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Cancer stem cells from solid tumors for personalized therapeutics

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Cancer stem cell (CSC) remains a contentious issue in spite of its discovery over 15 years ago. In these studies we will present evidence for putative CSCs from mammary tumors; which has potential applications for other solid tumors as well. CSCs are generally isolated by cell sorting via flow cytometry using cell surface markers or by ALDEFLOUR assay. However, many studies have shown that these markers are not unique to CSCs. We have developed an innovative approach for the isolation of high purity CSCs which is based on the activation of "intracellular machinery for self renewal" by vitamin A/retinol. The cells exhibit typical properties of stem cells such as unlimited self renewal, clonal growth from single cell, differentiation into mammary specific lineages and also formation of highly aggressive metastatic tumors in NOD SCID mice. Almost 100% cells express mammary stem cell specific markers CD29 (β1-integrin), CD49f (α6-integrin). Vitamin A/retinol is generally associated with cell differentiation via its metabolite retinoic acid however, our studies have revealed that CSCs do not contain enzymes such as ADH1/4 and RALDH2 that metabolize vitamin A/retinol into retinoic acid and therefore, have impaired retinol metabolism. The studies have potential for translational applications for generating patient specific CSC lines and tumor grafts for drug discovery and pre-clinical efficacy for personalized therapeutics.

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