See Article page 1078.

Commentary: Filling up my truck from an oil tanker: Can big ‘omic’ data influence our clinical decisions?

R. Taylor Ripley, MD

R. Taylor Ripley, MD

CENTRAL MESSAGE

Severson and colleagues write an outstanding review with historical context for the complex molecular techniques for an integrated analysis of mesothelioma tumors by Hmeljak and colleagues.

Recently, a patient presented with a pleural effusion and a computed tomography-guided biopsy that revealed well-differentiated papillary mesothelioma. Doubting the diagnosis, I performed a video-assisted thoracoscopic surgery biopsy and obtained tissue from 3 independent areas of the chest. All 3 biopsies revealed well-differentiated papillary mesothelioma. The patient underwent an extended pleurectomy and decortication and the final pathology report read, “biphasic mesothelioma with both epithelioid and sarcomatoid components. The sarcomatoid component also shows features of desmoplastic mesothelioma. The epithelioid component shows focal superficial papillary configuration.” The pathology was essentially all subtypes of malignant pleural mesothelioma (MPM). Could ‘omics’ have clarified this diagnosis before resection?

Severson and colleagues¹ review The Cancer Genome Atlas study by Hmeljak and colleagues.² They report 74 MPM tumors that were characterized by a genomic, epigenomic, and transcriptomic integrated analysis.¹ To help understand the molecular findings, the authors provide a historical context to the development of these techniques. This article is an outstanding summary for readers who are not scientists.

Hmeljak and colleagues² noted the loss of regions or alterations in tumor suppressor genes (TSGs) such as *CDKN2A*, *NF2*, *BAP1*, *TP53*, *LATS2*, and *SETD2*. Additionally, with the use of clustering algorithms, they identified 4 groups of MPM. Severson and colleagues¹ compared these findings to several other noteworthy

publications that have surprisingly similar findings. For example, when Bueno and colleagues³ performed genomic analysis of 216 MPM tumors, they noted copy number loss in many of the same TSGs. They also found 4 different molecular subtypes based on RNA sequencing data. Significant overlap of the molecular subtypes occurred compared with histology. Blum and colleagues⁴ describe this overlap as histo-molecular gradient, which highlights that these histologies are not completely distinct entities. As the molecular techniques and software for integration have advanced, 2 consistent themes have emerged with MPM: First, loss of TSGs is the most frequent molecular event and, second, clusters of MPM tumors are not completely distinct.

Can we apply this ‘omic’ data to clinical decisions? As the cost decreases and the technology is refined, molecular techniques should assist if not supplant histology for diagnosis. Furthermore, Bueno and colleagues³ generated a ratio of *CLDN15/VIM* genes score from their analysis that discriminated between the different clusters that should further simplify diagnostics. However, sampling errors may be as likely with molecular diagnostics as with histology. Next, prognosis may improve by assigning clusters to help counsel our patients. Lastly, will these techniques help with treatment? For MPM, mutations tend to be

From the Division of General Thoracic Surgery, The Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, Tex.

Disclosures: Author has nothing to disclose with regard to commercial support.

Received for publication March 13, 2020; revisions received March 13, 2020; accepted for publication March 13, 2020; available ahead of print March 31, 2020.

Address for reprints: R. Taylor Ripley, MD, Division of General Thoracic Surgery, Department of Surgery, Baylor College of Medicine, Houston, TX 77030 (E-mail: R.Taylor.Ripley@bcm.edu).

J Thorac Cardiovasc Surg 2020;160:1086-7

0022-5223/\$36.00

Copyright © 2020 by The American Association for Thoracic Surgery

<https://doi.org/10.1016/j.jtcvs.2020.03.056>

loss of TSG. Unfortunately, loss of TSGs is not targetable—unlike driver mutations. Although the molecular landscape of MPM has emerged rapidly over the past few years, based on these analyses advancements in treatment are lacking. Further work may require targeting microRNA, epigenetics, or cellular energetics to advance treatment for patients with MPM. Ultimately, would ‘omics’ have helped our patient? I doubt it. Nevertheless, the authors of these studies provide invaluable information to help move our field forward.

References

1. Severson DT, De Rienzo A, Bueno R. Mesothelioma in the age of “omics”: before and after the TCGA. *J Thorac Cardiovasc Surg.* 2020;160:1078-83.e2.
2. Hmeljak J, Sanchez-Vega F, Hoadley KA, Shih J, Stewart C, Heiman D, et al. Integrative molecular characterization of malignant pleural mesothelioma. *Cancer Discov.* 2018;8:1548-65.
3. Bueno R, Stawiski EW, Goldstein LD, Durinck S, De Rienzo A, Modrusan Z, et al. Comprehensive genomic analysis of malignant pleural mesothelioma identifies recurrent mutations, gene fusions and splicing alterations. *Nat Genet.* 2016;48:407-16.
4. Blum Y, Meiller C, Quetel L, Elarouci N, Ayadi M, Tashtanbaeva D, et al. Dissecting heterogeneity in malignant pleural mesothelioma through histo-molecular gradients for clinical applications. *Nat Commun.* 2019;10:1333.