HOW ARE GENOMICS TRANSFORMING THE FUTURE OF ONCOLOGY?

Precision oncology, which defines cancers by their underlying genomic alterations, is revolutionizing the diagnosis and management of cancer.[1-5]

Fighting cancer by finding its fingerprint

- Oncology is evolving from thinking about cancer according to site of origin to thinking about cancer according to tumor genomics[1-4]

One of the stated goals of precision oncology is to optimize and tailor each patient's treatment approach based on the genomic profile of the patient's cancer.[2-6]

Precision oncology is advancing rapidly[2,4]

- Understanding a patient's genomic drivers can help determine a more tailored approach to cancer care, which may potentially prevent cycles of trial and error and associated adverse physical and financial impact[2,3,6]
- As cancer biology advances, both the number and rate of discovery of actionable genomic alterations continue to rise[2,5,7]

While treatments are still being developed, it is estimated that over 50% of patients may have an actionable alteration[5,8-10,a]

- Individual genomic alterations may be rare; however, alterations in totality are found in a significant percentage of patients with cancer[5,8-10,a]
- Targeting genomic alterations may lead to better outcomes for patients with cancer[1-8]

FISH, fluorescence in situ hybridization; IHC, immunohistochemistry; NGS, next-generation sequencing; RT-PCR, reverse transcription-polymerase chain reaction.

[a]Large retrospective series have documented that 80% to 90% of patients tested will have potentially actionable genomic alterations.[5] A genomic alteration is typically defined as actionable when there is a potential therapeutic target that will mitigate the oncogenic consequences of the disrupted pathway, though across clinical studies, the definition of actionable can vary substantially.[5,8]

Investigators saw a 7X increase in the number of people estimated to benefit from precision oncology over 12 years[11,a]

Significant improvements were seen in ORR, OS, PFS, and QOL for patients with certain well-characterized molecular alterations with available targeted therapies compared with conventional chemotherapies[1,8,10-14]

The data-driven difference

Significantly increased PFS[12]

53% Risk of progression[12,b]

$0 Increase in health care costs per PFS week[12]

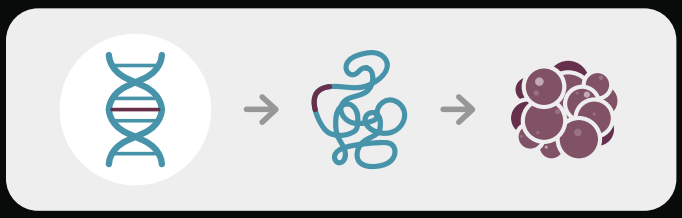
[a]From 2006-2018.

[b]When adjusted for age, sex, histologic diagnosis, and number of previous lines of treatment.[12]

Point mutations and pathogenic gene fusions are among the most common genomic alterations driving cancer[13]

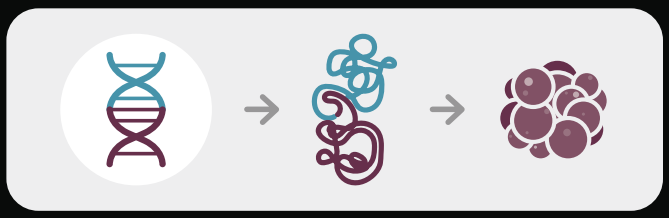
Point mutations

(eg, *KRAS*, *BRAF*, and *EGFR*) are changes in DNA base pair(s)[7,15]



Pathogenic gene fusions

(eg, *ALK*, *NTRK*, *ROS1*, *MET*, and *NRG1*) typically occur when 2 different genes join to form an abnormal hybrid gene[7,16,17]



What difference can targeting pathogenic gene fusions make for your patients?
Learn more at **FindTheFusions.com**

NRG1, neuregulin 1; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; QOL, quality of life.

References: 1. Adashek JJ, Subbiah V, Kurzrock R. From tissue-agnostic to N-of-one therapies: (R)evolution of the precision paradigm. *Trends Cancer*. 2021;7(1):15-28. doi:10.1016/j.trecan.2020.08.009 **2.** Personalized Medicine Coalition. *The Personalized Medicine Report 2020: Opportunity, Challenges, and the Future*. Accessed May 2, 2023. https://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PMC_The_Personalized_Medicine_Report_Opportunity_Challenges_and_the_Future.pdf **3.** Rodriguez-Rodriguez L, Hirshfield KM, Ganesan S. Preface: introduction to precision medicine oncology. In: Rodriguez-Rodriguez L, ed. *Precision Medicine Oncology: A Primer*. Rutgers University Press; 2020:ix-xii. **4.** El-Deiry WS, Goldberg RM, Lenz H-J, et al. The current state of molecular testing in the treatment of patients with solid tumors, 2019. *CA Cancer J Clin*. 2019;69(4):305-343. doi:10.3322/caac.21560 **5.** Schwartzberg L, Kim ES, Liu D, Schrag D. Precision oncology: who, how, what, when, and when not? *Am Soc Clin Oncol Educ Book*. 2017;37:160-169. doi:10.1200/EDBK_174176 **6.** Lassen UN, Makaroff LE, Stenzinger A, et al. Precision oncology: a clinical and patient perspective. *Future Oncol*. 2021;17(30):3995-4009. doi:10.2217/fon-2021-0688 **7.** Malone ER, Oliva M, Sabatini PJB, Stockley TL, Siu LL. Molecular profiling for precision cancer therapies. *Genome Med*. 2020;12(1):8. doi:10.1186/s13073-019-0703-1 **8.** Kris MG, Johnson BE, Berry LD, et al. Using multiplexed assays of oncogenic drivers in lung cancers to select targeted drugs. *JAMA*. 2014;311(19):1998-2006. doi:10.1001/jama.2014.3741 **9.** Priestley P, Baber J, Lolkema MP, et al. Pan-cancer whole-genome analyses of metastatic solid tumours. *Nature*. 2019;575(7781):210-216. doi:10.1038/s41586-019-1689-y **10.** Zhao S, Zhang Z, Zhan J, et al. Utility of comprehensive genomic profiling in directing treatment and improving patient outcomes in advanced non-small cell lung cancer. *BMC Med*. 2021;19(1):223. doi:10.1186/s12916-021-02089-z **11.** Marquart J, Chen EY, Prasad V. Estimation of the percentage of US patients with cancer who benefit from genome-driven oncology. *JAMA Oncol*. 2018;4(8):1093-1098. doi:10.1001/jamaoncol.2018.1660 **12.** Haslem DS, Van Norman SB, Fulde G, et al. A retrospective analysis of precision medicine outcomes in patients with advanced cancer reveals improved progression-free survival without increased health care costs. *J Oncol Pract*. 2017;13(2):e108-e119. doi:10.1200/JOP.2016.011486 **13.** Zhang R, Dong L, Yu J. Concomitant pathogenic mutations and fusions of driver oncogenes in tumors. *Front Oncol*. 2021;10:544579. doi:10.3389/fonc.2020.544579 **14.** Shin DH, Lee D, Hong DW, et al. Oncogenic function and clinical implications of *SLC3A2-NRG1* fusion in invasive mucinous adenocarcinoma of the lung. *Oncotarget*. 2016;7(43):69450-69465. doi:10.18632/oncotarget.11913 **15.** Gunter C. Point mutation. National Human Genome Research Institute. Updated February 3, 2023. Accessed March 28, 2023. https://www.genome.gov/genetics-glossary/Point-Mutation **16.** Drilon A, Duruisseaux M, Han J-Y, et al. Clinicopathologic features and response to therapy of *NRG1* fusion–driven lung cancers: the eNRGy1 Global Multicenter Registry. *J Clin Oncol*. 2021;39(25):2791-2802. doi:10.1200/JCO.20.03307 **17.** Latysheva NS, Babu MM. Discovering and understanding oncogenic gene fusions through data intensive computational approaches. *Nucleic Acids Res*. 2016;44(10):4487-4503. doi:10.1093/nar/gkw282

Merus closing in on cancer