Key Summary of Published Article

OncoKB: A Precision Oncology Knowledge Base

Background

- Specific genetic information about tumors can help oncologists match patients to targeted cancer therapies; thus, sequencing tumor DNA is becoming part of routine oncology care.
- However, determining the clinical implications of gene variants in tumors can be difficult. One reason for this difficulty is the lack of a comprehensive and reliable database that is integrated into clinical care.
- **Objective:** Clinical and research fellows, including faculty members at Memorial Sloan Kettering Cancer Center and scientists from Quest Diagnostics, developed OncoKB, a database of oncogenic effects and treatment implications of tumor gene variants.

Methods

- Four levels of evidence for biomarker utility were used to classify variants. These levels were based on standard FDA-approved treatments for the indication, FDA-approved treatments for another indication, NCCN guidelines, and/or results from preclinical and active clinical investigations.
- The following data were captured for tumor gene variants and categorized according to tumor type:
  - Biological relevance and effect
  - Prevalence
  - Prognostic information
  - Treatment-related information
  - Clinical trials
- A classification system was developed based on the level of evidence for clinical utility; the system included 4 levels related to drug response, 3 levels related to drug resistance, and 1 category to capture variants that have been biologically characterized but are not therapeutically actionable.
- Experts periodically inspect and update the information contained in OncoKB.

Results

- More than 3,000 unique variants in 418 genes implicated in cancer have been captured in OncoKB:
  - 109 variants in 17 genes associated with responses to standard and approved therapies
  - 77 variants in 26 genes with emerging investigational evidence of drug sensitivity
  - 3,098 variants in 357 genes that are biologically characterized but not therapeutically actionable

Conclusions

- OncoKB provides information about cancer-related variants that can help inform treatment decisions.
- The information contained in OncoKB is used for Memorial Sloan Kettering clinical sequencing reports and Quest Diagnostics OncoVantage™ reports. It is publicly available at oncokb.org and via the cBioPortal for Cancer Genomics.

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