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Editorial

Precision cancer medicine: where to target?

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The discovery of the first oncogene *Src* in 1976[1] opened up the field of molecular oncology and led to the discovery of oncogenes and anti-oncogenes that are involved in the formation and progression of cancers[2]. Nearly 4 decades of research on the functions and molecular mechanisms of oncogenes and anti-oncogenes and the related cell growth signaling pathways, has led to the understanding that cancer is characterized by uncontrolled cell growth that is regulated by multiple growth factors, growth factor receptors, cytoplasmic growth signal transducers and nuclear transcription factors, which collectively control nucleotides synthesis, DNA replication and cell division. Cancer treatments have been developed to target both the growth regulatory mechanisms as well as the DNA replication/cell division machinery. The traditional chemotherapies mostly target the cell division machinery, including nucleotide metabolism, DNA replication and cell division[3, 4]. While such traditional chemotherapies are effective in killing cancer cells and blocking cancer cell growth, they suffer from the lack of targeting specificity as they are equally toxic to normal dividing cells, which are commonly present in the bone marrow, digestive tract and hair follicles. As a result, they result in severe side-effects such as myelosuppression, mucositis and hair loss. On the other hand, targeted cancer therapies, which are designed to attack the growth regulatory systems, particularly the genetically mutated and misbehaved specific cell growth pathway control molecules, have become increasingly popular in the past two decades. The targeted therapies have been proven to be more effective and less harmful to normal cells than the traditional cytotoxic or cytostatic chemotherapies, because the targeted molecules and their mutations are cancer cell-specific.

The promise of targeted cancer therapy relies on the discovery of key molecular mechanisms that are involved in regulating oncogenesis. Dozens of oncogenes and anti-oncogenes have been identified along the growth signal transduction pathways, from growth factors, receptor tyrosine kinases, cytoplasmic signaling kinases to nuclear transcription factors[5]. Key proteins in other growth-related pathways such as the cell death/survival pathways, protein degradation pathways are also found to play key roles in cancers[6-8]. Recently, immune cells and their regulatory pathways[9, 10], epigenetic modifications[11], and non-coding RNAs[12] were added to the growing list of cancer growth regulatory systems. The category of oncogenes and anti-oncogenes keeps expending. It is the discovery of the growth regulatory oncogenes and anti-oncogenes and the deep understanding of their functions and mechanisms that led to the discovery of a host of new generation anti-cancer drugs, which precisely target these oncogene and anti-oncogene products. Therefore, continuing discovery of genes and their products specifically function in promoting cancer cell growth is the basis of new anti-cancer drug development.

In this special issue of cancer research, we have invited a number of researchers who are actively involved in the discovery of growth regulatory molecules and anti-cancer drug development to write reviews on recent progresses and future directions of cancer drug discovery and cancer treatment, all of which aimed at developing novel cancer medicines to target precisely cancer cells. In this issue, Meng *et al*[13] and Wang *et al*[14] targeted one important family of kinases in cell growth control, the PI3K family, and described new inhibitors targeting distinct members of the PI3K family with more precision. Ge *et al*[15] focused on tumor angiogenesis from a novel aspect of endogenous angiogenesis inhibitors and their therapeutic potentials in cancer treatment. Sun *et al* described the function and dysfunction of one of the key cancer-attacking cells in the immune system, the natural killer cells, in hepatocellular carcinomas and discussed their potential use in NK cell-based cancer immunotherapy[16]. Li *et al*[17] and Le *et al*[18] discussed microRNAs and alternative splicing respectively as potential new diagnostic biomarkers and targets for drug discovery. Finally, Sun *et al*[19] reviewed recent findings in intra-tumor

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heterogeneity of cancer cells and their implications in guiding precision cancer treatment. All of these studies support the new exciting development in cancer medicine in order to tailor effective cancer treatment precisely based on the molecular signatures of cancers in target.

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