In This Issue

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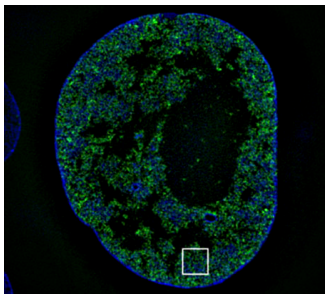
Unwrapping new histones



Novel histone variants (green) speckle the nucleus of a human cell.

Wiedemann et al. have discovered two novel kinds of histones, the protein spools for DNA.

DNA strands usually coil around four histones—H2A, H2B, H3, and H4. But in certain situations, cells install alternatives. For example, CENP-A, a variant of H3, replaces conventional H3 at centromeres. Researchers haven't identified a new version of the H3 histone for 20 years, but Wiedemann et al. wondered if others remained to be discovered.

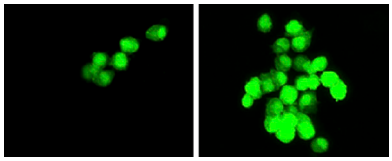
Searching the human genome for genes that resemble histone H3.1 revealed two close matches, which the researchers named H3.X and H3.Y. The genes occur in two other primates, the chimp and the rhesus macaque, but not in any other mammals with sequenced genomes or in other eukaryotes.

H3.X and H3.Y had previously been pegged as pseudogenes, but Wiedemann et al. showed that cells from several kinds of tumors—including bone, breast, and lung—make small amounts of RNA for one or both alternative histones. Healthy cells in the testis and much of the brain also tested positive for the variant histone RNA. The proteins might be useful in particular situations—cells could swap histones during stress, for example. When cells were crowded, the number of them expressing the variant histones shot up sixfold, the researchers found. Knockdown experiments suggested that H3.X and H3.Y promote cell growth.

The new histones remain mysterious in many ways. The researchers aren't sure why only primates appear to have them. And because only the H3.Y protein was detected in human cells, it's possible that the H3.X gene does not yield a protein and instead codes for a regulatory RNA.

Wiedemann, S.M., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.201002043.

Go on, satellite cells, be all that you can be



miR-1 and miR-206 curb the replication of satellite cells (left), compared with controls (right).

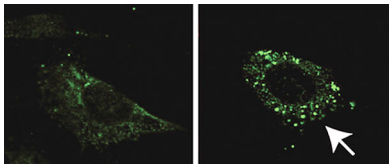
Two microRNAs enable adult muscle stem cells to reach their full potential, Chen et al. reveal. The regulatory molecules block a transcription factor that curtails the cells' differentiation.

Most of the time, muscle stem cells, or satellite cells, do little except slowly divide. After an injury, however, they activate and help build new muscle fibers. The transcription factor Pax7 is necessary for stem cell maintenance under normal conditions. Once the cells are activated, Pax7 switches on the genes necessary for early differentiation. But Pax7 also stops the cells from terminally differentiating, so Pax7 must be shut down to allow the differentiation program to proceed. To find out how, Chen et al. focused on microRNAs, which they had previously shown were crucial during embryonic muscle development.

By tracking the differentiation of cultured satellite cells, the researchers identified two microRNAs—miR-1 and miR-206—that were necessary for the process. The team found that boosting the amounts of miR-1 and miR-206 in satellite cells slowed their division and sped up their specialization. Both microRNAs reduced Pax7 levels but, because an individual microRNA can quell multiple target genes, Chen et al. speculate that miR-1 and miR-206 shut down other genes involved in stem cell maintenance.

Chen, J.-F., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.200911036.

With HMGB1's help, cells dine in



Sites of autophagy (green) are reduced in cells lacking HMGB1 (left) compared with control cells (right).

Like some people, cells eat when they are under pressure—but they consume parts of themselves. Tang et al. show that a multi-function protein helps control this form of cannibalism.

Cells often respond to hunger or stress by digesting some of their contents. The process, known as autophagy, helps free nutrients and clean up cytoplasmic trash such as worn-out organelles and misshapen proteins. Tang et al. discovered a link between this form of cellular recycling and the protein HMGB1. Inside the nucleus, HMGB1 bends DNA so that transcription factors can gain access to important regulatory genes. HMGB1 has an extracellular role, too. Dying cells shed the protein to trigger inflammation.

The researchers wanted to determine whether HMGB1 also has a function in the cytosol. They found that starving cells transfer HMGB1 from the nucleus to the cytosol. Once there, HMGB1 induces autophagy—self-eating slowed in cells lacking the protein. HMGB1 flips a key autophagy switch, separating the proteins Beclin1 and Bcl-2, which normally cling to each other to suppress the pathway.

Stressed-out cells hike their production of reactive oxygen species, which change HMGB1's behavior, Tang et al. discovered. Oxidation of a particular cysteine in HMGB1 springs the protein from the nucleus. Oxidation of two other cysteines enables HMGB1 to bind Beclin1 and separate it from Bcl-2. This suggests that blocking HMGB1 could benefit cancer patients, since tumor cells often rev up autophagy to withstand chemotherapy, immunotherapy, and radiation treatment.

Tang, D., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.200911078.