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Bioinformatics in cancer therapeutics—hype or hope?

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Bioinformatics should be viewed broadly as the use of mathematical, statistical, and computational methods for the processing and analysis of biologic data. The genomic revolution would not be possible without the sophisticated statistical algorithms on which DNA sequencing, microarray expression profiling and genomic sequence analysis rest. Although data management and integration are important, data analysis and interpretation are the rate-limiting steps for achieving biological understanding and therapeutic progress. Effective integration of scientific bioinformatics into biology and the training of a new generation of biologists and statistical bioinformaticists will require leadership with a vision of biology as an information science.

Development and use of bioinformatics is essential for the future of cancer therapeutics. Most cancer treatments work for only a subset of patients and this is likely to remain true for many molecularly-targeted drugs. This results in a large proportion of patients receiving ineffective treatments and is a huge financial burden on our health care system. It is essential that we develop accurate tools for delivering the right treatment to the right patient based on biological characterization of each patient's tumor.

Gene-expression profiling of tumors using DNA microarrays is a powerful tool for pharmacogenomic targeting of treatments. A good example is the Oncotype DX™ assay (Genomic Health) recently described for identifying the subset of node-negative estrogen-receptor-positive breast cancer patients who do not require adjuvant chemotherapy.[1] Development of genomic tests that are sufficiently validated for broad clinical application requires the sustained effort of a team that includes clinical investigators, biologic scientists and biostatisticians. Accurate, reproducible, predictive diagnostics rarely result from the unstructured retrospective studies of heterogeneous groups of patients that are commonly deposited in the oncology literature, but never independently validated or broadly applied.[2] With proper focus and support, gene-expression-based diagnostic tests could be developed today to assist patients and physicians with a wide range of difficult decisions regarding the use of currently existing treatments. Development of such tests should be part of a new paradigm for future therapeutics.

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Bioinformatics is also essential for enhancing the discovery of new drugs. Many tumors consist of mixtures of subclones containing different sets of mutated, overexpressed and silenced genes. This heterogeneity makes the process of identifying good molecular targets very challenging. Most overexpressed genes and mutated genes may not represent good molecular targets because resistant subclones are present. The best target is a 'red dot' gene whose mutation occurs early in oncogenesis and dysregulates a key pathway that drives tumor growth in all of the subclones. Examples include mutations in the genes *ABL*, *HER-2*, *KIT*, *EGFR* and probably *BRAF,* in chronic myelogenous leukemia, breast cancer, gastrointestinal stromal tumors, non-small-cell lung cancer and melanoma, respectively. Effective development of therapeutics requires identification of red-dot targets, development of drugs that inhibit the red-dot targets, and diagnostic classification of the pathways driving the growth of each patient's tumor. Development and application of bioinformatics by multidisciplinary teams conducting focused translational research is essential for all steps of this process.

Taking advantage of genomic technologies to develop drugs effectively and target them to the right patients depends on the use of bioinformatics, in its broadest sense. The tools to achieve rapid advances in cancer therapeutics are available today. Rapid progress requires wisdom to establish innovative multidisciplinary approaches to focus our technologies and organize our talents for the delivery of a new generation of truly effective cancer treatments.

Supplementary information, in the form of a reference list, is available on the *Nature Clinical Practice Oncology* website.

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Competing interests
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