

different ribosomal proteins has been characterized; Diamond-Blackfan anemia is associated with haploinsufficiency in multiple different ribosomal proteins (but not RPSA) and results in bone marrow failure as well as multiple developmental defects. However, in these patients, there is no evidence of splenic abnormalities, and the current study found no evidence of hematologic abnormalities (or developmental abnormalities) in the patients harboring the RPSA mutations.

REVIEWER COMMENTS. The importance of this study is that many of these cases developed invasive bacterial infection early in childhood, most often involving *Streptococcus pneumoniae* (61%) with a high mortality rate (45%) (Mahaoudi N, et al. *J Pediatr.* 2011;158[1]:142–148, 148.e1). Thus, isolated congenital asplenia has overlapping features with recently defined TLR defects (eg, MyD88, IRAK4 deficiency) in that both are associated with childhood invasive bacterial infections that have a high mortality rate. Consequently, any child with invasive bacterial infection should be evaluated for absence of a spleen (presence of Howell-Jolly bodies, directed imaging studies) as well as studied for other congenital immune defects associated with this clinical presentation. In view of the autosomal dominant transmission of some cases of isolated congenital asplenia, family members of an affected patient should also be evaluated for possible asplenia.

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HIV AND INFECTIOUS DISEASES

Chronic Progressive HIV-1 Infection Is Associated With Elevated Levels of Myeloid-Derived Suppressor Cells

Vollbrecht T, Stirmer R, Tufman A, et al. *AIDS.* 2012;26(12):F31–F37

PURPOSE OF THE STUDY. Myeloid-derived suppressor cells (MDSC) consist of a heterogeneous population of progenitor cells and immature myeloid cells that are potent suppressors of T-cell function in many tumor models. The purpose of this study was to evaluate the possibility that MDSC play a role in HIV-induced immunosuppression.

STUDY POPULATION. Ninety-seven patients participated in this study: 16 healthy controls; 20 HIV-infected individuals with suppressed viral loads; 49 HIV-infected treatment-naive individuals; 2 individuals with hepatitis C co-infection; 4 HIV-infected individuals failing to respond to treatment; and 8 individuals with lung cancer as positive controls.

METHODS. Flow cytometry analysis was performed on freshly isolated peripheral blood mononuclear cells. MDSC were defined as CD11b+CD14-CD33+CD15+.

CD4+CD25+, FoxP3+ regulatory T cells were also analyzed. Mixed lymphocyte reactions and proliferation assays were used to measure suppressor function.

RESULTS. Subjects with progressive or chronic uncontrolled HIV infection had significantly higher levels of MDSC than healthy controls. Subjects with lung cancer, as expected, had elevated MDSC. In HIV-infected individuals, percent MDSC correlated positively with elevated viral load (>50 000/mL) and low CD4 count (<250/mm³). In addition, effective antiretroviral therapy was associated with normalization of MDSC number; individuals with elevated MDSC before antiviral therapy had significant reductions in MDSC after initiation of therapy. MDSC number was correlated with generation of CD4+CD25+FoxP3+ regulatory T cells. Finally, MDSC directly impaired the proliferative capacity of T cells of healthy donors and HIV controllers.

CONCLUSIONS. Uncontrolled HIV infection is associated with elevated levels of MDSC. These cells potentially contribute to the impaired T-cell responses characteristic of progressive HIV disease.

REVIEWER COMMENTS. The variety of hematopoietic cells seems endless, and as new cell types are defined, they routinely seem to be affected by HIV infection. MDSC are a case in point. The relevance of these cells in tumor biology has recently been better defined. It has long been known that chronic inflammation creates a tumor-inducing environment. It is now speculated that infiltrating MDSC inhibits effective immunologic control of evolving malignant cells. The current study suggests that MDSC may contribute to the immunopathogenesis of HIV. Are these cells contributing to the immunologic suppression associated with HIV, or are they a regulatory response to HIV-associated persistent immune activation? As described in an accompanying Editorial Comment (Macatangay BJ, et al. *AIDS.* 2012;26[12]:1567–1569), dampening the effects of MDSC could be important in purging latent HIV reservoirs in approaches aimed at curing HIV disease. However, understanding the immunoregulatory networks involved in HIV pathogenesis is likely critical for the design of effective HIV immune-based therapies.

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Vaccine-Induced Plasma IgA Specific for the C1 Region of the HIV-1 Envelope Blocks Binding and Effector Function of IgG

Tomares GD, Ferrari G, Shen X, et al. *Proc Natl Acad Sci U S A.* 2013;110(22):9019–9024

PURPOSE OF THE STUDY. A recently completed Phase III vaccine trial demonstrated a 32% estimated efficacy. An

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