**H. pylori mobilizes cells**

*Helicobacter pylori* infects the gastric track of more than half of the human population and is associated with an increased occurrence of invasive gastric cancers. On page 249, Churin et al. explain how this widespread bug turns tumors metastatic by corrupting a growth factor receptor.

*H. pylori* mobilizes infected epithelial cells on its course to pathogenicity. The authors now show that mobilization results from activation of the hepatocyte growth factor (HGF) receptor c-Met. During development and differentiation, HGF-induced activation of c-Met initiates cell migration events. Inhibition of c-Met expression by siRNA blocks *H. pylori*-induced motility. *H. pylori* corrupts c-Met signaling, however, by injecting host cells with the protein CagA. Binding of CagA to c-Met resulted in modulation of receptor activity and recruitment of PLCγ, a mediator of cell polarity necessary for motility. CagA–PLCγ interactions mobilized infected cells through an ERK-dependent MAP kinase pathway, as inhibitors of MAP kinases or PLCγ blocked motility.

Unlike the gastric tumor cell line, a polarized canine kidney cell line does scatter in response to HGF. *H. pylori* also induced c-Met–mediated motility in these cells, but did so through a PI3K-dependent pathway rather than through PLCγ, indicating that the bug uses alternative routes to motility depending on the cell type. The authors hope to look at animal models next to determine whether inappropriate activation of c-Met and the resulting mobilization of gastric cells is responsible for increased incidences of metastatic cancers in *H. pylori* infections.

**Choosing replication origins**

After mitosis, cells prepare for the next round of DNA replication by assembling complexes of proteins on chromatin that will carry out the task of copying the genome. Prereplication complexes (preRCs) assemble during telophase, but studies of the dihydrofolate reductase locus in mammalian cells have indicated that, during G1, only a subset of preRCs are designated for use as origins of replication. On page 257, Li et al. demonstrate that the same is true for origins throughout the genome.

Li et al. compared origins used by mammalian cells in vivo with those chosen in isolated mammalian nuclei undergoing premature replication in frog cytoplasmic extracts. Comparison of the two sets of origins revealed that, soon after mitosis, few of the sites used matched. About two hours after mitosis, the sites used in vitro were clustered into domains surrounding in vivo sites, but the actual sites fired still did not necessarily correspond. This domain selection was previously suggested by examinations of the timing of replication of whole chromosomal domains and is known as the timing decision point.

Five hours after mitosis, the sites chosen in vitro were more likely to be the same sites used in vivo. This site selection is known as the origin decision point. Thus, as for the DHFR locus, the general choice of origins used is not random, but why origin selection should be regulated is unclear. Perhaps origins are placed near genes that encode replication proteins so that they are activated early by passage of the replication fork. Alternatively, origins may be regulated to prevent collision of RNA and DNA polymerases. If the latter is true, origin choice may change during differentiation to accommodate transcriptional differences.

**Say NO to insulin**

Insulin stimulates its own secretion from pancreatic β cells through rapid nitrosylation of glucokinase (GK), according to results by Rizzo and Piston on page 243.

When glucose levels are low, an inhibited form of GK associates with insulin-containing granules in pancreatic β cells. Rizzo and Piston have determined that this localization is mediated through interaction with neuronal nitric oxide synthase (nNOS). Insulin treatment disrupted this association through nitrosylation of a GK cysteine residue. Activation of nNOS and the resulting nitrosylation of GK may be mediated through a rise in intracellular calcium, a known response of GK by preventing granule binding. Release of the enzyme into the cytoplasm and the accompanying conformational change—both of which required NO production—activated GK.

GK induces secretion of the granules, thus promoting local increases in insulin levels. A recently developed drug for the treatment of type II diabetes is a GK activator. The new results suggest that the drug may activate GK by preventing granule binding. Piston plans to test this possibility in the near future.