VIII CRG ANNUAL SYMPOSIUM
"STEM CELLS, DIFFERENTIATION AND CANCER"

15/16 October 2009, Barcelona (Spain)

Organizers: Miguel Beato, Thomas Graf, Luciano Di Croce, Salvador Aznar-Benitah and Bill Keyes.

The CRG symposia have been highly successful in bringing together some of the best scientists in their field. For the upcoming VIIIth symposium we have merged the fields of stem cell research and differentiation with that of cancer.

Differentiation and cancer have long been considered as being two sides of the same coin, in particular in the case of leukemias. Thus, many leukemias essentially represent differentiation diseases, in which specific oncogenes (often over-expressed or fused transcription factors) cause the proliferation of aberrantly or incompletely differentiated blood cells. Some of the successful therapies revolve around the concept to enable their differentiation, bringing the cells into a resting state, the best example of which is the treatment of PML RAR induced promyelocytic leukemia with retinoic acid. This field has been pioneered by Pier Giuseppe Pellici.
More recently a strong link has also been established between stem cells and cancer. Studies in the 90s by John Dick and colleagues showed that acute myeloid leukemia is a heterogeneous population, consisting of a small fraction of cells with self-renewal potential (the 'cancer stem cells') and the bulk of the leukemic cells that are essentially non-dividing cells. This concept has now been extended to other types of tumors, such a mammary and colon carcinomas) although it appears not to be a universal principle of all cancers.

The question of whether or not a given tumor contains a subset of self renewing cells with tumor initiating potential is not just of academic interest, as it strongly influences the approaches chosen for therapy. If a defined subset of cancer stem cells can be identified, all efforts should be directed at eradicating them; if essentially all cells in a tumor proliferate, the approach must be directed at the bulk of the population.

Interestingly, there are now several studies that establish a connection between stem cells, differentiation and cancer. For example, it has been shown in mouse models by Tariq Enver and others, that certain types of leukemias induced by aberrant transcription factors originate not from stem cells, as it had been originally assumed, but from committed progenitors, which are then directed to acquire self-renewal potential and to exhibit a stem cell specific gene expression signature. In addition, as shown by Robert Weinberg and colleagues, mammary epithelial cells induced to become tumorigenic by undergoing an epithelial to mesenchymal transition acquire stem cells properties. Together, these findings suggest that at least some forms of cancer arise by the reprogramming of differentiated cells under the influence of aberrant transcription factors, and undergo extensive remodelling of their epigenetic machinery. This remodelling may also involve specific microRNAs, as has been shown for a number of tumor types. All of the above mentioned scientists will participate at the conference.

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Additionally, the field of epidermal stem cells (and its links with cancer) will be represented by two leading scientists in the field. Both Fiona Watt and Elaine Fuchs have made seminal contributions to isolate, and characterize epidermal stem cells. They have identified key pathways that control their behaviour during homeostasis and cancer onset and progression. As well, they have studied in recent years how and when epidermal stem cells are specified early during embryonic development, and how they make lineage choices to form the entire epidermal compartment. More specifically, they have described a role for wnt TGFb, Bmp and Notch signalling as essential players in epithelial stem cell differentiation and lineage commitment.

The role of one of the best-characterized oncogenes, Myc, and its contribution to the establishment and maintenance of the cancer phenotype will be discussed by Gerard Evan. Finally, the importance of epigenetic gene programming and reprogramming, telomers, either at specific loci or genome-wide will be illustrated by Wolf Reik, Maria Blasco, and Richard Young.

Thus, this symposium will gather some of the worldwide leaders in the fields of stem cells, differentiation and cancer and promises to become a magnet for the attendance of the scientific community in Spain working in these areas.

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