

PERSPECTIVES

portin- β for FG nucleoporins by altering the relative positions of HEAT repeats 5 and 6 (7, 8); this change also facilitates cargo release.

\beta和许多它的结合伙伴的相互作用界面。FG核孔蛋白结合在importin- β 的外侧，凸面表面。importin- β 结合在HEAT重复5和6的主要位点之间(7, 8, 15)。然而，importin- β 的结合伙伴主要与内侧，凹面表面交互。RanGTP结合在HEAT重复1到8的氨基端(4)。而主要的螺旋IBB域结合在凹面表面，该表面包含了HEAT重复7到19(3)。IBB域和importin- β 展示了广泛的相互作用，涉及超过40个静电、疏水性和范德瓦尔斯接触。色氨酸残基(尤其是色氨酸-864)在importin- β 中帮助稳定IBB域的螺旋构象。通过这种方式，importin- β 确保了特定的高亲和力结合(16)。相比之下，PTHRP(甲状腺激素相关蛋白)的NLS结合在importin- β 氨基端(HEAT重复2到6)并与其RanGTP结合位点重叠(9)。该NLS主要以 β -片层构象存在，其结合方式类似于经典NLSs结合importin- α (6)。尽管PTHRP-NLS和IBB域在importin- β 上的结合位点部分重叠，但它们的分子架构不同，两者都可以结合importin- β (9)。

SREBP-2缺乏经典的NLS，正如Lee等(10)所描述的，通过其二聚体螺旋-环-螺旋 zipper(HLHZ)域结合importin- β 。正如研究者们所展示的，晶体结构揭示了importin- β :SREBP-2复合物的新颖结合方式。importin- β 必须结合到一个非凡的范围内的不同蛋白上，以执行其核运输和核装配任务。这在分子层面提出了非凡的需求。

在复合物中，二聚体HLHZ域主要被HEAT重复7和17的长 α 螺旋所夹持，它们像筷子一样夹住货物。与IBB域的 α 螺旋不同，HLHZ域的 α 螺旋垂直于进口in- β 超螺旋的中心轴。为了适应这种结合，importin- β 移动HEAT重复7和17的长螺旋，并采取更扭曲和开放的构象。这种方式带来的变化是戏剧性的，氨基端区域旋转20 \AA (22°)。与PTHRP-NLS和IBB域不同，importin- β 和SREBP-2的HLHZ域之间的结合主要通过疏水性相互作用实现；电荷互补性并不那么重要。Lee等(10)也指出，importin- β 序列中可能存在的重复提供了结合货物的方便途径，而且可能也适用于FG核孔蛋白(15)。

总的来说，importin- β :货物复合物的构象多样性表明，未结合的importin- β 是灵活的，可以适应不同的结合伙伴。这种灵活性与自由的importin- β 相比，更容易受到蛋白酶降解(3)。尽管高分辨率结构尚未获得，但importin- β 的同源物可能提供了一个类似的灵活支架，以促进对底物的识别(14)。相比之下，尽管importin- α 与多种底物结合，但这些结合方式并不涉及主要的构象变化，即使它们能加速货物的释放(17)。

That importin- β must bind to a remarkable range of different proteins to carry out both its nuclear trafficking and nuclear assembly tasks exerts extraordinary demands on molecular

recognition capabilities. Such demands are made even more pressing by the necessity for importin- β to bind to and release many of its partners in a spatially and temporally defined sequence. Molecular recognition usually involves matching of complementary interfaces between interacting proteins, and it is not uncommon for relatively small structural alterations to be present at the interface associated with binding, or for domains of molecules to rotate around a hinge. However, the conformational changes observed when importin- β binds to its partners, particularly when it binds to SREBP-2, involve an unusually large distortion. Although stacking of 19 tandem HEAT repeats generates an extensive interaction surface that enables importin- β to bind to a wide range of different molecules, importin- β supplements this ability with a remarkable degree of conformational flexibility. In this way, it is able to greatly increase its versatility in recognizing and releasing its different binding partners. As more crystal structures of importin- β bound to different cargo proteins become available, it will be fascinating to see how the interplay of surface structure and conformational dynamics is exploited to accomplish a variety of different tasks.

References

1. K. Weis, *Cell* **112**, 441 (2003).
2. Y. M. Chook, G. Blobel, *Nature* **399**, 230 (1999).
3. G. Cingolani et al., *Nature* **399**, 221 (1999).
4. I. R. Vetter et al., *Cell* **97**, 635 (1999).
5. Y. M. Chook, G. Blobel, *Curr. Opin. Struct. Biol.* **11**, 703 (2001).
6. E. Conti, E. Izaurralde, *Curr. Opin. Cell Biol.* **13**, 310 (2001).
7. R. Bayliss et al., *Cell* **102**, 99 (2000).
8. R. Bayliss et al., *J. Biol. Chem.* **277**, 50597 (2002).
9. G. Cingolani et al., *Mol. Cell* **10**, 1345 (2003).
10. S. J. Lee et al., *Science* **302**, 1571 (2003).
11. B. Fahrenkrog, U. Aebi, *Nature Rev. Mol. Cell Biol.* **4**, 757 (2003).
12. C. Zhang et al., *Curr. Biol.* **12**, 498 (2002).
13. A. Harel et al., *Mol. Biol. Cell* **14**, 4387 (2003).
14. N. Fukuhara et al., *J. Biol. Chem.* M309112200 (2003).
15. J. Bednenko et al., *J. Cell Biol.* **162**, 391 (2003).
16. C. Koerner et al., *J. Biol. Chem.* **278**, 16216 (2003).
17. Y. Matsuura et al., *EMBO J.* **22**, 5358 (2003).

OCEAN SCIENCE

The Many Shades of Ocean Blue

Hervé Claustre and Stéphane Maritorena

In satellite data over the South Pacific gyre, Earth's largest oceanic desert (see the figure), Dandonneau et al. [page 1548 of this issue (1)] have detected areas that are greener than the surrounding deep blue waters. They suggest that these "hotspots" are not

H. Claustre is at the Observatoire Océanologique de Villefranche, Laboratoire d'Océanographie de Villefranche, CNRS-INSU, 06238 Villefranche-sur-Mer, France. E-mail: claustre@obs-vlfr.fr S. Maritorena is at the Institute for Computational Earth System Science, University of California, Santa Barbara, CA 93106, USA. E-mail: stephane@icesc.ucsb.edu

vegetal oases, but rather result from residues and by-products of marine life accumulated by physical processes. This detrital material would be incorrectly interpreted as phytoplankton biomass from satellite ocean color data. The study provides further evidence that the current paradigm—the greener the open ocean waters, the higher their phytoplankton content—has its limitations.

For nearly 25 years, ocean color has been used as a proxy for algal biomass. Empirical algorithms (2) for mapping the global phytoplankton distribution from space rely on

mean statistical relationships between the chlorophyll a concentration [Chla] (a proxy for phytoplankton biomass) and the blue-to-green (B/G) reflectance ratio (an optical index for water color). The resulting [Chla] maps are used to estimate the contribution of phytoplankton to global CO₂ fixation (3) and investigate long-term changes in vegetal biomass (4).

However, there is increasing evidence that the simple empirical relationship between [Chla] and B/G ratio does not always hold. Which optically active components cause these deviations, and where do they occur? Answers to these questions should shed light on regional ecosystem structure and functioning.

Phytoplankton itself is one of the first candidates to be examined. Marine phyto-

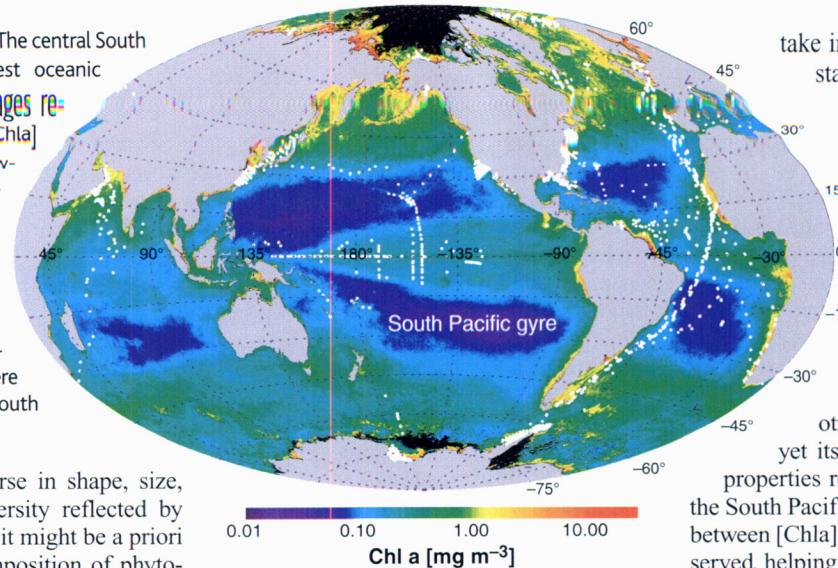
Colors of an oceanic desert. The central South Pacific gyre is Earth's largest oceanic desert. SeaWiFS satellite images reveal its consistently low [Chla] (deep blue and purple). However, some nuances in the blue color of these waters can be detected (1). Only 20% of available measurements (white symbols) for ocean color algorithms development have been collected in the Southern Hemisphere (and less than 2% in the South Pacific between 0° and 60°S).

plankton are highly diverse in shape, size, and pigmentation, a diversity reflected by their varying color. Thus, it might be a priori possible to track the composition of phytoplankton communities from space. For example, *Emiliania huxleyi* is covered with calcium carbonate plates that, when released in the water, give it a milky turquoise color, easily captured by satellite (5). *Trichodesmium* sp.'s gas vesicles and specific pigmentation may also allow its remote detection (6). However, apart from *E. huxleyi* and *Trichodesmium* sp., discriminating phytoplankton types from space is difficult, because detected nuances could easily be confounded with noise.

Besides phytoplankton, colored dissolved organic matter (CDOM) and submicrometer detritus particles also affect the optical properties of oceanic waters. CDOM is responsible for a large (sometimes dominant) fraction of the visible blue light absorbed by the water (7). Assessments of [Chla] from empirical ocean color algorithms can be skewed by the presence of such dissolved material.

Absorption by submicrometer particles is generally small compared to that of phytoplankton or CDOM. However, these particles are a major source of backscattered light in the open ocean. Underestimates of [Chla] at high latitudes have been attributed to low backscattering, possibly because of low concentrations of submicrometer particles, either detritus or living (bacteria, viruses) (8). Conversely, a phytoplankton bloom could rapidly be transformed into detrital material by viruses (9), leading to overestimates of [Chla].

Recent studies have also suggested that fine desert dust trapped in the upper layer of the ocean might depress the B/G ratio, causing overestimates of [Chla] (10). Dust deposition is associated with the dissolution of iron, an important phytoplankton fertilizer. Future studies aiming to assess the impact of desert dust deposition on marine biogeochemical cycles must discriminate between the enhanced backscattering due to the dust and the increased pho-



plankton biomass due to fertilization (11).

The story becomes even more complex with the presence of bubbles, which make the water appear greener (12). Hence, the rougher the sea state and the higher its bubble content, the more standard algorithms would overestimate [Chla].

Present empirical models are not well suited to capture the impact of these optically active components. Furthermore, ocean color algorithms have been established from data collected mostly in the Northern Hemisphere, with few data points from very oligotrophic areas. They might therefore not represent the Southern Hemisphere well, particularly the central part of the gyres, which also experience lower dust deposition. Semianalytical algorithms must be developed that explicitly

take into account the various substances that affect ocean color in both hemispheres (7, 13).

Further in situ investigations in the Southern Hemisphere are also needed, especially in remote areas such as the South Pacific gyre investigated by Dandonneau *et al.* (1) (see the figure). This vast oceanic biome is the most oligotrophic water body on Earth, yet its optical and biogeochemical properties remain largely unexplored. In the South Pacific gyre, new types of nuances between [Chla] and ocean color might be observed, helping to explain the various shades of ocean blue.

References

- Y. Dandonneau *et al.*, *Science* **302**, 1548 (2003).
- J. E. O'Reilly *et al.*, *J. Geophys. Res.* **103**, 24937 (1998).
- D. Antoine *et al.*, *Global Biogeochem. Cycles* **10**, 57 (1996).
- M. C. Gregg, M. A. Conkright, *Geophys. Res. Lett.* **29** (15), 10.1029/2002GL014689 (2002).
- P. Holligan *et al.*, *Nature* **304**, 339 (1983).
- A. Subramaniam *et al.*, *Deep Sea Res. II* **49**, 107 (2002).
- D. A. Siegel *et al.*, *J. Geophys. Res.* **107**, 3228 (2002).
- H. M. Dierssen, R. C. Smith, *J. Geophys. Res.* **105**, 26301 (2000).
- W. M. Balch *et al.*, Abstract 663, ASLO/TOS Ocean Research Conference, Honolulu, Hawaii, 15 to 20 February 2004.
- H. Claustre *et al.*, *Geophys. Res. Lett.* **29** (10), 10.1029/2001GL014056 (2002).
- J. K. B. Bishop *et al.*, *Science* **298**, 817 (2002).
- D. Stramski, J. Tegowski, *J. Geophys. Res.* **106**, 31345 (2001).
- H. Loisel, D. Stramski, *Appl. Opt.* **39**, 3001 (2000).

IMMUNOLOGY

The Paracaspase Connection

Li Yu and Michael J. Lenardo

Successful immune responses depend on the regulation of many genes to guide the biological effects of T and B lymphocytes. To accomplish this, various incoming signals must be integrated and then distributed to a diverse set of gene expression outputs. The transcription factor NF-κB serves as a key signal integrator in this process in ways that no one could have imagined when it was first identified as a DNA binding factor (1, 2). On page 1581 of this issue and in the most recent issue of *Immunity*, the laboratories of Dixit and Mak, respectively, reveal that a mouse pro-

tein called MALT1/Paracaspase (MPC) is a crucial regulator of NF-κB activity in B and T cells (3, 4).

Numerous cytokines, chemical mediators, and cell surface receptors, including the antigen receptors of B and T lymphocytes, activate NF-κB. Nuclear NF-κB can bind to and regulate the DNA control elements of a wide variety of immune response genes [reviewed in (5)]. The centerpiece of the NF-κB pathway is the IκB kinase (IKK) complex (6). IKK is formed from three subunits (IKKα, IKKβ, and IKKγ/NEMO) that transduce diverse upstream signals into the phosphorylation and degradation of IκB, the inhibitory binding partner that restrains NF-κB in the cytoplasm. When IκB is degraded, NF-κB is

The authors are in the Laboratory of Immunology, National Institute of Allergy and Infectious Diseases, Bethesda, MD 20892, USA. E-mail: mlenardo@nih.gov