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### RESEARCH BRIEF

Evolutionary Pathways in BRCA1-Associated Breast Tumors .... 503  

**Précis:** BRCA1 loss of heterozygosity is frequently preceded by PTEN loss or TP53 mutation in BRCA1-mutant breast cancers.

### RESEARCH ARTICLES

Modulation of Activation-Loop Phosphorylation by JAK Inhibitors Is Binding Mode Dependent ... 512  

**Précis:** Type II JAK inhibition prevents the sustained activation loop phosphorylation observed after treatment with type I ATP-competitive JAK inhibitors.
Forced Mitotic Entry of S-Phase Cells as a Therapeutic Strategy Induced by Inhibition of WEE1 524

Précis: In combination with chemotherapy, WEE1 inhibitors can force cancer cells with incompletely replicated DNA into mitosis, leading to abnormal mitoses and cell death.

miR-23a Promotes the Transition from Indolent to Invasive Colorectal Cancer 540

Précis: Upregulation of miR-23a in the early stages of colorectal cancer stimulates cell migration and invasion.

Gene Signatures Associated with Mouse Postnatal Hindbrain Neural Stem Cells and Medulloblastoma Cancer Stem Cells Identify Novel Molecular Mediators and Predict Human Medulloblastoma Molecular Classification 554

Précis: Murine medulloblastoma cancer stem cells that recapitulate distinct human molecular medulloblastoma subtypes can be valuable preclinical models.

Martins and colleagues determined the order of BRCA1 LOH, PTEN loss, and TP53 mutation in single cells from breast tumors with germline BRCA1 mutations. Surprisingly, BRCA1 LOH was rarely the initiating event, and wild-type BRCA1 expression was not lost in every cell within a tumor. Instead, PTEN loss occurred first in the majority of cases, particularly in basal-like tumors, and TP53 mutation was the initiating event in most luminal tumors. These findings provide insight into the evolution of BRCA1-mutant breast cancers and suggest that BRCA1 loss is not a rate-limiting step in breast tumorigenesis. For details, please see the article by Martins and colleagues on page 503.