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## LETTERS

edited by Jennifer Sills

### Promoting Engineering

IN HIS EDITORIAL "SCIENCE IN THE WHITE HOUSE" (1 MAY, P. 567), Office of Science and Technology Policy (OSTP) Director John Holdren outlined the role that OSTP plays in the formulation of science and technology policy in President Obama's White House.

America's science, technology, and engineering infrastructure can be used to drive America's economic recovery. Now is the time to add "Engineering" to Dr. Holdren's title and the organization he directs. Engineering is the practical application of science to commerce or industry. The multitude of economic recovery options outlined by the president (for example, a new energy grid, green energy solutions, and efficacious health care) cannot happen without engineering expertise. History shows us an encyclopedia of technological advances that simply would not have occurred without strong engineering expertise. From radar, to nuclear weapons and energy, to space travel, to robotic

**Director John P. Holdren.** Is it time to add "Engineering" to the Office of Science and Technology Policy?



EUGENE C. ECKSTEIN

surgery and engineered tissue implants, the tripartite arrangement of science, technology, and engineering has always been the combination for successful advancement.

What better way to raise the stature of engineering than to include it in the title of the individual tasked with advising the president on how to capitalize on America's science, technology, and engineering expertise? This change is fully consistent with President Obama's stated desire that more young people choose engineering as their career.

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### Do Not Underestimate Science

IN THE LETTER "THE HARD PROBLEM" (24 April, p. 463), E. J. Neafsey comments on a previous Letter by M. J. Farah and N. Murphy ("Neuroscience and the soul," 27 February, p. 1168), which claimed that neuroscience may eventually be able to explain all aspects of being human. Neafsey asserts that Farah and Murphy's Letter demonstrates "a somewhat naïve and simple faith in scientific progress." He then refers approvingly to the philosopher David Chalmers's characterization of consciousness as the "hard problem" that will forever defy a reductionist, scientific explanation (1).

However, philosophers deal in belief systems and personal opinions, not in natural laws and facts. They ask interesting questions and pose challenging dilemmas, but they have an unimpressive historical record of prognostication. August Comte, father of positivism, wrote in 1835 that we shall never know what stars are made of (2). A few decades later, the chemical composition of stars was deduced by spectral analysis of their light (3).

Francis Crick, a scholar with a far better track record of prediction, stated in an interview in 1996, "It is very rash to say that things are beyond the scope of science" (4).

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4. Interview "The scientific search for the soul" with Jeffrey Mishlove as part of the *Thinking Allowed* series, NPR (1996).

### Immune System: Success Owed to a Virus?

IN HIS NEWS FOCUS STORY "ON THE ORIGIN of the immune system" (1 May, p. 580), J. Travis addresses the mysterious origins of the immune system's ability to create specific antibodies. He first describes how this occurs: *RAG* enzymes mediate a recombination process that results in specific lymphocyte receptors and immunoglobulin. He then explains the pre-

vailing theory about the origins of the process: These *RAG* enzymes were originally transposons. However, no specific transposon with these properties has been identified. In fact, the closest transposon relative to the *RAG1* protein is the so-called transib family of DNA transposons, which do not contain anything resembling a *RAG2* protein (1).

I recently proposed an alternative explanation. Numerous other enzymes—including retroviral integrases, RNase H, the RNA Induced Silencing Complex Argonaute proteins, and possibly other DNA viruses—use a similar magnesium-dependent catalytic site

### Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 3 months or issues of general interest. They can be submitted through the Web ([www.submit2science.org](http://www.submit2science.org)) or by regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

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for nucleic acid cleavage (2). More plausible than a “*RAG* transposon” is the insertion of an infectious DNA virus resembling a herpes virus adjacent to the *RAG2* protein in a primordial deuterostome (3). DNA viruses such as the herpes viruses encode a recombinase resembling the *RAG1* protein more closely than that of DNA transposon transposases, and they are also part of the regulatory network shared by the *RAG* genes and recombination of the VDJ regions, consistent with the subsequent arms race between herpes viruses and the immune system.

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## Immune System: “Big Bang” in Question

J. TRAVIS’S NEWS FOCUS STORY “ON THE ORIGIN OF THE IMMUNE SYSTEM” (1 May, p. 580) strengthens the idea that there exists a “Big Bang” in the evolution of the immune system, namely the move from innate to adaptive immunity. Yet evidence accumulated during the past 10 years has shown that this idea requires caution, for at least three reasons: (i) Immune memory, supposedly a characteristic of adaptive immunity and therefore of higher vertebrates, does in fact exist in invertebrates (1, 2). (ii) Nonvertebrate immunity no longer appears to be “unspecific”; many forms of immune specificity exist in animals, and even in plants (3). (iii) The adaptive immune system never works on its own [a little-known fact first revealed 20 years ago (4) but subsequently neglected]. An antigen that is recognized by the adaptive immune system but not by the innate immune system will not, in general, trigger an immune response (5).

These studies show that immunity is ubiquitous in nature and that the boundary between adaptive and innate immunity is not as clear cut as has been claimed for decades (6). In light of these results, looking for evidence

for the immunological “Big Bang” is probably an inadequate strategy for studying the evolution of immunology.

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5. R. M. Steinman, D. Hawiger, M. C. Nussenzweig, *Annu. Rev. Immunol.* **21**, 685 (2003).
6. E. Vivier, B. Malissen, *Nat. Immunol.* **6**, 17 (2005).

## Immune System: Promethean Evolution

IN HIS NEWS FOCUS STORY “ON THE ORIGIN OF THE IMMUNE SYSTEM” (1 May, p. 580), J. Travis overlooked some important components of the Darwinian evolution of the acquired immune response. Travis, quoting molecular biologists, ascribes the “Big Bang” in immunological evolution to the adaptation of *RAG1* and *RAG2* enzymes from transposons (or something similar) to gene-segment splicers. However, it is possible that a mechanism that permitted this splicing function existed previously and that the true “Big Bang” was the development of the multiple V, D, and J regions—those regions that are spliced in order to create specific antibodies.

But even this is not the most interesting aspect of immunological evolution. Many years ago, Susumo Ohno, citing the Greek legend of the Titan brothers—forward-looking Prometheus and backward-looking Epimetheus—speculated that in contrast to almost all other physiological functions, immunology has developed an anticipatory mechanism (1, 2). Most physiological functions are Epimethean: They start with a primitive mechanism and then gradually adapt to meet environmental challenges. Thus, everything in Epimethean evolution depends on the response to past events and challenges.

In contrast, immunology functions as a forward-looking system (3). The evolution of

the various B cell gene segments, together with the adaptation of mechanisms to join them combinatorially, has enabled the generation of a magnificently large repertoire of specific antibodies. Almost any new pathogenic component will thus be covered, which is important in an environment where pathogens change far faster than the vertebrates can adapt.

Here was the real “Big Bang.” But then normal Darwinian (Epimethean) evolution intervened, as might have been expected. It entered the process in many forms. For example, given that the generator of diversity would necessarily produce lymphocytes that are specific to both foreign and self antigens, the latter had to be down regulated by various mechanisms to avoid the development of compromising autoimmunities.

We do not know precisely when the change from Epimethean (reacting) to Promethean (anticipating) took place, and there are no satisfactory intermediate forms (“missing links”) to indicate the steps along the way. But absence of proof is not proof of absence. We may with confidence recognize the Promethean “Big Bang” in immunology as one of the high points in the workings of Darwinian evolution.

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#### References and Notes

1. S. Ohno, *Perspect. Biol. Med.* **19**, 527 (1976).
2. S. Ohno *et al.*, *Progr. Immunol.* **4**, 577 (1980).
3. The neural networks of the brain are the only other known system with this capability.

## CORRECTIONS AND CLARIFICATIONS

**News Focus:** “A medical mystery in middle China” by R. Stone (12 June, p. 1378). On page 1380, in the first paragraph, the recommended daily intake of selenium should have been 70 micrograms, not 70 milligrams.

**News of the Week:** “Report finds no gender bias in faculty hiring, resources,” by J. Mervis (5 June, p. 1250). Sally Shaywitz, Yale University professor of pediatrics and co-director of the Center for Dyslexia and Creativity, served as co-chair of the report by the National Research Council, *Gender Differences at Critical Transitions in the Careers of Science, Engineering, and Mathematics Faculty*.

**News Focus:** “Biologists struggle to solve bat deaths” by R. Zimmerman (29 May, p. 1134). On page 1135, the statement that bats “arouse and triple their body temperature” was incorrect. During an arousal, the body temperature of a bat will increase approximately 10°C to about 24° to 30°C.

**Reports:** “Human substantia nigra neurons encode unexpected financial rewards” by K. A. Zaghloul *et al.* (13 March, p. 1496). Equation 1 in this paper was incorrect. The correct equation is as follows:

$$E_d[n] = 0.5 + 0.5 \sum_{i=1}^{n-1} R_d[n-i] \alpha_i^{-\tau} \quad n = 2, \dots, N$$