Editorial Comment

Morphoproteomics: A Novel Approach to Identify Potential Therapeutic Targets in Cancer Patients

Dongfeng Tan

Department of Pathology and Laboratory Medicine, Unit 85, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, USA

Received 18 October 2007; Accepted 22 October 2007; Available online 1 January 2008

Studies in early detection, risk assessment, and genetic and proteomic profiling have been conducted to identify new opportunities in prostate cancer detection and therapy [1]. The discovery of new targets and the application of targeted therapies are beginning to shape our understanding of the complex pathways that operate in this disease, leading to the development of pathogenesis-based therapies [2].

It has been suggested that prostate cancer, like many other solid tumors, is a group of heterogeneous clinical disorders that share some molecular and cellular characteristics but have variable clinical behaviors and prognoses. The question is whether more sophisticated measures than histopathologic analysis alone can be used to understand the heterogeneity that leads to these diverse clinical outcomes and to identify high-risk types that are suitable for management of cancer patients [3-5].

A study authored by Brown R et al and published in the current issue of the International Journal of Clinical and Experimental Pathology has taken a novel approach, morphoproteomics, to assessing potential therapeutic targets for patients with prostate cancer [6]. Although the principle is straightforward, the philosophy is especially meaningful. In brief, morphoproteomics combines the disciplines of histopathology, molecular biology, and protein chemistry to paint a portrait of the protein circuitry in diseased cells to uncover molecular targets amenable to specific intervention, thereby allowing therapy to be customized for individual patients. Preclinical studies have implicated the mammalian target of rapamycin (mTOR) pathway in cancer growth and progression [7]. Recently, Brown and his colleagues examined p-mTOR (Ser 2448) and p-p70S6K (Thr 389) expression in a well-defined cohort of prostate cancer [6]. This study is different from traditional immunohistochemical analysis; it combines the application of phosphor-specific probes directed against putative sites of activation (phosphorylation) on protein analytes and the evaluation of their cellular compartmentalization. Therefore, the conclusion of this study demonstrates the potential clinical utility of personalized medicine. In fact, this unique approach of using morphoproteomics to assess human cancer cells has recently proven its fidelity in other malignancies, including pediatric tumors, brain tumors, and mesenchymal tumors [8-10].

Although substantial work has been performed in the field of proteomic profiling in prostate cancer, routine clinical applications of these methods are not yet in place. Many unanswered questions remain, and new avenues are open for the application of these technologies in prostate cancer. Early detection and prediction of response to targeted therapies may benefit from the power of global gene and protein expression evaluations in prostate cancer patients and individuals at risk. These approaches hold substantial promise for clinical impact in prostate cancer [3, 4]. In the near future, one will not be surprised to see the possible
clinical application of morphoproteomics in malignant cells in the context of currently available pharmaceutical agents and opportunities for combinatorial approaches that involve one or more small molecule inhibitors and single-agent chemotherapeutic agents with relatively low toxicity profiles.

Please address all correspondences to Dongfeng Tan, MD, Department of Pathology and Laboratory Medicine, Unit 85, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030. Tel: 713-745-4977; Fax: 713-745-1105, Email: dtan@mdanderson.org

References