Frog skin isomerase identified

Alexander Jilek et al. have isolated and characterized an isomerase from the skin secretions of frogs of the subfamily Bombinae. Protective antibacterial and hemolytic peptides found on the skin of these frogs often contain a D-allo-isoleucine as the second amino acid, and such D-amino acids are derived posttranslationally from the corresponding L-amino acid via isomerase activity. The authors collected the skin secretions from Bombinae frogs and purified a 52-kDa protein that, when incubated with the N-terminal sequence of the protective skin peptide bombinin H, catalyzed the conversion of the second residue, L-isoleucine, to D-allo-isoleucine. Jilek et al. also carried out the reaction in tritiated water and demonstrated that the change of chirality proceeded via a deprotonation/protonation reaction at the α-carbon of the isoleucine. The authors showed that a histidine residue was part of the active site and that the isomerase did not require the presence of an apparent pyridoxal phosphate cofactor. The cloned isomerase gene from skin cDNA and genomic DNA was able to express the enzyme in Xenopus oocytes. A search of protein databases revealed the presence of homologs of the Bombina isomerase in several vertebrate species, including birds, fishes, and humans.

“Biosynthesis of a D-amino acid in peptide linkage by an enzyme from frog skin secretions” by Alexander Jilek, Christa Mollay, Christa Tippelt, Jacques Grassi, Giuseppina Mignogna, Johannes Müllegger, Veronika Sander, Christine Fehrer, Donatella Barra, and Günther Kreil (see pages 4235–4239)

MET and MYC coexpression in breast cancer

Alana Welm et al. demonstrate that coexpression of the protooncogenes MET and MYC leads to the formation of malignant breast cancer, whereas expression of either alone does not. Previous research by others has implicated both the MET gene, which encodes a transmembrane receptor tyrosine kinase, and the MYC gene, which encodes a transcription factor, in several types of cancer. In addition, the overexpression of MET is associated with a high risk of metastasis in breast cancer. Welm et al. infected cultured mouse primary mammary epithelial cells with a mouse retrovirus containing the wild-type human MET gene. The researchers transplanted the infected cells into mammary fat pads, and, at 10 weeks after transplantation, the cells appeared structurally disorganized and clustered abnormally. Through histological analysis, the researchers determined that the phenotype was similar to mammary intraepithelial neoplasia. However, the lesions did not progress to malignant tumors. When the researchers infected the MET-overexpressing neoplasms with a second retrovirus containing the human MYC gene, the glands progressed to discernable tumors in 10 weeks. Histological analysis of the tumors after 4 months revealed that they were mammary adenocarcinomas. Overexpression of either Met or Myc protein alone did not result in tumorigenesis. The authors found that both the nonprogressive neoplasms and adenocarcinomas displayed characteristics consistent with the transformation and expansion of mammary progenitor cells.

“MET and MYC cooperate in mammary gland neoplasia” by Alana L. Welm, Suwon Kim, Bryan E. Welm, and J. Michael Bishop (see pages 4324–4329)

Remote sensing of biogeochemical change

Climate change altered arctic aquatic ecosystems

Instructive immunotherapy destroys tumors
Remote sensing of biogeochemical change

Researchers used airborne imaging spectroscopy and photon transport modeling to measure how invading plants are changing the biochemistry of tree canopies across mountainous Hawaiian rain forests. Invasions must be advanced to be detected by conventional remote sensors that rely on canopy emergence or dominance by an invader; and, even then, only the distribution of invaders, and not ecosystem-level effects of invasion, can be gleaned. To catch early changes in an ecosystem, Gregory Asner and Peter Vitousek used equipment mounted on high-altitude aircraft to measure the biogeochemistry of forest canopies in Hawaii Volcanoes National Park. The technology used recent advances in spectroscopic transport models that trace photons through the canopy, as well as advanced airborne sensors with performance comparable to ground-based laboratory sensors. The researchers learned that the invading Canary Islands tree Myrica faya has doubled nitrogen concentrations and water content in the Hawaiian forests as it replaces native trees, whereas the invasive herb Hedychium gardnerianum has reduced nitrogen concentrations but substantially increased water content. These changes in biochemistry show where biological invasion is occurring, as well as whether the invasion has had a substantial effect on the entire ecosystem.

“Remote analysis of biological invasion and biogeochemical change” by Gregory P. Asner and Peter M. Vitousek (see pages 4383–4386)

Climate change altered arctic aquatic ecosystems

A survey of arctic lake communities has uncovered extensive species changes over the past 150 years, most likely because of climate change. John Smol et al. examined species composition changes recorded in 55 stratigraphic profiles from sediments deposited in a wide range of arctic lakes and ponds. The team examined shifts in the siliceous remains of diatom and chrysophyte algae, and the chitinous remains of small invertebrate crustaceans and insect larvae. These microfossils serve as reliable proxies for water quality and habitat availability. The authors found that the diversity and proportions of algal and invertebrate remains have changed dramatically since 1850, indicating that biological communities are markedly different compared with previous centuries or even millennia. The team says climate warming has shortened the duration and extent of lake ice cover, creating different habitats and longer growing seasons for lake biota. The population changes were largest in regions where the greatest relative warming appears to have taken place, principally in the most northerly regions investigated. However, consistent changes were observed throughout many arctic regions, leading the authors to conclude that the hopes of finding pristine arctic environments untouched by climate change have dwindled.


Instructive immunotherapy destroys tumors

The immune system has difficulty suppressing tumors, partially because of the limited number of T cells capable of recognizing and eliminating tumor cells. Lili Yang and David Baltimore developed an “instructive immunotherapy” method to reprogram the immune system by engineering mouse hematopoietic stem cells (HSCs) to produce T cells in vivo of defined antitumor specificity. The authors isolated HSCs from mouse bone marrow and, using a bicistronic retroviral vector, delivered genes encoding both the α and β chains of T cell receptors (TCRs) specific for a model tumor antigen. Yang and Baltimore injected the engineered HSCs into irradiated mice, which successfully reconstructed the bone marrow and hematopoietic lineages. The HSCs expressed tumor-specific TCRs for up to 8 months, suggesting that these stem cells may be able to maintain the TCRs for a lifetime. Many of the HSCs matured into functional CD4 and CD8 T cells, which responded to the tumor peptide antigen by proliferating and producing cytokines. Although these T cells were able to partially resist a challenge with tumor cells carrying the antigen, the tumor could be suppressed completely by boosting the mouse’s immunity through injection of dendritic cells pulsed with cognate tumor peptides.

“Long-term in vivo provision of antigen-specific T cell immunity by programming hematopoietic stem cells” by Lili Yang and David Baltimore (see pages 4518–4523)