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がんトランスレーショナル・リサーチ:新規がん治療開発への挑戦

Cancer translational research: Challenges to the production of a promising new treatment

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Translational research (TR) has been described in various ways such as- "taking research from bench-to bedside;" "bridging basic research and medical innovation;" "translating research into medical practice;" "translating science into better healthcare." Even if there are some differences in the definitions, the end point of translational research is the same: The production of a promising new treatment. Approximately 40 years ago when I started cancer translational research, the existing chemotherapeutic regimens using classical cytotoxic agents had obvious limitations. The production of truly active agents is limited, the therapeutic index is very narrow, and the high inter-individual variability of the drug kinetics makes it difficult to optimize the therapy for each patient. Much efforts had to be focused on the studies how to effectively use the limited number of drugs. Recent decades have yielded unprecedented advances in understanding the biological mechanisms underlying cancer development, progression, and symptomatology, which has led us to a new treatment strategy, precision medicine with truly active target drugs. The cancer treatment has been changed dramatically. Even so, still there are many obstacles in the way to the goal: Only partial inhibition of signaling pathways provided, Severe toxicity in combination, Highly plastic and adaptable proliferation or cell survival signal pathways in cancer, Acquired resistance by means of up-regulation of the partially inhibited pathway, mutation of the target, or activation of alternative pathways. The real complexity of tumor biology including epigenetic mechanisms, secondary genomic events and heterotypic interactions of multiple distinct cell types in the tumors remain the least understood. Mainly focusing on the recent researches, my (our) approximately 40 years of challenges in cancer translational research will be introduced along with describing the current issues and the future plans.