

## Letter

# The future of mammary stem cell biology: the power of *in vivo* transplants - authors' response

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See related letter by Lindeman *et al.*, <http://breast-cancer-research.com/content/10/3/402>

and related review article by Smith and Medina, <http://breast-cancer-research.com/content/10/1/203>

The letter from Lindeman and coworkers [1] conveys their concern regarding the future of prospective isolation and characterization of individual cells that may be characterized as mammary stem cells upon *in vivo* transplantation. As they have pointed out, the difficulties encountered in identifying specific mammary epithelial subtypes by different levels of fluorescence (particularly for membrane components that decorate most if not all mammary epithelial cells) leads to differential reporting and 'resultant confusion' and 'underscores the need for improved standardization'.

Our 're-evaluation' [2] sought to highlight these concerns for those mammary and nonmammary biologists, who have been regaled in the current literature with glowing claims of the prospective isolation of normal and 'cancer stem cells'. Despite tremendous efforts to isolate stem and progenitor subpopulations from mammary glands using surface markers, the following critical questions remain; where is the stem cell located?; what constitutes a niche environment?; and what critical molecular mechanisms regulate these interactions? Our understanding of mammary 'stem cell' and 'progenitors' will be greatly enhanced when these questions are answered. *In vivo* lineage-tracing experiments will be critical in resolving these issues. The mouse mammary fat pad represents a powerful and under-utilized site for the rigorous delineation of the complex interaction between mammary epithelial cells (of all subtypes), their stromal counterparts and extrinsic signals, which are indispensable to mammary gland growth, development, and differentiation. It was recently demonstrated that admixtures of mammary epithelial cells and cells from adult male seminiferous tubules produce chimeric glands, in which both testicular and mammary cell progeny play interchangeable roles in mammary growth, development, and differentiation [3]. This experimental model holds great promise for the subsequent identification of the cellular,

stromal and extrinsic signals necessary to specify, initiate, generate, and maintain a fully functional mammary gland population, and has been extended to include cells from other adult organs.

## Competing interests

The authors declare that they have no competing interests.

## References

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2. Smith GH, Medina D: **Re-evaluation of mammary stem cell biology based on *in vivo* transplantation.** *Breast Cancer Res* 2008, **10**:203.
3. Boulanger CA, Mack DL, Booth BW, Smith GH: **Interaction with the mammary microenvironment redirects spermatogenic cell fate *in vivo*.** *Proc Natl Acad Sci USA* 2007, **104**:3871-3876.