ABSTRACTS

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CHARACTERIZATION OF CANINE MAMMARY TUMOR INITIATING CELLS WITH STEM CELL POTENTIAL

Cocola C.1*, Anastasi P.2*, Astigiano S.3, Sanzone S.1, Cellamare N.1, Piscitelli E.1, Vilardo L.1, Sala E.1, Bertoli G.1, Beccaglia M.2, Veronesi M.C.2, Barbieri O.3, Reinbold R.4, Luvoni G.C.2, Zucchi I.1

1-ITB-CNR, Via Cervi 93, 20090 Segrate-Milan, Italy.; 2-Department of Veterinary Clinical Sciences, Obstetrics and Gynaecology, University of Milan, Italy; 3-IST L.go R. Benzi 10, 16132 Genova Italy; 4-Max Planck Institute, D48149 Muenster, Germany.

Corresponding author: cecilia.luvoni@unimi.it *These authors contributed equally to this work.

Introduction - Breast cancer research has substantially relied on rodent and human tumor cell lines, and on mouse models expressing breast cancer inducing (oncogenic) or repressing transgenes. Recent data suggests that mammary carcinogenesis may be driven by cancer stem cells (CSCs) derived from mutated adult stem or progenitor cells in which deregulation of self-renewal or progenitor cells by the stem cells has occurred. It has become apparent that species differences between rodent and human cancer stem cells exist in the development of tumors and suggest that alternative species model systems would contribute to the study of human oncogenesis. It has been recently reported that spontaneous mammary cancers in cats and dogs make excellent models for human breast cancer (1). These findings have generated renewed interest in determining the universal mechanisms by which cancer stem cells become independent of extra-cellular signals of the normal mammary microenvironment and knowledge of mammary carcinogenesis would be greatly enhanced across all species.

Objectives - With the goal to identifying the emerging concepts universal in tumor development from cancer stem cells, we have generated a dog cancer stem cell model system. Insight into the hierarchical organization of canine tumors as abnormal tissues that originates from, and are maintained by cancer stem cells, should provide a mammalian tumor model system more similar to human than the rodent system.

Results - Using normal and tumoral dog mammary tissues, we isolated and propagated putative normal/cancer stem cells as mammospheres in long-term non-adherent cultures. Both normal and tumoral mammary cells showed self-renewing and multi-lineage differentiation capacity and generated complex branched tubular structures in vitro. We plan to analyze these cells for the expression of specific stem and cancer stem cell markers and determine which are in common and unique to human normal/cancer stem cells. In 2 cases these cells have been injected into NOD/scid mice for serial transplantation studies in order to characterize their tumor formation potential and the dynamic of tumor formation at the single cell level as previously described (2). Work is in progress in identifying and characterizing the earliest precursor/progenitor cells, and mechanisms and pathways by which tumors are seeded. This work was financially supported by FONDAZIONE CARIPLO.

References