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Status quo and prospects of the translational research on lung cancer in China

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To shed light on the development and prospects of lung cancer translational research in China, a questionnaire survey has been designed and distributed via a domestic medical and life science website-DXY (http://www.dxy.cn/), including the concept of translational medicine, EGFR mutations in lung cancer, EML4-ALK fusion gene, IPASS study, OPTIMAL study, lung cancer GWAS, prospects and recommendations and other contents. DXY is the largest online academic portal for five million Chinese physicians and life science professionals, with average daily page views of 1.8 millions. It was established in 2000, and now has over 2.6 million registered members. DXY features >100 columns to facilitate communication, information sharing and collaboration of medical professionals within practically all sub-specialties of clinical medicine, basic medical research, life sciences, and pharmaceutical sciences. The specialties and titles of the 291 clinicians who responded to the survey are depicted in *Figure 1*.

Translational medicine is a new concept in the international medical community highlighted by both medical professionals and the media (1,2). The new concept, however, is composed of existing contents, which are generated at the very beginning of medicine. As early as the Han Dynasty in China two thousand years ago, the famous doctor Hua Tuo had extracted powder for anesthesia from the plant Ephedra and applied it in clinical treatment. In 1992, the concept of "bench to bedside" was first raised in the journal *Science* (3), and translational research was first mentioned in 1994. In 1996, *Lancet* used "translational medicine" as a new term for the first time (4). In 2003, then-NIH Director Elias A. Zerhouni made it clear (5) at the NIH Roadmap (NIH Roadmap) that the core of translational medicine was to quickly and effectively convert medical and/or biology preclinical into theories, techniques, methods and drugs available clinical practice, i.e. to set up a fast track from bench to bedside (B2B). The survey results showed that 96 (33%) did not know anything about the concept of translational medicine, while only 22 (7%) had known three years ago, with the majority having learned the idea in the near three years. Overall, 94 (32%) learned the concept through the DXY website and others through academic conferences (24%), peers (10%) and journals (12%).

The development and application of molecular targeted therapy agents is of epoch-making significance in the treatment of non-small cell lung cancer. The continuous research advancement from the discovery of EGFR mutations to the clinical application of TKI and in turn to the study of the mechanism in TKI acquired resistance has constituted a cyclying pattern back and forth between the clinical and basic medicine field, which serves as a good interpretation of B2B mode. Although it has been more than 20 years since the discovery of EGFR mutations, EGFR-TKI has not been clinically applied until 2001, a gap of more than 10 years between the discovery of mutations to the application of targeted drugs. With the development of pharmacogenetics, proteomics and other preclinical subjects, the time to application will be sharply reduced. The lung cancer-promoting EML4-ALK fusion genes were first found (6) in animals in 2007, followed by the research of ALK-inhibitor Crizotinib, of which the clinical trial came to success in this year (7). It was about three years from the revelation of ALK fusion genes to the trial stage. However, more than 50% participants did not know the translational research about the above lung cancer targeted therapy, shows this survey.

The IPASS study, a clinical trial led by Chinese scholars that clearly demonstrated the role of EGFR-TKI in the first-line individualized therapy for NSCLC patients with EGFR mutations (8), suggested better efficacy and longer progression-free survival (PFS) than chemotherapy in patients with EGFR mutations. As shown in the study, patients with

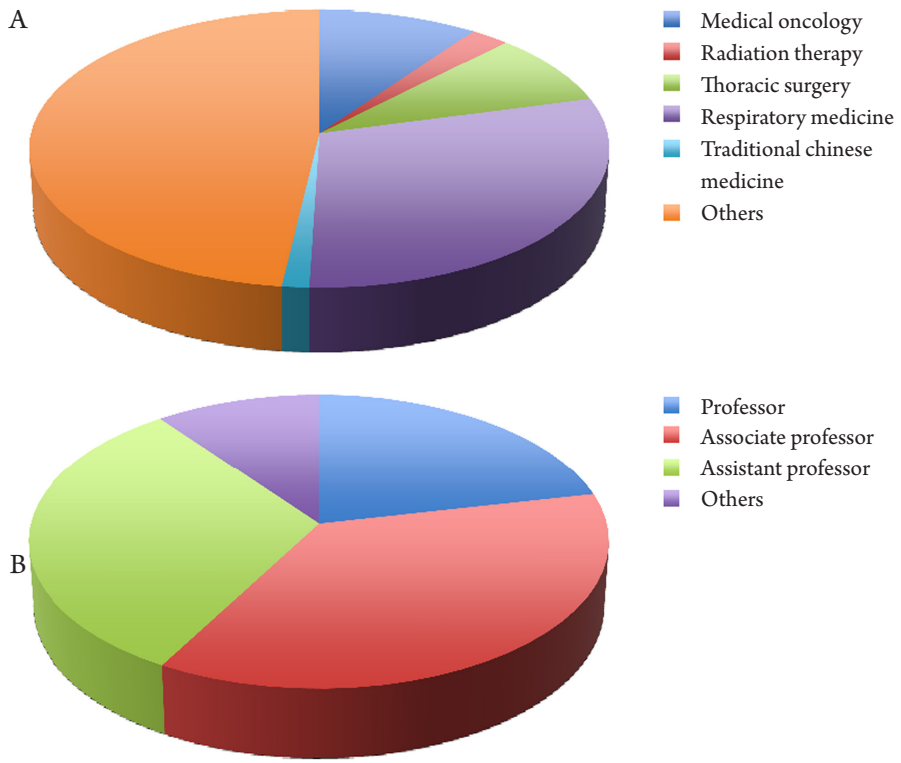

Figure 1 The specialties (A) and titles (B) of the 291 clinicians who responded to the survey.

EGFR mutations would have better outcomes than wild-type EGFR patients regardless of medication, which also suggested that genetic characteristics were the basis for individualized treatment planning. The OPTIMAL study, another Chinese-led research (9), demonstrated the fundamental role of erlotinib in the first-line individualized treatment for advanced NSCLC patients with EGFR mutations in the Chinese population. Similarly, more than 50% participants did not know the two renowned clinical trials on lung cancer therapy.

Genome-wide association study (GWAS) is used to analyze the association of common genetic variants (single nucleotide polymorphisms and copy number) within the whole genome of common genetic variants, providing an overall profile of the disease in a single analysis, which is suitable for research into complex diseases. Shen Hongbing and his team compared the genomes of more than 8,000 lung cancer patients and more than 9,000 healthy candidates, and identified 6 risk loci for lung cancer using GWAS (10). Developed in recent years, GWAS has been widely applied in the research of susceptibility genes associated with cancer, hypertension, diabetes and other complex diseases. As shown in the results of this survey, 60% of respondents believed that the lung cancer GWAS was a powerful tool for identifying susceptibility genes, though there was still a long way to go as to accurate location and functional studies of the relevant genes or loci as well as translational research such as development of the targeted agents.

Translational medicine is also underway in China. A number of universities, research institutions, hospitals and biopharmaceutical companies have conducted cooperations on translational research, and specialized translational medical centers have been established, such as Biomedical Research Institute, Fudan University; Central South University Xiangya Translational Medical Research Center; Health Sciences Center jointly formed by Shanghai Institute of Life Sciences and Shanghai Jiao Tong University School of Medicine; and Beijing Union Medical College Hospital Translational Medical Center. More and more studies have shown significant genotype differences between races among lung cancer patients. Chinese investigators have also conducted population-based studies and achieved positive results in this regard. Nevertheless, in view of the gap between the level of Chinese translational medical research and that of European and American ones, improvement is necessary in the following aspects: (I) Further popularizing the concept of translational medicine by establishing an exchange and communication platform for both preclinical and clinical institutions using the rich clinical resources in China; (II) Developing plans for translational medical research centers and participating more international multicenter lung cancer studies; (III) Establishing relevant academic organizations, such as the Translational Medicine

Society; (IV) Developing professional web sites, either a translational medicine site or a comprehensive portal, so as to promote the exchange and dissemination of translational medicine; and (V) Publishing translational medicine journals: from 2003 to 2009, eight journals in this regard have been published, such as the Journal of Translational Medicine in 2003, and the Science Translational Medicine founded by American Association for the Advancement of Science (AAAS) in September 2009. In March 2012, the *Translational Lung Cancer Research* (TLCR) journal was founded, with the hope to provide a favorable academic platform for the development of translational research on lung cancer.

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