LETTERS

Retraction

IN THE REPORT "LYSOPHOSPHATIDYLCHOLINE as a ligand for the immunoregulatory receptor G2A" by Kabarowski *et al.* (*1*), we concluded that the lysolipid lysophosphatidylcholine (LPC) and a related molecule, sphingosylphosphorylcholine (SPC), directly bound to and served as agonists of the G protein–coupled receptor G2A. Concerns about the reproducibility of portions of the data lead us to retract this paper.

Critical data in the paper showed direct and specific binding of radiolabeled LPC or SPC to G2A in cell homogenates. The primary data generated by Dr. Zhu for these binding studies are not available for evaluation. During investigation of engineered point mutants of the G2A receptor, we were unable to repeat these radiolabeled ligand-binding studies following similar protocols. Alternative protocols with purified membrane fractions (*2*, *3*) expressing high levels of the G2A receptor or whole-cell–based radioligand binding studies (*4*–*6*) also failed to establish direct G2A binding. This calls into question the major conclusion that LPC and SPC are direct ligands for G2A.

In attempts to reproduce LPC stimulation of intracellular calcium responses, only 50% of single MCF 10A cells expressing G2A responded to LPC in single-cell assays identical to those originally employed. Only about half of these gave robust responses similar to those shown in the *Science* paper. Similar assays of intracellular calcium release using bulk cell populations failed to detect any reproducible G2A-mediated response to LPC. Data generated by Dr. Kabarowski demonstrating cellular migration dependent on LPC addition and G2A receptor expression have been reproduced and extended in independent work (*7*–*9*). We believe these data to be accurate and reproducible and therefore conclude that G2A is an effector of LPC action in certain cell-types. However, these data cannot distinguish between a direct action of the lysolipid on the receptor and an indirect action in which the lysolipid modifies another receptor or process that in turn regulates the G2A receptor.

We sincerely regret the confusion that this paper may have caused for the readers of *Science*.

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Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 6 months or issues of general interest. They can be submitted through the Web (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.

Scientific Priorities in North Korea

IN HIS EDITORIAL "TALKING WITH NORTH Korea" (17 Sept., p. 1677), N. P. Neureiter endorses the idea of scientific cooperation as a tool for engaging the isolated Democratic People's Republic of Korea. This view is echoed by R. Stone in his article "A wary pas de deux" (News Focus, 17 Sept., p. 1696), and each recommends an approach that is both constructive and cautious. We agree but, along with caution, we recommend more urgency to the engagement process. The international and Korean scientific communities should first concentrate on still-widespread food insecurity and a largely dysfunctional health care system before turning its attention to such things as cloning rabbits or breeding supergoats, as mentioned in the article.

Researchers performing embryo transfer on a rabbit in a clean room at the Institute of Experimental Biology in Pyongyang, North Korea.

CREDIT: R. STONE/*SCIENCE*

Throughout the 1990s, North Korea experienced what even its leaders acknowledged was a "march through hardship," including a famine whose most severe years were in 1996 and 1997. Up-to-date, empirical data on mortality were not permitted to be collected inside the country. It became necessary to adopt an indirect approach to data collection, which we did by interviewing a total of 2692 North Korean migrants and asylum seekers who had crossed into China in 1999 to 2000.

In a retrospective household survey of the period 1995–98, we found evidence of elevated crude (all ages, all causes) mortality (peaking at 31.5 per 1000 in 1997), declining fertility, and rising out-migration (*1*, *2*). About 35.8% of deaths (353 of 986) to the 9958 household members during the interval were linked to malnutrition and infectious disease, compared with 11.6% of deaths in 1986 (*3*). A health care system that once produced life expectancies and infant mortality rates comparable to those of South Korea on approximately one-tenth of South Korea's per capita GNP is now overwhelmed by a rising tide of communicable disease, scarce supplies of essential drugs, antiquated equipment, and shortages of heating fuel and electricity in the hospitals and clinics.

In the face of these critical needs, North Korea is increasing some restrictions on foreign aid organizations working inside the country (*4*). Western scientists must join with colleagues in South Korea, China, and elsewhere in Asia to engage with our counterparts in North Korea to promote innovations in the agricultural and health sciences and many other fields, while understanding that North Korean scientists and intellectuals are an elite political class who derive their status and their livelihood from the state. Science to promote state prestige may be different from that which is in the immediate public interest. Engagement must seek to advance science in North Korea for the betterment of all its people.

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Response

I CERTAINLY HAVE NO DISAGREEMENT WITH THE priorities suggested for engagement with

North Korea by Robinson, Lee, and Burnham. The only problem is that it takes two to tango. I recall that the United States discussed the general idea of exchanges with North Korea at the time of Secretary of State Albright's trip there—the idea was rejected by the North Koreans. The intriguing element of the present initiative is that North Korea has actually proposed the start of some cooperative scientific activity ("A wary pas de deux," R. Stone, News Focus, 17 Sept., p. 1696). If this is real and if they are truly prepared to follow up, I think we should accept this opportunity to begin meaningful cooperation with the North Korean scientific community. Until we have taken a first step toward a cooperative relationship in nonsensitive areas of science, I think it is not useful to try to dictate the priorities for their limited capacity to cooperate with us.

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North Korea and Renewable Energy

IN HIS NEWS FOCUS ARTICLE "NUKES FOR windmills: quixotic or serious proposition?" (17 Sept., p. 1698) (and the broader article on North Korean science, "A wary pas de deux," 17 Sept., p. 1696), R. Stone quotes an unofficial envoy of the Democratic People's Republic of Korea (DPRK) as suggesting that the DPRK would be willing to abandon its nuclear program in exchange for clean energy technologies. The desire of North Koreans for renewable small-scale energy systems is consistent with what we have learned in our contacts with DPRK researchers and engineers in the context of our North Korean wind power project (*1*).

The key energy elements of the 1994 Agreed Framework between the United States and the DPRK—the two large (1 GW) light-water reactors (LWRs) and the 500,000 tonnes/year of heavy fuel oil that were to have been provided to the DPRK until the reactors were completed—were political compromises with severe practical drawbacks. The LWRs could not be operated safely without an interconnection to South Korea's grid, and the bottom-of-the-barrel, high-sulfur heavy fuel oil has reportedly accelerated degradation of an already dilapidated thermal power plant fleet (*2*).

Small and mini hydroelectric systems are a good match to the DPRK's terrain and climate, and parts of the DPRK seem to have at least a fair wind resource. Renewable options put the focus on economic redevelopment on the local level, rather than on the less tractable national level.

Renewable energy systems are not going to be enough by themselves to makeover the DPRK's energy sector in the near term, but can certainly contribute to the redevelopment of the DPRK energy infrastructure. They are also relatively resistant to diversion to military use and would engage a broad group of North Korean citizens with visitors from the outside as technological skills are transferred.

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Inflammation and Life-Span

IN THEIR REVIEW "INFLAMMATORY EXPOSURE and historical changes in human life-spans" (17 Sept., p. 1736), C. E. Finch and E. M. Crimmins reinforce earlier suggestions that many diseases and disabilities of older age have their roots in previous exposures to infectious agents and other sources of inflammation in early life. Interesting developments of the inflammatory hypothesis for geriatric illness may come from genetic studies on inflammatory molecules (*1*). Our recent findings allow us to suggest that different alleles at different cytokine genes coding for pro- (IL-6 or IFN-γ) or anti-inflammatory (IL-10) cytokines may affect individual life-span expectancy by influencing the type and intensity of the immune-inflammatory responses against environmental stressors (*2–5*). The conclusion is that people who are genetically predisposed to weak inflammatory activity have a better chance of living longer if they don't catch any infectious diseases.

Our data prompt consideration of the role that antagonistic pleiotropy plays in diseases and in longevity (*6*). Our immune system has evolved to control pathogens, so pro-inflammatory responses are likely to be evolutionarily programmed to resist fatal infections (*7*). Yet genetic backgrounds promoting pro-inflammatory responses play an opposite role in cardiovascular diseases and in longevity (*8–10*), such that cardiovascular diseases are a late consequence of evolutionary programming for a pro-inflammatory response to resist infections at an early age. Genetic polymorphisms responsible for a low inflammatory response may better control inflammatory responses involved in atherogenesis and reduce the risk of atherogenesis complication. So, these polymorphisms might result in an increased chance of long life-span in an environment with reduced antigen (i.e., pathogens) load.

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C. E. FINCH AND E. M. CRIMMINS' REVIEW on the role of reduced inflammation and increased human life-span was most compelling ("Inflammatory exposure and historical changes in human life-spans," 17 Sept., p. 1736). The link between nutrition and inflammation was especially intriguing, especially for those of us involved in Darwinian nutrition issues. With the advent of agriculture, human communities introduced grains, cereals, and other foods whose ratio of omega-6 to omega-3 fatty acids is out of kilter with ancient hominid consumption patterns, a shift that tends to aggravate inflammatory and autoimmune diseases (the pre-agricultural omega-6:omega-3 ratio was approximately 2:1; the ratio in contemporary Americans is as high as 10:1) (*1*). This is being addressed to some degree by food manufacturers and consumer choices, although there is vast room for improve-

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ment. And although it may indeed turn out that, as Finch and Crimmins suggest, "future increases in life expectancy from reduced inflammatory causes may be relatively small," quality of life should be improved considerably as informed populations shift their dietary and life-style patterns to ones that are in harmony with our evolved nature.

I would suggest the elimination of dietary wheat and rye. These grains are especially rich in alkylresorcinols—phenolic lipids that were found to significantly raise thromboxane A2 levels in platelets (*2*). These compounds are absorbed in vivo (*3*). In patients with platelet adherence under way, the release of thromboxane A2 together with ADP can result in the evolution of a platelet thrombus that can lead to a myocardial infarction. Interestingly, it is well established that myocardial infarctions occur most often in the morning hours (*4*–*6*). It is tempting to posit that the inflammation-driven or informed process that underlies thrombus formation may be accelerated by a post-breakfast dietary influx of fats and cereal-derived alkylresorcinols.

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Response

WE AGREE WITH THE DARWINIAN PERSPECTIVES in these Letters, which extend our briefly noted point (p. 1736) that adaptive inflammatory responses to short-term infections can show antagonistic pleiotropy with delayed adverse effects during aging. Payne further notes that diets since the neolithic have increasingly included cultivars containing pro-inflammatory and prothrombotic micronutrients. Of course, these staples were widely used during the 250 years we considered in our Review. It is hard to determine how much of the recent increased longevity is due to improved resistance to infections by consumption of fresh fruit and vegetables year round. However, modern populations show synergistic effects of low levels of antioxidants and high levels of inflammation on old age mortality (*1*).

A further Darwinian question raised by Caruso *et al.* is the role of polymorphisms in genes that influence inflammation and that also show antagonistic pleiotropy. Another example is the apolipoprotein E isoforms (*2*) in which apoE4, the ancestral allele, is associated with elevated cholesterol and can be proinflammatory and prothombotic. The adaptive value of apoE4 during the early reproductive years may depend on the levels of intercurrent infections, such that apoE3, which reduces the risk of dementia, may have become increasingly important to longevity advances as infectious disease waned. Because IL-10 polymorphisms, mentioned by Caruso *et al.*, show evidence of active selection in high disease environments (*3*), one may ask if shifts in inflammatory gene polymorphisms have contributed to the historical changes in longevity.

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