

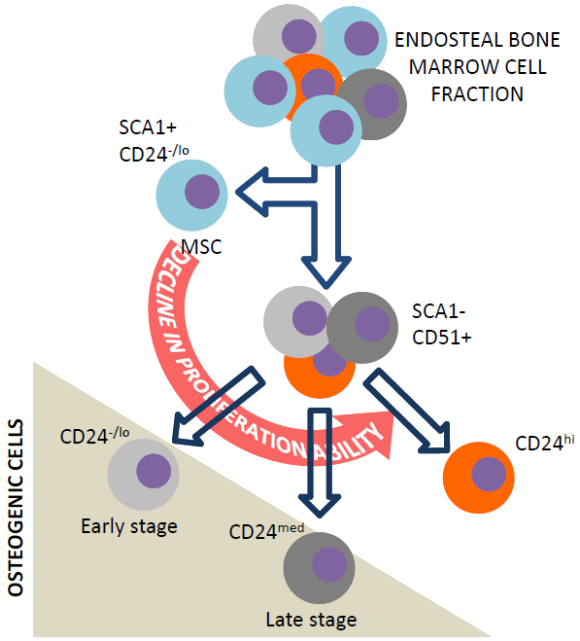

Figure 1: Schematic representation of the endosteal stromal marrow cells dynamics, as identified by Sca1/CD24 level of expression.

By contrast, the Sca1$^-$CD24^{hi} cells did not express any osteogenic markers, nor they give rise to CFU-ALP or adipocytes. The nature of this last cell population is still to be determined, and its characterization may give new insight on the complexity of the stromal cell compartment. The dynamics of cell populations proposed for osteogenic lineage is summarized in Figure 1. Further highlighting the complexity of the stromal cell compartment is the finding that, within the Sca1$^+$ Endosteal compartment, only a single Sca1$^+$CD24$^{-/lo}$ MSC population was found. As expected, these cells do not express osteogenic molecular markers, but maintain the multipotent ability to differentiate towards both osteogenic and adipocyte lineages when

cultured in the appropriate conditions. The approach presented should allow to further characterize differentiation potential and to in-dept understand the hierarchical organization of osteogenic cell lineages over the other lineages during skeletogenesis and bone repair. Moreover, the identification of CD24 as a novel cell surface marker to discriminate osteoprogenitors, based on its level of expression, gives important new information on the complexity of stem/progenitor cells within the MSCs.

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