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Key Difficulties Associated with Cancer Biology

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Supplement Aims and Scope

This supplement is intended to focus on key difficulties associated with cancer biology. The supplement is intended to address drug resistance, tumor microenvironment and metastasis, although other relevant sub-topics may be included at the discretion of the guest editors.

Clinical Medicine Insights: *Oncology* aims to provide researchers working in this complex, quickly developing field with online, open access to highly relevant scholarly articles by leading international researchers. In a field where the literature is ever-expanding, researchers increasingly need access to up-to-date, high quality scholarly articles on areas of specific contemporary interest. This supplement aims to address this by presenting high-quality articles that allow readers to distinguish the signal from the noise. The editor in chief hopes that through this effort, practitioners and researchers will be aided in finding answers to some of the most complex and pressing issues of our time.

While cancer research has made dramatic progress with advances in technologies and knowledge base, it is accompanied with new challenges, too. For example, resistance to classical cytotoxic chemotherapeutics, to immunotherapies and molecularly targeted therapies is now a major problem that clinicians and researchers are facing. Tumor tissues and their interaction with surrounding tumor microenvironment and communicating factors are found to be working in tumorigenesis with a more important role than people previously expected. In quite a few types of cancers, metastasis, instead of tumor origination or the development of tumorigenic tissues at the primary site, is the lethal factor for prognosis. This supplement would focus on a few of those key challenges we are facing, and try to give a brief solution/method/plan for future studies.

Recent advances of cancer biology are largely related to dramatic development in Next Generation Sequencing (NGS) technologies and fast growing methods in molecularly targeted therapies and immunotherapies. In 2014, Housman *et al.* summarized various mechanisms that could result in drug resistance in cancer (PMID: 25198391), and followed by an interesting discussion about cellular origin of acquired resistance to targeted therapy in lung cancer (PMID: 26937615). These studies shed light on how cancer cells may respond to targeted therapy and facilitate the development of 2nd and even 3rd generation drugs for cancers carrying specific variants. Meanwhile, as tumor-stroma interaction has been studied for quite a while, stromal cells, tumor-infiltrating leukocytes and interactions between them become more and more of interest, especially in their role of re-shaping anti-tumor immunity and responsiveness to immunotherapy, given the fact that immunotherapy is taking an essential role in clinical treatment options for cancer patients, and recent progress was summarized by Turley *et al.* (PMID: 26471778). In addition, tumor metastasis and related therapeutic associations were reviewed by P. Steeg (PMID: 27009393), covering both the molecular targets and tumor microenvironment in metastasis.

The diagnosis and treatment of prostate cancer is rapidly evolving. While early stage prostate cancer (localized or regional at diagnosis) has a pretty high 5-year relative survival rate (>99%) (PMID: 26742998), advanced metastatic

castration-resistant disease is ultimately a lethal one. This thematic issue features the key difficulties associated with cancer biology in the realm of prostate cancer. Boudadi and Antonarakis address the important issue of resistance to currently available novel androgen-targeted signaling agents enzalutamide or abiraterone and potential ways to circumvent such resistance. El-Amm and Aragon-Ching address the use and utility of bone-targeted agents in metastatic prostate cancer, especially as it deals with the bone microenvironment. Lastly, Lohiya and Sonpavde tackle the varying mechanisms of action, resistance and novelty of using chemotherapy not just in the castration-resistant disease but also in early hormone-sensitive disease in the era of the ECOG CHAARTED trial.

In this supplement, we would cover resistance to trastuzumab and strategies to overcome it, immune targeting in triple negative breast cancer, microenvironment in prostate cancer, resistance to novel anti-androgen therapies in castration-resistant prostate cancer (CRPC) treatment, and markers to anti-angiogenic therapies in colorectal cancer. This field is emerging fast and we hope the pioneering works done and published by this supplement will encourage more exciting work to overcome those key challenges in cancer.

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