Epigenetics, Differentiation, and Cancer

Loss of imprinting (LOI, a change in DNA methylation) of the gene encoding insulin-like growth factor-2 (IGF-2) correlates with the development of human colorectal cancer and may serve as a possible marker for cancer screening. To determine if this epigenetic change, which modestly increases IGF-2 expression, has a causal role in tumorigenesis, Sakatani et al. (p. 1976, published online 24 February 2004) created a mouse model of LOI. The LOI mice developed twice as many intestinal tumors as did controls, and their normal intestinal epithelium was shifted toward a less differentiated state, a pathological change also detected in humans with LOI. Thus, epigenetic changes may affect cancer risk by altering the maturation state of the normal tissue from which tumors arise.

Arming Sticklebacks

Parallel evolution is seen in sticklebacks that colonized freshwater streams and lakes around the world at the end of the last ice age 10,000 to 20,000 years ago. A common change in freshwater species is loss of the extensive body armor of marine species. A single major locus controls the armor phenotype. Colosimo et al. (p. 1928; see the Perspective by Gibson) now show that the gene primarily responsible for these changes is ecdysplasin, and that almost all low-armor populations share a common ancestry for this gene. However, this is not because a single low-armor population migrated around the globe. Instead, the low armor allele of ecdysplasin, which originated well before the last ice age, is present cryptically around the globe. Instead, the low armor allele of ecdysplasin, which originated well before the last ice age, is present cryptically around the globe. Instead, the low armor allele of ecdysplasin, which originated well before the last ice age, is present cryptically around the globe. Instead, the low armor allele of ecdysplasin, which originated well before the last ice age, is present cryptically around the globe.

Leading and Lagging

A vigorous debate has been waged about whether rapid climate changes were triggered by shifts between distinct ocean circulation states, or whether changes in the location and strength of deepwater formation were driven by climate. Piotrowski et al. (p. 1933; see the news story by Kerr) analyzed the Nd-isotopic compositions of the iron and manganese oxides (a proxy for deep ocean circulation) of two cores from Cape Basin in the southeast Atlantic Ocean, and compared them to the carbon isotopic composition of benthic foraminifers (a proxy for climate and the global carbon cycle) from the same cores. They found that, during both the last glaciation and the last deglaciation, the global carbon budget changed before ocean circulation strengthened. This lead-lag relationship is not observed during the abrupt millennial warming events during the last ice age, indicating that ocean circulation could have been a trigger for them.

High-Energy Milky Way

The Milky Way Galaxy is full of high-energy emissions, produced by pulsars, supernovae, and unknown sources. Aharonian et al. (p. 1938) used the High Energy Stereoscopic System (HESS) of four telescopes arrayed in Namibia to search for the highest energy gamma-ray emissions (energies greater than 10^{22} electron volts) in the central part of the Galaxy. They found eight new high-energy emitters, some of which are associated with pulsar wind nebulae or supernova remnants. Determining the source of these emissions and understanding the mechanisms that lead to these highest energy particles will eventually help to resolve the mystery of the source of the Galactic cosmic rays that bombard Earth.

A Capacity for Sensing

Electrical detection can greatly simplify gas sensing. For low-power applications, chemiresistors, which detect gases through changes in dielectric constant, can offer higher stability than sensors based on chemiresistive polymers. However, the response times of chemiresistors can be slow (on the order of minutes to respond and recover). Snow et al. (p. 1942) show that response times can be reduced to the order of a few seconds for common organic vapors by using single-walled carbon nanotubes as one of the electrodes. Fringing fields that radiate from the nanotube’s surface polarize adsorbed molecules and enhance the capacitive response. The coatings used to make the device chemically selective can thus be made thinner, which decreases diffusion limitations and improves the response time.

Remote Interference

Atoms in a Bose-Einstein condensate (BEC) have the property of all being in the same phase. The phase difference of two separate BECs can be measured by allowing the clouds of atoms to collide, thereby producing an interference pattern in the atom density. Using the associated wavelength of such atomic ensembles has already been demonstrated in sensitive interferometric measurements and metrology. However, colliding the separate BECs has so far been a destructive process. Saba et al. (p. 1945; see the Perspective by Javanainen) use light scattering to couple a small portion of the atoms from each BEC and show that an interference pattern can be produced. The almost nondestructive technique should provide a method to continuously probe the phase difference between two spatially separate BECs without the need to destructively split and collide the atomic clouds.

Feeding the Five Trillion

More prokaryotic cells are present in the gut microflora than there are eukaryotic cells in the human body, but almost nothing is...
known about their contribution to their host. Sonnenburg et al. (p. 1955) reveal that a prominent gut occupant Bacteroides thetaiotaomicron harvests otherwise indigestible nutrients from our diet contents such as plant polysaccharides until that supply is exhausted. Then the bacteria can turn to the host’s mucopolysaccharide secretions to supplement their energy supply. Thus, although the floral composition tends to stay constant, its metabolic activities shift according to energy supply.

Conformational Signaling

In bacteria, sigma $\sigma^{54}$ factors that bind to core RNA polymerase (RNAP) are required for specific promoter recognition and initiation of transcription. Unlike holoenzymes containing other $\sigma$ factors, $\sigma^{54}$-RNAP is transcriptionally silent until it binds to an ATP-dependent activator protein. Now Rappas et al. (p. 1972) have determined a 20 Å resolution cryo-electron microscopy structure of $\sigma^{54}$ in complex with the binding domain of its activating protein [PspF$_{1-275}$] containing an ATP transition-state analog. Combining this with a 1.8 Å crystal structure of apo PspF, comparison to an alternative conformation of a homologous activator (NtrC1) and mutational analysis, they suggest that nucleotide hydrolysis transmits a conformational signal that frees two loops to interact with $\sigma^{54}$.

Top Dog?
The role of apex predators in ecological communities and the potential ubiquity of resulting “trophic cascades,” have led to the idea that the world is green because predators limit herbivores, protecting plant communities from restriction by herbivory. Croll et al. (p. 1959) studied seven Aleutian Islands on which Arctic foxes were introduced long ago for the fur trade, and seven that remained fox-free. Foxes preyed on the native seabirds, thereby reducing the import of guano, changing soil fertility, and inducing major changes in the plant community. Fertilization of plots on an island with foxes allowed the vegetation to change to resemble that of fox-free islands. Thus trophic cascades have the capacity for effects beyond the immediate food web, and connectivity exists between marine and terrestrial ecosystems.

Modeling Gene Regulation

Modeling gene regulation is a fundamental goal in systems biology (see the Perspective by Isaacs et al.). Rosenfeld et al. (p. 1962) combine modeling with experiments in their analysis of gene networks. The quantitative function relating transcription factor concentration and gene factor production is termed Gene Regulation Function (GRF). Biochemical parameters, noise, and cellular states affect the GRF. Noise in gene expression results from fluctuations in factors such as mRNA and protein abundance and environmental conditions. Pedraza and van Oudenaarden (p. 1965) now model and test networks in which gene interactions are controlled and quantified in single cells. Quantitation of noise propagation will assist in understanding the complex dynamics of gene networks in prokaryotic and eukaryotic systems and will assist in designing synthetic networks.

Biochemical Prehistory

The transition from an early RNA-based biochemistry to one that was (and is) based on proteins required a set of components that could convert the nucleic acid code for amino acids into the actual amino acid. The set of aminoacyl–transfer RNA (aa-tRNA) synthetases does just that, attaching the amino acid to its cognate tRNA, which is then used by the ribosome to translate the genetic code into proteins. There is, however, evidence that some of the 20 canonical amino acids are relative latecomers, and Sauerwald et al. (p. 1969) show that cysteine may be one of these add-ons. Archaea that lack the aa-tRNA synthetase for cysteine rely on an alternative pathway (likely a relic) in which phosphoserine is attached to tRNA and then enzymatically converted in an anaerobic, pyridoxal phosphate–dependent reaction to cysteiny1–tRNA.