frontiers in ONCOLOGY

SPECIALTY GRAND CHALLENGE ARTICLE
published: 29 March 2011
doi: 10.3389/fonc.2011.00002

The grand challenges to cellular and molecular oncology

Lorenzo Galluzzi*[1,2,3] *and Guido Kroemer*[1,4,5,6,7]

[1] *INSERM, Villejuif, France*
[2] *Institut Gustave Roussy, Villejuif, France*
[3] *Université Paris-Sud 11, Villejuif, France*
[4] *Metabolomics Platform, Institut Gustave Roussy, Villejuif, France*
[5] *Centre de Recherche des Cordoliers, Paris, France*
[6] *Pôle de Biologie, Hôpital Européen Georges Pompidou, Paris, France*
[7] *Université Paris Descartes, Paris, France*

**Correspondence: kroemer@orange.fr*

In the last decade, our molecular and cellular understanding of cancer has been tremendously ameliorated. It has been demonstrated that, in some cellular settings, microRNAs (miRNAs) can exert *bona fide* oncogenic or oncosuppressive functions (Croce, 2009) and that cancer cells often, if not always, exhibit an extensive metabolic rewiring (Kroemer and Pouyssegur, 2008); the compartment of cancer stem cells has been intensely studied (Visvader and Lindeman, 2008); the concepts of oncogene/non-oncogene addiction (Luo et al., 2009) and of immunogenic cell death (Zitvogel et al., 2010) have been founded; and novel modalities of programmed cell death have been characterized (Vandenabeele et al., 2010), just to mention a few examples. These advances in our fundament knowledge of molecular and cellular cancer biology are rapidly being translated into ever more reliable diagnostic and prognostic biomarkers as well as into a large armamentarium of novel therapeutic tools. Personalized anticancer strategies, which at the end of the 1990s held great expectations, have now turned into a clinically exploitable reality. Moreover, there is now an emerging tendency to conceive tumors as micro-ecosystems that are composed by a heterogeneous population of cancer (stem) cells as well as a plethora of distinct stromal cells, including fibroblasts and endothelial cells, which either promote or limit tumor growth at the metabolic, architectonic, trophic, and immunological levels.

New knowledge generates new questions, and there also remain several old unresolved issues. For instance, do cancer stem cells occupy a physical niche within solid tumors of do they represent a functional compartment only? How can we exploit cancer stem cell biology to increase their sensitivity to therapy? How can we induce the immunogenic demise of tumor cells and hence circumvent their resistance to conventional anticancer regimens? What components of the molecular machinery for necroptosis might be exploited for the generation of novel cytotoxic agents that do not operate via apoptosis? How can we target the tumor-stroma for developing safe and efficient anticancer strategies? Will nanoparticles and other molecular targeting devices progress until clinical applications? These are only some of the great questions that will drive the work of us, as cellular and molecular oncologists, for the next few years. We must concentrate our efforts to reach an ever more precise characterization of the mechanisms that underlie the origin, survival, and therapeutic response of cancer. It can be anticipated that this will lead to the development of new, efficient approaches for the treatment of this dreadful disease.

ACKNOWLEDGMENTS

Lorenzo Galluzzi is financed by Apo-Sys. Guido Kroemer is supported by the Ligue Nationale contre le Cancer (Equipe labellisée), Agence Nationale pour la Recherche (ANR), European Commission (Active p53, Apo-Sys, ChemoRes, ApopTrain), Fondation pour la Recherche Médicale (FRM), Institut National du Cancer (INCa), and Cancéropôle Ile-de-France.

REFERENCES

Croce, C. M. (2009). Causes and consequences of microRNA dysregulation in cancer. *Nat. Rev. Genet.* 10, 704–714.

Kroemer, G., and Pouyssegur, J. (2008). Tumor cell metabolism: cancer's Achilles' heel. *Cancer Cell* 13, 472–482.

Luo, J., Solimini, N. L., and Elledge, S. J. (2009). Principles of cancer therapy: oncogene and non-oncogene addiction. *Cell* 136, 823–837.

Vandenabeele, P., Galluzzi, L., Vanden Berghe, T., and Kroemer, G. (2010). Molecular mechanisms of necroptosis: an ordered cellular explosion. *Nat. Rev. Mol. Cell Biol.* 11, 700–714.

Visvader, J. E., and Lindeman, G. J. (2008). Cancer stem cells in solid tumours: accumulating evidence and unresolved questions. *Nat. Rev. Cancer* 8, 755–768.

Zitvogel, L., Kepp, O., and Kroemer, G. (2010). Decoding cell death signals in inflammation and immunity. *Cell* 140, 798–804.

Received: 18 January 2011; accepted: 18 March 2011; published online: 29 March 2011.
Citation: Galluzzi L and Kroemer G (2011) The grand challenges to cellular and molecular oncology. Front. Oncol. ***1****:2. doi: 10.3389/fonc.2011.00002*
This article was submitted to Frontiers in Molecular and Cellular Oncology, a specialty of Frontiers in Oncology.