

Targeted Therapies in Cancer: Myth or Reality?

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Volume 610

TARGETED THERAPIES IN CANCER

Edited by Francesco Colotta and Alberto Mantovani

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Francesco Colotta
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Targeted Therapies in Cancer:

Myth or Reality?

 Springer

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Introduction

Cancers share a restricted set of characteristics crucial to the tumor phenotype: proliferation in the absence of external growth stimuli, avoidance of apoptosis and no limits to replication, escape from external growth-suppressive forces and the immune response, an inflammatory micro-environment with new blood vessel formation, and an ability to invade normal tissues. In the last 20 years, the molecular determinants of these behaviors are becoming increasingly well understood. This has changed the current paradigm underlying the drug discovery process intended to identify novel therapies to fight cancer.

In the past most efforts to identify novel therapies to cancer were focused on the empirical observation of natural or chemically synthesized molecules that inhibited cancer cell growth *in vitro* and/or *in vivo*. Most often, the molecular mechanisms underlying the observed anti-cancer activities of empirically discovered anti-cancer agents were discovered afterwards. Cornerstones of currently used chemotherapeutic armamentarium have been discovered according to this “empiricism-based paradigm.”

The “molecular target paradigm” is focused on the molecular determinants of aberrant cancer behavior. Conceptually, this paradigm starts with the identification and molecular characterization of proteins that are mutated or over-expressed in cancer cells, and that are believed to play a key role in cancer cell biology. High throughput screening and modern medicinal chemistry, along with sophisticated techniques like computational chemistry and modeling, lead to rapidly identifying hits and then leads that specifically and potently inhibit the activity of proteins mutated or over-expressed in cancer. Recombinant approaches have also been successfully used to generate molecular-targeted biologicals that specifically hit proteins aberrantly expressed in cancer cells.

The global effort sustained by the scientific community and the pharmaceutical industry to discover new approaches to fight cancer is impressive. Thousands of scientists are devoted to this mission and the global investment is in the order of several billion Euros. The “targetcentric” paradigm in cancer drug discovery is widely accepted and used in the pharmaceutical industry and represents the current standard approach to cancer drug discovery.

In September 2005 an International Meeting on “Targeted Therapies in Cancer: Myth or Reality” was held in Milan. This successful meeting sponsored by

Nerviano Medical Sciences (www.nervianoms.com) was intended as a forum for scientists and clinicians working in cancer drug discovery and therapy to share their reflections and experiences on how the paradigm shift from empiricism to molecular-targeted therapies is contributing to the translation of basic knowledge into new therapies for cancer patients. This book collects the contributions given by scientists and clinicians, from academia and industry, who participated in this meeting.

We hope that this book contributes to the improvement of our approach to cancer drug discovery and helps us find new, more efficacious and better tolerated drugs for cancer patients. It provides an overview of diverse approaches ranging from drug discovery to cellular therapy. Although this change in paradigm has been useful, its entry into the clinical arena was associated with unforeseen problems including the emergence of resistance, unexpected side effects and failures. Time is, therefore, ripe for a critical cultural reflection on the state of the art, prospects and limitations. Ultimately, is targeted therapy in cancer a myth or a reality?

Francesco Colotta
Alberto Mantovani

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