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Understanding how distinct tumor cell clones communicate in glioblastoma

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Tumor cell heterogeneity constitutes a major challenge in cancer treatment. It has been shown thatinteractions between genetically different tumor cell subclonesin glioblastomacan affect the overall tumor growth.

To identify further signaling pathways and factors that contribute to interclonal effects we have usedthe U343 cell culture system, which consists of a panel of cell clones derived from a single glioblastomatumor, including U343MG, U343MGa, U343MGa31L and U343MGaCl2:6.

Here we show that U343MG cells have invasive capacity *in vitro* and express elevated mRNA levels of mesenchymal genes, including SNAI2, LAMC1 and FN1. In contrary, the other clones are less invasive and express high mRNA levels of the stem cell factor SOX2 and the astrocytic marker GFAP. By genomic copy number analysis a set of common gains and losses indicated a common ancestor, while specific alterations illustrated how the different clones had evolved. By co-culture and conditioned media experiments we found that U343MG elicited differentiation and growth inhibitory effects on U343MGaCl2:6 in co-culture via Notch signaling, and inhibited the proliferation of U343MGa31L via secreted factors. Gene-expression,proteomicand functional genomic approaches will pinpointthe specific pathways that elicit these inter-clonal effects.

Our studies show that different tumor cell subclones in a single glioblastomamay affect each other´s growth and differentiation via secreted and cell-associated factors. Massive single-cell analyses and further studies of fresh tumor samples will tell what combinations of interacting cell types may prevail in glioblastoma. Knowledge about cell-to-cellcommunicationin glioblastomamayprovidenovel therapeutic targets.

Biography:

Monica Nistér is a professor of pathology since 2002 at the Department of Oncology – Pathology, Karolinska Institutet, Karolinska University Hospital, Sweden. Her major research interests are to characterize the cancer cell heterogeneity and cancer stem cells in brain cancer, and to study the involvement of growth factor stimulation and p53 loss of function as well as epigenetic mechanisms and mitochondrial dynamics in cancer. Dr. Nistér has authored 120 peer-reviewed articles, a majority of whichin the cancer field, especially onbrain cancer. She has a PhD degree in Pathology (Tumor Biology) from Uppsala University in 1987 and became professor of experimental pathology at the same university in 1999.