Commentary

Translational significance of multi-dimensional omics

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Kadara H, Choi M, Zhang J, *et al.* Whole-exome sequencing and immune profiling of early-stage lung adenocarcinoma with fully annotated clinical follow-up. Ann Oncol 2016. [Epub ahead of print].

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So far, the surgery, radiotherapy, chemotherapy, targeted therapy and biological therapy have been the five major fields for cancer therapy. These enormous developments, especially tyrosine kinase inhibitors (TKIs) and immune checkpoint inhibitors, are inseparable from the support of big data. On a macro level, several large-scale public database projects, such as The Cancer Genome Atlas (TCGA), International Cancer Genome Consortium (ICGC), Gene Expression Omnibus (GEO) and Surveillance Epidemiology and End Results (SEER), have generated an overwhelming amount of cancer genomics data and epidemiological information (1-4). At the individual level, liquid biopsy, next generation sequencing and radiomics make individual medicine more accurately. At the cellular level, single-cell sequencing, diverse non-coding RNA and exosomes have become research focuses.

Although lung cancer incidence rates have begun declining since 2000, it is still the leading cause of cancer-related mortality worldwide in the last ten years for both sex (5). Lung adenocarcinoma (LUAD) and lung squamous cell carcinoma (LUSC) account for the major part of pulmonary cancer. Recent advances in the development of immunotherapy and target therapy against LUAD contrast sharply with the minor progress in LUSC.

These two studies performed whole-exome sequencing (WES) and comprehensive immune profiling of a unique set of LUAD and LUSC samples to further understand the clinically relevant prognostic markers (6,7). The authors concluded that diverse gene mutation may impact the immune marker expression and clinical outcome. In terms of LUAD, TP53 mutation was associated with elevated PD-L1 expression, on the contrary PIK3CA mutation exhibited markedly down-regulated PD-L1 expression. In the aspects of LUSC, ADCY8 and PIK3CA mutations were associated with markedly decreased tumoral PD-L1 expression. These interesting results revealed an unknown correlation between genome alteration and tumoral immune modulation.

Predictive biomarkers for immune checkpoint inhibitors have been hot topics recently. How to choose the patients who can benefit from immunotherapy is an urgent problem to be solved. Recently, Gibney *et al.* (8) summarized seven reliable predictive markers, including PD-L1 expression, tumor-infiltrating lymphocytes, T-cell receptor clonality, mutational or neoantigen burden, peripheral blood markers and immune gene signatures. Currently, PD-L1 expression is clinically feasible biomarker. The correlation between molecular mutation and PD-L1 expression can provide an alternative selection for immunotherapy. But it remains to be further investigated.

However, there are several limitations to this study, including the lack of clinical information and inadequate data mining results. In addition, the unclear baseline characteristics of subgroup patients affected the authenticity for genome markers' predictive value for prognosis. Of note, the major limitation of big data studies is that there

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is insufficient clinically translational significance. TCGA have been generated an overwhelming amount of cancer genomics data from multiple different technical platforms, including LUAD and LUSC. WES data has been further investigated by combine survival information and several immune markers in the current studies, which did not fully transform back to clinical issue. Further gene ontology and pathway enrichment analysis can be investigated.

In the era of big data supported scientific research, we need to insist on the path that initiated from clinical issues and back to clinic.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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