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Cancer stem cells in lung cancer: The resident evil!

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Abstract

Lung cancer is a main cause of cancer-related deaths worldwide. Its prevalence is increasing due to the widespread smoking habits and accumulation of atmosphere pollutants. In our laboratory hexavalent chromium [Cr(VI)] was selected to induce human bronchial cells malignant transformation because of its increasing occupational relevance. BEAS-2B cell line was malignantly transformed into the RenG2 system using low density culture in the presence of Cr(VI). Two derivative cell lines (DRenG2 and DDRenG2) were attained following serial rounds of injection in nude mice. Metabolic studies using [^{18}F]fluoro-2-deoxyglucose and nuclear magnetic resonance spectroscopy performed in all the cell lines revealed a more glycolytic phenotype for the derivatives, compatible with a quiescent phenotype. Subsequent karyotype and real time PCR-based characterization identified different cellular sub-populations within each cell line, strengthening the hypothesis on the CSCs presence. The sphere-formation assay, used to search for CSCs presence, revealed the presence of CSCs only in the derivatives, suggesting that a dedifferentiation process featured the formation of CSCs during RenG2 derivation in mice. The involvement of the mice stroma in this process was uncovered by surgical isolation of mouse stromal cells of the subcutaneous compartment and subsequent co-culture with RenG2 cells for 30-60 days (time needed to induce tumors with RenG2), which resulted in the emergence of a CSCs sub-population. A cytokine multiplex array performed in the conditioned medium of the co-cultured cells along with comparative genome hybridization array analysis performed in all the cell lines revealed a panel of potential paracrine orchestrators of this stromal-induced dedifferentiation process.

Biography

Carlos Rodrigues has 27 years old and is a last year PhD student at the University of Coimbra, Portugal. He has finished his graduation in Biology at the same University in 2008. Since the last year of his graduation he has been focusing his research in trying to understand the molecular mechanisms underlying cancer stem cells during lung carcinogenesis as well as their role in the metastatic disease. So far he has already published 14 papers (2 original research paper, 1 review and 11 proceedings) and two additional manuscripts in preparation.