EDITORS' CHOICE

EDITED BY GILBERT CHIN AND JAKE YESTON

CELL BIOLOGY

Caught in the NET

When circulating neutrophils are challenged by microbes, they can transform themselves into neutrophil extracellular traps or NETs, which are constructed out of chromatin (from the nucleus) and granule proteins (from the cytoplasm). These NETs grab hold of and sequester bacteria—and in doing so, they keep them within the range of antimicrobial enzymes and peptides.

Fuchs *et al.* show that this process involves a new type of cell death program. After neutrophils are stimulated, the normal segregation of chromatin into regions that are actively transcribing genes and those that are inactive disappears, and the nuclei become deformed. Subsequently, intracellular membranes, including the nuclear envelope and also granule membranes, disintegrate; this leads to the mixing and assembly of the NET components, which are then released from the dying cell as its plasma membrane ruptures. This sequence of cell death is distinct from other known forms of programmed cell death and appears to involve reactive oxygen species (superoxide and peroxide) that are produced by NADPH oxidase. Chronic granulomatous disease patients are deficient in this enzyme and cannot make NETs, which may explain in part why they suffer recurrent infections. Thus, even with their last breath, neutrophils contribute to the fight against invasive microbes. — SMH

J. Cell Biol. **176**, 231 (2007).

Extracellular NETs (yellow fibers) bind bacteria (orange).

CHEMISTRY

Through the Looking Glass

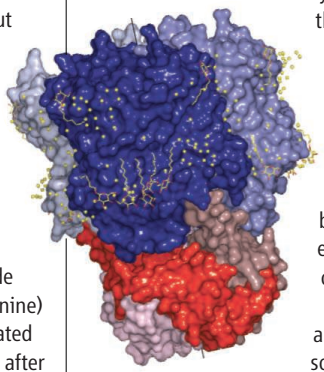
Amino acids exist predominantly as L isomers, although the mirror-image D isomers figure in several biochemical pathways. Pyridoxal phosphate-dependent enzymes racemize amino acids for this purpose by binding them through a hydrogen bond–stabilized imine linkage. Park *et al.* have prepared a small-molecule receptor that binds amino acids through a similar motif but also incorporates a chiral binaphthyl backbone. When L amino acids are bound in the presence of triethylamine base, they are selectively epimerized by proton exchange to the D isomers in order to relieve steric constraints imposed by the framework. The authors could efficiently invert the configurations of 13 chiral amino acids, including those with acidic or basic side chains. Selectivities ranged from 7:1 (for alanine) to 20:1 (for threonine). Acid hydrolysis liberated the epimerized product from the framework, after which the receptor could be recycled. — JSY

J. Am. Chem. Soc. **129**, 10.1021/ja067724g (2007).

BIOCHEMISTRY

Three of a Kind

Nitrogen is, of course, an essential element for life, and the primary mode by which microbes acquire nitrogen is by ammonia uptake through the trimeric ammonia channel AmtB. Two crystal structures of bacterial AmtB (and one of archaeal Amt1) revealed that each monomer features a passageway for ammonia (NH_3) and a pseudosymmetric pair of five transmembrane helix domains (for more on how this dual topology arrangement might have evolved, see Rapp *et al.*, Reports, *Science* Express, 25 January 2007). When intracellular nitrogen is limiting, the primary AmtB regulator—the trimeric protein GlnK—dissociates to allow ammonia entry; an unregulated channel (and persistent ammonia influx) would be fatal given its effect on pH homeostasis.



The AmtB (blue)–GlnK (red) complex, with detergent (yellow).

Gruswitz *et al.* and Conroy *et al.* have solved the structure (at 2.0 and 2.5 Å, respectively) of the bacterial AmtB-GlnK complex, and Yildiz *et al.* have contributed an electron microscopic study of the archaeal Amt1-GlnK1 complex. They find that an extended region of GlnK referred to as the T loop, which contains an arginine residue at its tip, inserts into the cytoplasmic vestibule of AmtB and physically impedes the passage of ammonia. All five hydrogens of the guanidinium cation find partners on the interior surface of the AmtB pore, which seems fitting because the channel has, after all, adapted to conduct ammonia. How is such an intimate association disrupted? As intracellular nitrogen drops, the small molecule 2-oxoglutarate accumulates and binds to GlnK (precisely where is not quite clear yet) along with Mg-ATP; these interactions and perhaps ATP hydrolysis may be involved in the extension and retraction of the T loop. — GJC

Proc. Natl. Acad. Sci. U.S.A. **104**, 42; 1213 (2007); *EMBO J.* 10.1038/sj.emboj.7601492 (2007).

IMMUNOLOGY

Keeping It Brief

The cytokine interleukin-2 (IL-2) is both produced by and exerts strong effects on T cells. Despite its fundamental importance for T cell development and immune regulation, IL-2 is only fleetingly expressed, consistent with a need to keep the potent effects of this growth factor under tight control.

Villarino *et al.* have investigated the management of IL-2 expression by helper T (T_H) cells and find that several feedback mechanisms exist to ensure the brevity of its expression. Selection cytokines—including some that use receptors bearing the common γ chain—exhibited the ability to suppress IL-2 expression. Most potent

CREDITS (TOP TO BOTTOM): V. BRINKMANN/MAX PLANCK INSTITUT FOR INFECTION BIOLOGY; GRUSWITZ *ET AL.*, PROC. NATL. ACAD. SCI. U.S.A. **104**, 42 (2007)

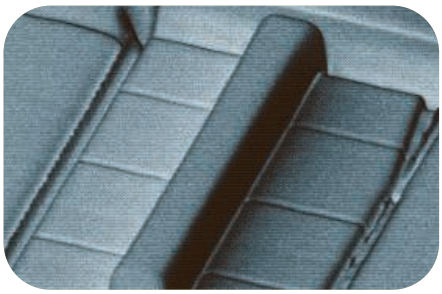
among these was IL-2 itself, and it was at its best in combination with one or more of the other cytokines. Negative feedback was also mediated by the intracellular STAT family of transcription factors, which assist with the differentiation of T_H1 and T_H2 cells. These in vitro observations were supported by in vivo experiments, in which treatment of mice with recombinant IL-2 measurably reduced the levels of IL-2 produced after immunization. It will be of interest to investigate whether these pathways cooperate in distinct ways to control early T cell immunity, regulatory T cells, and the formation of T cell memory. — SJS

J. Exp. Med. 10.1084/jem.20061198 (2007).

MATERIALS SCIENCE

Wiggling into Something Thinner

Nanoscale features can be fabricated in polymer thin films by room-temperature forging or embossing, in which the material undergoes inelastic flow from beneath a die to create an impression. The thinness of the layer remaining below the die is limited by friction, the shear strength of the material, and the pressure created by material building up outside the die, as well as by the amount of force the die itself can tolerate before it deforms. Cross *et al*. show that applying a small-amplitude shearing motion (approximately 10 nm) in the plane of



Nanoscale die used to pattern films.

the film activates surface flow. The shear motion not only allows much thinner layers to be formed but also decreases the number of defects that often limit the yield of structures with the necessary critical dimensions for a given application. Finite element simulations were used to confirm the underlying mechanism. — PDS

Nano Lett. **7**, 10.1021/nl0624566 (2007).

CLIMATE SCIENCE

A Splash of Cold Water

During the last degalciation, a large and rapid injection of glacial meltwater from the Laurentide Ice Sheet to the North Atlantic (called meltwater pulse 1a, or mwp-1a) raised sea level by ~20 m in only about two centuries. This enormous freshwater addition has variously been posited as the trigger of the Bølling warming period 14,600 years ago or as the cause of the Older Dryas cold event that terminated the Bølling 14,000 years ago; uncertainty about the age of mwp-1a has prevented resolution of these conflicting claims. Stanford *et al.* present a record of North Atlantic Deep Water (NADW) flow intensity from Eirik Drift that, combined with previously published improved dating for mwp-1a, establishes a relatively minor 200-year weakening of NADW flow 14,600 years ago, coincident with mwp-1a. The data also show that no discernible sea-level rise accompanied the clear NADW slowdown during the Younger Dryas. These results demonstrate that NADW formation and climate are not controlled exclusively by the magnitude or rate of meltwater addition, because the largest meltwater pulse resulted in the relatively minor Older Dryas whereas the climatologically much more dramatic Younger Dryas was not associated with discernable rises in sea level. Thus, the location of meltwater additions may be important. — HJS

Paleoceanography **21**, PA4103 (2006).

GENETICS

Not Cheaper by the Dozen

Fitness, defined as an individual's reproductive success, is measured by the number of offspring, and parents with more offspring are generally considered fitter. However, Penn and Smith show that in married couples in preindustrial societies, the survival of both the mother and the father depended on the number of offspring the wife had and families with fewer children had more surviving grandchildren. In an analysis of 21,000 records of survival in late 19th-century Utah, survival rates of the parents and children were significantly lower in the largest families, that is, those with 12 or more children. The negative effect of bearing children on fitness was stronger in females, lasted after menopause, and was evident even in women with only 1 to 3 offspring. However, after the birth of the fourth child, the risk of death became significantly greater in fathers, too. In addition, those children with the largest number of siblings were less likely to survive to the age of 18, with the youngest siblings at greatest risk. The ability of human females to survive long after the loss of reproductive function has previously been explained by the positive effect a mother's survival has on the success of her offspring; without a mother, survivorship of the children is lowered. Nevertheless, this study demonstrates that there may be a selective pressure for females to stop reproducing before they complete child rearing. — LMZ

Proc. Natl. Acad. Sci. U.S.A. **104**, 553 (2007).