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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 ERBB2 (HER2) amplification (FISH). The targeted next generation sequencing assay used in this study found an ERBB2-GRB7 putative gene fusion that has not been previously reported. The fusion retains the kinase domain of ERBB2 (uniprot.org) which suggests that it could result in ERBB2 activation. The 17q12-21 amplicon which includes both ERBB2 and 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 GRB7 can function as an ERBB2-dependent oncogene. GRB7 encodes an adaptor protein that interacts with ERBB2 and has been shown in a preclinical study to enhance its transformative capacity and increase ERBB2 phosphorylation in fibroblasts. For details, see the article by Ross and colleagues on page 2668 of this issue.