WEB WATCH

Bugs on the Web

- http://microbiol.org/
  http://www.microbiology-direct.com/

The beauty of the Internet is the ease with which networks can be generated by linking related sites. The Microbiology Network is at the centre of one such web, and aims to serve as a "communication resource for the microbiologist".

The Microbiology Network provides a starting point for various sites of interest to microbiologists, including a 'resource centre' with information on several areas — from contract testing to microbiology software or laboratory equipment and supplies. The site also includes a list of user groups, a page for discussion groups, and 'file libraries', which aim to act as a "repository for computer files of interest to biologists and health care workers in industry, academics, and private practice".

Another web site doing a similar job is Microbiology Direct. Launched in July 2000, this site has a slick design and easily navigable layout. Like The Microbiology Network, its strength lies in the plethora of links to related sites, handily divided into categories (genomics, journals and methods, for instance).

The comprehensive gallery of images includes video clips and links to other photo galleries, and the 'research topics' section contains links to several areas, from phylogenetics and nomenclature to public health microbiology. Many of the 'teaching resources' links are both educational and entertaining, and the news links are regularly added to and updated (an advantage of this site compared with The Microbiology Network). Together, these sites provide a great launch pad for microbiology online.

Alison Mitchell

STEM CELLS

Forever young

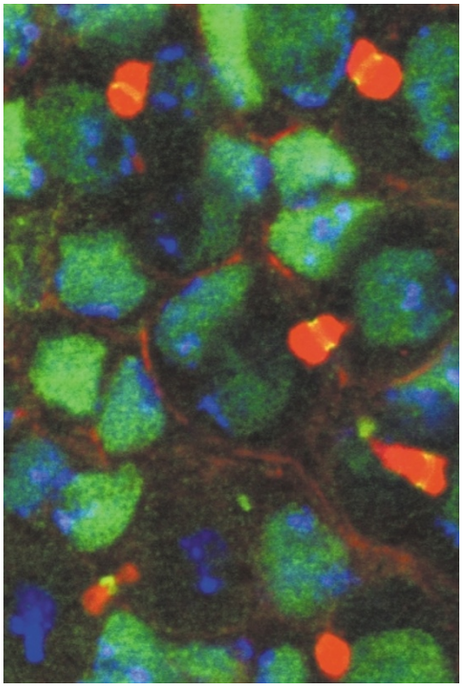
We all know that stem cells can generate any of the body's tissue types, but how do they renew themselves to prevent their own demise? Now, two reports in *Science* reveal some of the biological instructions for self-renewal. They have found that cells in the *Drosophila* testes act as a microenvironment and activate the JAK–STAT (Janus kinase–signal transducer and activator of transcription) signalling pathway, which determines the fate of stem cells.

In male *Drosophila*, the sperm stem cells lie at the tip of the testis, surrounding a cluster of cells called a hub. When the stem cell divides, the daughter cell maintaining contact with the hub remains a stem cell, whereas the cell that is displaced away becomes a blast cell and begins to develop into a male germ cell. What governs the destiny of each cell was unclear.

Kiger and colleagues, and Tulina and Matunis investigated whether cues from within the hub were important. Both groups focused on the JAK–STAT pathway as it is known to activate target genes in both *Drosophila* and mammals. They created mutants for the JAK homologue hopscotch (Hop) or the STAT homologue Stat92E in stem cells, and found that if mutants lacked an active JAK–STAT pathway, the stem cells differentiated but did not self-renew. By contrast, ectopic or constitutive JAK–STAT signalling greatly expanded stem-cell numbers — as shown by the presence of Anillin (red in the picture) or spectrosomes.

But how is the JAK–STAT pathway activated in these cells? Both groups found that cells in the hub act as a microenvironment by expressing a localized source of a signalling molecule called Unpaired, which activates the JAK–STAT pathway in adjacent stem cells. Both groups found that misexpression of Unpaired was sufficient to cause expansion of the germline stem-cell population.

So, it seems that signals within the hub create a stem-cell microenvironment and that any daughter cells that



are displaced will embark on a journey of differentiation into mature germ cells. Signals from surrounding cells that promote differentiation of displaced cells could help prevent excessive stem-cell proliferation, whereas hubs that lack stem cells could instruct both daughters of a neighbouring stem cell to self-renew and repopulate the microenvironment. Although this model will need to be

TRANSCRIPTION

A unique switch

Although histone methylation is known to regulate gene transcription through chromatin modification, no transcription factor has yet been identified as a direct target for methylation. In *Science*, however, Evans and colleagues now describe a unique molecular switch, which enhances the transcription of nuclear receptor (NR)-dependent genes and blocks the transcription of cyclic-AMP-response-element-binding protein (CREB)-dependent genes. This switch is based on the controlled methylation of histones and the transcriptional cofactors CREB-binding protein (CBP)/p300.

CBP/p300, which possess intrinsic histone acetyltransferase (HAT) activity, and coactivator-associated arginine methyltranferase (CARM1), which has intrinsic histone methyltransferase (HMT) activity, are transcriptional coactivators of NR-dependent genes. The cofactor, activator of retinoid and thyroid receptors (ACTR), also possesses HAT activity and interacts with both CBP/p300 and CARM1.

Evans and co-workers used an *in vitro* chromatin-based NR-dependent transcription system to characterize the interplay between the p300-HAT and CARM1-HMT activities. They observed the most striking transcriptional enhancement in the presence of p300, CARM1 and ACTR, indicating that a trimeric coactivator complex might be required for maximal activation of NR-dependent genes.

Using a CARM1-HMT-defective mutant, the authors showed that this HMT activity is essential for the enhancement of NR-dependent transcription. They also showed that p300-acetylated histones are more effectively methylated by CARM1 than are nonacetylated histones, indicating that CARM1 might be an NR cofactor through which acetylation and methylation cooperate to modify chromatin and stimulate transcription.

Using a similar system, the authors found that although CBP/p300 enhance this transcription, CARM1 inhibits it, and this inhibition was not observed using a CARM1-HMT-defective mutant. Evans and colleagues found that, in addition to methylating histones, CARM1 also specifically methylates CBP/p300.

As CREB-dependent transcription is determined by the strength of the interaction between the KIX domain of CBP/p300 and the kinase-inducible domain (KID) of CREB, the authors proposed that CARM1-dependent methylation of CBP/p300 inhibits CREB signalling by disrupting this interaction.

Using *in vitro* methylation assays with GST–KIX fusion proteins, the authors found that CARM1 predominantly methylates a single arginine residue in CBP and p300 that is localized to the external surface of the KIX–KID complex. Methylation of this site disrupts the formation of this complex, but does not affect the NR-related functions of CBP/p300.

The authors identified a potential