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PREDICTIVE BIOMARKERS AND PERSONALIZED MEDICINE
ABOUT THE COVER

This image is taken from a bone metastasis in a patient with stage IV relapsed invasive CDH1 mutated lobular carcinoma of the breast. The tumor was negative for \textit{ERBB2 (HER2)} amplification (FISH). The targeted next generation sequencing assay used in this study found an \textit{ERBB2-GRB7} putative gene fusion that has not been previously reported. The fusion retains the kinase domain of \textit{ERBB2} (uniprot.org) which suggests that it could result in \textit{ERBB2} activation. The 17q12-21 amplicon which includes both \textit{ERBB2} and \textit{GRB7} is frequently amplified in breast cancer and preclinical studies suggest that it may be a recombination hotspot. An expression screening study has reported that \textit{GRB7} can function as an \textit{ERBB2}-dependent oncogene. \textit{GRB7} encodes an adaptor protein that interacts with \textit{ERBB2} and has been shown in a preclinical study to enhance its transformative capacity and increase \textit{ERBB2} phosphorylation in fibroblasts. For details, see the article by Ross and colleagues on page 2668 of this issue.

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