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Bose and colleagues functionally characterized 13 somatic HER2 mutations identified by genome sequencing in breast cancers lacking HER2 gene amplification. Protein structure analysis showed that these mutations largely clustered in either the HER2 tyrosine kinase or extracellular domain. Many of these were gain-of-function mutations that enhanced HER2 kinase activity and downstream signaling, promoted anchorage-independent growth, and accelerated tumor formation, suggesting that HER2 mutations may be driver events in breast cancer. Although several mutations conferred resistance to lapatinib, all mutations were sensitive to the irreversible HER2 kinase inhibitor neratinib. These findings suggest that patients with HER2 mutation–positive breast cancer may benefit from HER2-targeted therapies. For details, please see the article by Bose and colleagues on page 224.

For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org. Online-only News stories include the following:

- Ibrutinib Impresses in Early Trials
- NCAB Gains New Members
- EMA Boosts Transparency for Trials
- Cancer Screening Participation Shows Some Dips
- Proton Therapy Appears to Be Less Cost-Effective
- Study Reveals Global Shifts in Causes of Death

ON THE COVER

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