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Editorial

Tumor suppression

Cancer affects 1 in 3 adults and 1 in 330 children worldwide. According to the latest update by the International WHO Agency for Research on Cancer http://www.iarc.fr/en/media-centre/pr/2013/pdfs/pr223_E.pdf, there were about 14 million new cases of cancer and 8 million deaths owing to this disease in 2012. Projections suggest that there will be approximately 20 million new cases per year in the not-so-distant year 2025. The most commonly diagnosed cancers worldwide are lung (13.0% of the total), breast (11.9% of the total), and colorectal (9.7% of the total) cancers with deaths from lung, liver and stomach cancer being in the top 3. These statistics are alarming but highlight the need for innovative, multi-disciplinary and joint ventures to battle cancer.

Our understanding of cancer initiation and progression has increased exponentially since the first proto-oncogene, Ras, was identified in 1993. Genetics and epigenetics play a major role in our molecular understanding of the pathogenesis of cancer, as cancer is predominantly a genetic disease. Numerous research groups all over the world, including those of Bert Vogelstein, Robert Weinberg, Douglas Hannahan, Scott Lowe, Tyler Jacks, Tak Mak, Julian Downward, Michael Karin and the late Stanley Korsmeyer to mention a few, have contributed significantly to the advances made in the field. Numerous publications using animal models, in vitro cell culture, genome wide association studies and samples from cancer patients have demonstrated that cancer-causing signaling pathways are complex and influenced by multiple insults. Distinct genes initiate and maintain the cancer phenotype and are the target of therapeutic intervention. Targeted therapy has worked well for some cancers, such as Her2 inhibitors for breast cancer and c-ABL inhibitors for leukemia. However, there is a great need to rethink drug discovery strategies as we move forward, and we are in dire need for a better understanding of pathways regulating the appearance, growth and propagation of cancer cells and how multiple pathways are connected.

This Special Issue attempts to inform and encourage cancer researchers to think about several emerging avenues in cancer signaling involving tumor suppression. The review by Dr. Giancotti on how a cancer cell undergoes dysregulation provides a comprehensive introduction to the topic. Several contributions describe emerging aspects of p53 biology, including novel roles for cytoplasmic p53 (Comel et al.) and p53-mediated regulation of several microRNAs (Li et al.). Tumor-associated microRNAs and their potential in personalized cancer therapy are also discussed in this Special Issue. Updates on numerous tumor suppressor pathways, including PML, RASSF, angiomotins, VHL, ING and NF2/Merlin, are comprehensively described in several reviews. A contribution on pyruvate kinase M2 (PKM2) (Iqbal et al.) emphasizes that cancer can be considered a metabolic disease due to the switch from aerobic metabolism to anaerobic metabolism during growth and metastasis. This review highlights the imperative need to understand the energetic state of tumor cells, so as to design novel therapeutics capable of starving the cell of this energy source and inducing its demise. Lastly, a timely review on autotaxin (Benesch et al.) underscores the importance of the microenvironment of a tumor cell in the complex interplay between stromal and tumor factors. Autotaxin is a secreted enzyme that regulates the production of lysophosphatidate, which is involved in regulating growth and migration of cells, and is a field that warrants attention.

As we learn more about the complex molecular circuitries that suppress tumor growth and progression, extensively reviewed in this Special Issue, we might stand a better chance at finding ways to eradicate cancer through rational drug design. Bert Vogelstein estimated several years ago that over 90% of cancer-causing genes are mutated tumor suppressor genes rather than oncogenes. Thus, understanding the molecular mechanisms involved in tumor suppression will greatly aid in the battle against cancer.

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