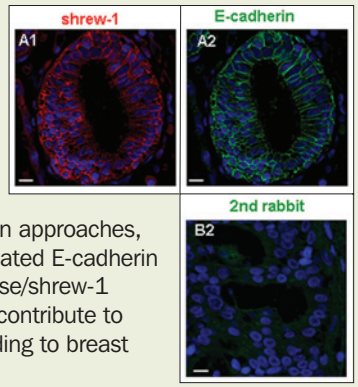
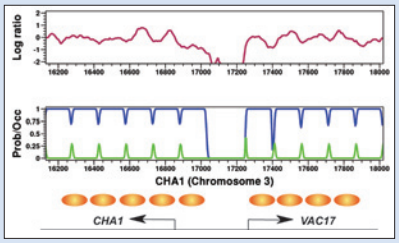
E-cadherin Surface Levels in EGF-stimulated Cells Depend on Adherens Junction Protein Shrew-1
Julia Christina Gross, Alexander Schreiner, Knut Engels, and Anna Starzinski-Powitz



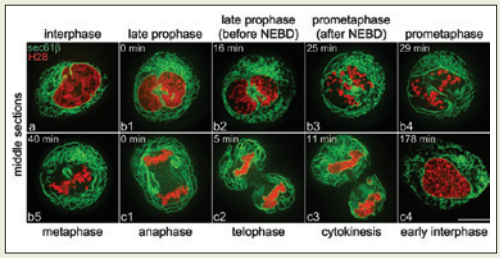
Loss of the tumor suppressor E-cadherin has been proposed to facilitate metastatic spread of ductal breast cancers by inducing epithelial–mesenchymal transition. In a significant number of breast cancers tyrosine kinase growth factor receptors (RTKs), such as HER2 and EGFR, are amplified. Their activation has been proposed to enhance E-cadherin endocytosis. However, the mechanism remains rather elusive. Shrew-1/AJAP1 is a recently identified adherens junction–associated transmembrane protein that internalizes with E-cadherin upon activation on RTKs. By means of complementary gain- and loss-of-function approaches, the authors show that shrew-1 upregulation and depletion respectively enhances and abrogates EGF-stimulated E-cadherin endocytosis. Overexpression of shrew-1 leads to preformation of an E-cadherin/EGF receptor Her-2/src-kinase/shrew-1 signalling complex and accelerated E-cadherin internalization but not cadherin degradation. These findings contribute to the understanding of E-cadherin regulation and provide further insight into putative pathological factors leading to breast cancer.



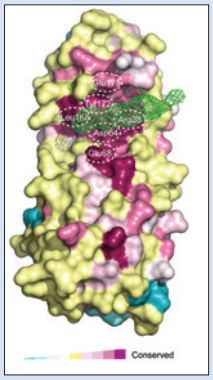
Chromatin-dependent Transcription Factor Accessibility Rather than Nucleosome Remodeling Predominates during Global Transcriptional Restructuring in *Saccharomyces cerevisiae*
Karl A. Zawadzki, Alexandre V. Morozov, and James R. Broach

Nucleosomes not only serve as the fundamental unit of chromatin organization but also participate in regulation of genes they package. Previous studies have indicated that nucleosomes function as nonspecific repressors of gene expression. Examination of the regulation of specific genes has prompted a model in which induction correlates with removal of nucleosomes from gene promoters while repression is associated with addition of nucleosomes. In this study the authors determined precise nucleosome positions across the entire yeast genome both before and after glucose addition, a condition resulting in transcriptional change in almost half of all genes. Surprisingly, little correlation was observed between changes in gene expression and changes in promoter nucleosome occupancy. Rather, the authors found that nucleosome occupancy predominantly defines which transcription factor binding sites are available for participation in regulation. Thus, in yeast, regulation by chromatin-delimited accessibility appears to predominate over regulation by chromatin remodeling.

Cisternal Organization of the Endoplasmic Reticulum during Mitosis
Lei Lu, Mark S. Ladinsky, and Tom Kirchhausen



Cell division is accompanied by dramatic alterations in the functional and morphological organization of membrane-bound organelles. How does mitosis affect the structure of the endoplasmic reticulum (ER)? By means of rapid 3-D imaging of single live cells, the authors show that during mitosis most of the ER is organized as an extended array of cisternae, with a few remaining ER tubules associated with the spindle. In contrast, the ER of interphase cells exhibits the characteristic reticular organization, with convolved perinuclear ER cisternae connected to ER tubules present mostly in the cell periphery. The prevalence of extended mitotic ER was confirmed using high-resolution EM tomography of samples preserved by high-pressure freezing and freeze substitution. The authors go on to show that microtubules are required for maintenance and generation of tubular ER. Simple addition of nocodazole to interphase cells, which mimics in part the massive mitotic microtubule reorganization, also results in the tubule-to-cisternae ER transformation. This reflects the importance of active, cytoskeleton-based mechanisms to stabilize tightly curved ER membranes.



Structural Basis of Ist1 Function and Ist1-Did2 Interaction in the MVB Pathway and Cytokinesis
Junyu Xiao, Xiao-Wei Chen, Brian A. Davies, Alan R. Saltiel, David J. Katzmann, and Zhaohui Xu

The ESCRT (**e**ndosomal **s**orting **c**omplex **r**equired for **t**ransport) machinery mediates a series of topologically similar membrane deformation events: multivesicular body (MVB) sorting, enveloped virus budding, and abscission during cytokinesis. ESCRT-III subunit polymerization is not understood, but has been implicated in deforming membranes during these membrane budding/scission events. Ist1 has been identified as an ESCRT-III–associated protein (via direct interaction with the Did2 subunit), but its mechanism was unclear. Structural determination of the Ist1 amino-terminal domain (Ist1NTD) revealed remarkable similarity to the previously described ESCRT-III subunit fold, identifying Ist1 as a divergent ESCRT-III subunit. Moreover, cocrystallization of Ist1NTD in complex with the Did2 carboxyl-terminus identified a previously unappreciated pocket formed by Ist1 that binds Did2. This pocket contributes to the intermolecular association between Ist1 and Did2 but may also represent a conserved mechanism by which ESCRT-III subunits are auto-inhibited. These studies identify Ist1 as a divergent ESCRT-III subunit and reveal a novel ESCRT-III interaction surface that may contribute to both auto-inhibition and intersubunit associations. ■