

Seminar series FOR2127 – Selection and adaptation during metastatic cancer progression

Thursday, 17 May 2018
Hörsaal, Biopark I
14.00 h

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“Characterization and therapeutic targeting of cancer stem-like cells in glioblastoma and metastatic tumors”

Like normal tissues, tumors such as glioblastoma or colorectal cancer are structured according to a hierarchy that includes two main components. At the hierarchy's apex there is a (small) subpopulation of 'cancer stem-like cells' (CSCs) able to self-renew, namely to endlessly propagate, and support tumor aberrant histogenesis, regeneration, and dissemination. At the hierarchy's base there is an (ample) subpopulation of cells that, unlike CSCs, have limited self-propagation ability, and tend to abnormally differentiate and die. This model implies that, to cure the tumor, CSCs must be eradicated. This goal is challenging, as CSCs are often inherently resistant to therapies that so far have proven effective against the hierarchical basis of tumor cells, therapies that also include the most innovative agents, targeted at the genetic alterations driving cancer pathogenesis. To improve therapeutic outcomes, it is crucial, on the one hand, to identify and attack the molecular and genetic mechanisms underlying CSC resistance to conventional chemo- and radio-therapy, or to agents targeted at molecular lesions, and, on the other hand, to expose CSC vulnerabilities. During the seminar, the role of tyrosine kinase receptors such as MET and EGFR family members in sustaining the 'CSC phenotype' in glioblastoma and metastatic colorectal cancer, and the preclinical outcomes of their therapeutic targeting, will be discussed. Moreover, recent data on isolation and characterization of CSCs from 'cancers of unknown primary site', that clinically present as disseminated tumors of elusive histological origin, will be presented.

Selected reading:

Luraghi P, Bigatto V, Cipriano E, Reato G, Orzan F, Sassi F, De Bacco F, Isella C, Bellomo SE, Medico E, Comoglio PM, Bertotti A, Trusolino L, Boccaccio C. A Molecularly Annotated Model of Patient-Derived Colon Cancer Stem-Like Cells to Assess Genetic and Nongenetic Mechanisms of Resistance to Anti-EGFR Therapy. *Clin Cancer Res.*, 2018, 24:807-820.

De Bacco F, D'Ambrosio A, Casanova E, Orzan F, Neggia R, Albano R, Verginelli F, Cominelli M, Poliani PL, Luraghi P, Reato G, Pellegatta S, Finocchiaro G, Perera T, Garibaldi E, Gabriele P, Comoglio PM, Boccaccio C. MET inhibition overcomes radiation resistance of glioblastoma stem-like cells. *EMBO Mol Med.*, 2016, 8:550-68.