basal/stem cell-like state by inducing the activation of *de novo* enhancers, which drive the transcriptional activation of oncogenic pathways. MYC-driven epigenetic reprogramming favours the formation and maintenance of TICs endowed with metastatic capacity. Moreover, oncogenic pathways activated by MYC-modulated enhancers are associated with basal-like breast cancer in patients with a poor prognosis.

Conclusion MYC-driven tumour initiation relies on a cell reprogramming process, which is mediated by activation of MYC-dependent oncogenic enhancers, thus establishing a therapeutic rational for treating basal-like breast cancers.

PO-299 *IN VIVO* SHRNA SCREENING TO IDENTIFY QUIESCENCE-RELATED GENES REQUIRED FOR AML GROWTH

[1]G De Conti*, [2]G Melloni, [1]ME Boggio Merlo, [3]M Mazza, [4]UA Cammarata, [1]L Luzi, [1]E Colombo, [1]PG Pelicci. *[1]European Institute of Oncology, Experimental Oncology, Milano, Italy; [2]Harvard Medical School, Center for Biomedical Informatics, Boston, USA; [3]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori IRST, Laboratorio di Bioscienze, Meldola, Italy; [4]San Raffaele Hospital, Istituto San Raffaele Telethon per la Terapia Genica SR-Tiget, Milano, Italy*

10.1136/esmoopen-2018-EACR25.330

Introduction AML is hierarchically organised with at the apex Leukaemia Stem Cells (LSCs), a rare cell population able to initiate and sustain the tumour growth. LSCs share many functional properties with normal Hematopoietic Stem Cells (HSCs) including self-renewal capacity and quiescence. Quiescent LSCs can survive to radiation and chemotherapy acting as a reservoir for leukaemia relapse, the major cause of death for AML patients. Therefore, LSCs quiescence is critical for leukaemia maintenance and few evidences suggest that quiescence regulation in pre-leukemic phase plays a pivotal role for leukemogenic process as well.

Material and methods We analysed the transcriptional deregulations induced by the expression of different leukemic oncogenes in HSCs and we examined the contribution of representative quiescence related genes in AML growth by *in vivo* RNA interference screening.

Results and discussions The transcriptional profile of oncogene-expressing HSCs is enriched in a quiescent stem cell gene signature, compared to normal HSCs. Therefore, we hypothesised that enhancement of the quiescent phenotype in HSCs could be a shared mechanism for leukaemia development and maintenance. The *in vivo* shRNA screening allowed the identification of genes whose silencing in AML blasts was sufficient to significantly decrease *in vitro* self-renewal and delay leukaemia growth *in vivo*.

Conclusion We identified quiescence-related genes, commonly deregulated by leukemic oncogenes at pre-leukemic level, which may offer new therapeutic targets in a wide group of AML patients.

PO-300 UNVEILING AND EXPLOITING CANCER STEM CELL EDITING AND IMMUNOGENICITY FOR PRECISION MEDICINE

[1]M Musella*, [2]C Galassi, [1]G Manic, [2]R De Maria, [1,3]I Vitale, [1,2]A Sistigu. *[1]IRCCS Regina Elena National Cancer Institute, UOSD Cellular Networks Molecular Target Therapies, Rome, Italy; [2]Catholic University 'Sacro Cuore', General Pathology and Physiopathology, Rome, Italy; [3]University of Rome 'Tor Vergata', Biology, Rome, Italy*

10.1136/esmoopen-2018-EACR25.331

Introduction Immunogenic chemotherapy (IC) induces immunogenic cell death (ICD), which, similar to viral infection, leads to a cancer-cell autonomous Type-I-Interferon (IFN-I) signalling. This immunological signature is crucial for effective antitumor responses but may paradoxically promote the emergence of a rare population of cancer stem cells (CSCs) acting as a chemoresistant niche within the tumour and roots for metastasis and relapse. In this study, we have investigated the role of IFN-I during IC in inducing a cancer editing program resulting in the appearance of poor immunogenic CSCs.

Material and methods Human and murine tumour cell lines were treated *in vitro* with ICD-inducers or IFN-I as control and the induction of CSC were analysed by cytofluorometry, quantitative real time (qRT)-PCR, 3D culture and functional assays. Free and vesicle-mediated nucleic acid transfer during ICD has been characterised by co-culture experiments. IC-induced CSC immunogenicity has been studied through cytofluorometry, microfluidic devices and *in vivo* experiments. All experiments have been done in triplicate and statistical significance evaluated by two-tailed Student's *t* test and two-way ANOVA.

Results and discussions The transient/acute induction of IFN-I during ICD is followed by the appearance of a rare population of CSCs. Both free nucleic acids and extracellular vesicles are released during tumour ICD constituting the upstream inducers of IFN-I-mediated reprogramming of neighbouring cells. IC-induced CSCs display epithelial-to-mesenchymal transition traits, multidrug resistance and regenerative properties, and a significant tumorigenic potential when inoculated in immunodeficient and immunocompetent mice. As expected, tumour growth and size are reduced in the presence of an intact immune system. Experiments on microfluidic devices reveal a poor immunogenic potential of CSCs, further confirmed by the expression of immune checkpoint blockers.

Conclusion Our results pinpoint a surprising link between ICD, IFN-I and CSCs. Elucidating the mechanisms of CSC editing together with a deep characterisation of CSC (immune) properties could be crucial to prevent tumour relapse. This could undoubtedly have dramatic implications for the clinical management of cancer in an era of terrific development of precision combined chemo-immune therapy.

Poster Presentation: Cancer Genomics, Epigenetics and Genomic Instability

Genomic Alterations in Cancer

PO-301 DIAGNOSIS OF GLIOMA TUMOURS USING CIRCULATING CELL-FREE DNA

V Palande*, D Raviv-Shay, M Frenkel-Morgenstern. *Bar-Ilan University, Faculty of Medicine, Safed, Israel*

10.1136/esmoopen-2018-EACR25.332

Introduction Gliomas are the most frequent tumours of brain, and they make up about 30% of all brain and central nervous system tumours, and 80% of all malignant brain tumours. Diagnosis of different glioma tumour types and their tumour grade is an essential step to suggest a right treatment for the glioma patients. Existing standard diagnostic technique for glioma tumour includes tissue biopsy, which is a highly invasive and hence a risky technique for the patient's health. 'Liquid biopsy'