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Deregulation of *c-myc* and *GNL3* in tumorspheres from *in vitro* transformed cell lines

Chiara Mondello[1], Ilaria Chiodi[1], Bartolo Bono[1], Martina Peritore[1], Giulia Monticone[1], Mariavittoria Pizzinga[1], Roberta Frapolli[2] and Maurizio D'Incalci[2]
[1]Institute of Molecular Genetics, CNR, Italy
[2]Institute for Pharmacological Research "Mario Negri", Italy

According to the cancer stem cell (CSC) hypothesis, only a subset of tumor cells, sharing features with normal stem cells, are endowed with tumorigenic potential. The origin of CSCs is elusive; however, evidence has been reported that they can originate form bulk tumor cells through a dedifferentiation process or, as shown in *in vitro* transformed cell lines, during neoplastic transformation of differentiated cells.

To investigate the possible generation of CSCs during propagation of *in vitro* transformed cell lines, we exploited a cellular system derived in our laboratory from telomerase immortalized human fibroblasts, which recapitulates fibroblast neoplastic transformation. To isolate potential CSCs, we used the tumorsphere approach. Growing cells in the absence of serum and in the presence of growth factors, we obtained spheres with a frequency ranging between 2-10%. Sphere cells could be replated for at least six times and showed increased Sox2 expression, suggesting that they are endowed with self-renewal potential and stemness features. However, preliminary *in vivo* tumorigenic assays failed to show an increased tumorigenicity of sphere cells. Moreover, compared to adherently growing cells, sphere cells were characterized by a reduced expression of genes involved in tumorigenesis and stemness, as c-myc, GNL3 and Notch, as well as an increased expression of the tumorsuppressor microRNA miR34a. These observations suggest that tumorsphere formation might not always be an effective method to isolate highly tumorigenic cells and that CSC properties and tumorigenicity could be dissociated features. Experiments are in progress to determine the c-myc down-regulation mechanism and its possible functional meaning.

Biography

Chiara Mondello is Senior Researcher and group leader at the Institute of Molecular Genetics of the National Research Council in Pavia (Italy). Her main interests concern the study of genome instability and cellular transformation in mammalian cells. She has published more than 60 papers in peer-reviewed journals and several chapters in books. She has been the Editor of the book "Multiple pathways in cancer development" (Transwell Research Network).

mondello@igm.cnr.it