

tion with ALPS in the Italian population (odds ratio, 28.6; 95 percent confidence interval, 1.9 to 830.6).

Third, the unpublished data on two additional perforin mutations in the patient described in the report that Rieux-Laucat et al. cite² do not rule out a role for N252S, since three causal mutations of a gene in the same patient have been reported in persons with other diseases.^{3,4} Finally, the detection by Rieux-Laucat et al. of a *Fas* mutation and N252S in a patient with ALPS and his healthy father supports the possibility, suggested in our report, that other environmental or genetic factors may contribute to ALPS.

Rita Clementi, M.D.

Policlinico San Matteo
27100 Pavia, Italy

Marina Ferrarini, M.D.

Marco Bregni, M.D.

Istituto Scientifico San Raffaele
20132 Milan, Italy
marco.bregni@hsr.it

1. Molleran Lee S, Villanueva J, Sumegi J, et al. Characterisation of diverse PFR1 mutations leading to decreased natural killer cell activity in North American families with haemophagocytic lymphohistiocytosis. *J Med Genet* 2004;41:137-44.

2. Stepp SE, Dufoucq-Lagelouse R, Le Deist F, et al. Perforin gene defects in familial hemophagocytic lymphohistiocytosis. *Science* 1999;286:1957-9.

3. Monaghan KG, Feldman GL, Barbarotto GM, Manji S, Desai TK, Snow K. Frequency and clinical significance of the S1235R mutation in the cystic fibrosis transmembrane conductance regulator gene: results from a collaborative study. *Am J Med Genet* 2000;95:361-5.

4. Hojo S, Fujita J, Miyawaki H, Obayashi Y, Takahara J, Bartholomew DW. Severe cystic fibrosis associated with a deltaF508/R347H + D979A compound heterozygous genotype. *Clin Genet* 1998;53:50-3.

Federal Funding for Stem-Cell Research

TO THE EDITOR: In your editorial (Oct. 21 issue),¹ you correctly state that if U.S. biomedical researchers are sidelined in pursuing stem-cell research, “our children and grandchildren may need to leave the United States to benefit from treatments other nations are currently developing.” This result would be unfortunate but surmountable. Worse for the American scientific community would be the

“brain drain” effect on U.S. scientists who would leave to pursue cutting-edge research elsewhere.

Robert Matz, M.D.

Mount Sinai School of Medicine
New York, NY 10029-6574
robert.matz@msnyuhealth.org

1. Drazen JM. Embryonic stem-cell research — the case for federal funding. *N Engl J Med* 2004;351:1789-90.

Diastolic Heart Failure

TO THE EDITOR: Aurigemma and Gaasch (Sept. 9 issue)¹ do not mention diabetes mellitus as a frequent cause of diastolic heart failure. In the Strong Heart Study,² the investigators reported an extremely high prevalence (80 percent) of left ventricular diastolic dysfunction among normotensive persons with diabetes. The relationship was independent of other confounding factors, such as blood pressure, systolic function, and age, and it was stronger for patients with worse glycemic control. Others have also reported a high frequency of diastolic dysfunction among normotensive patients with diabetes.³ Increased matrix collagen, interstitial fibrosis, myocardial microangiopathy, and myocyte hypertrophy are common findings in the diabetic heart⁴ that can lead to diastolic dysfunction. Tight glycemic control

decreases the risk of heart failure in patients with diabetes,⁵ although the most appropriate treatment regimen is uncertain.

Miguel A. Arias, M.D.

Alberto Alonso, M.D.

Francisco García-Río, M.D.

Hospital Universitario La Paz
28046 Madrid, Spain
maapalomares@secardiologia.es

1. Aurigemma GP, Gaasch WH. Diastolic heart failure. *N Engl J Med* 2004;351:1097-105.

2. Liu JE, Palmieri V, Roman MJ, et al. The impact of diabetes on left ventricular filling pattern in normotensive and hypertensive adults: the Strong Heart Study. *J Am Coll Cardiol* 2001;37:1943-9.

3. Boyer JK, Thanigaraj S, Schechtman KB, Perez JE. Prevalence of ventricular diastolic dysfunction in asymptomatic, normotensive patients with diabetes mellitus. *Am J Cardiol* 2004;93:870-5.