onset breast cancer in two aunts. The patient’s mother had a cerebellar astrocytoma, two vaginal tumors, and a malignant nevus (Fig. 2A).

The germ-line PTEN genes of the child and her father had a base change, c.334C→G. Although this change putatively encodes an L112V missense mutation, PTEN messenger RNA (mRNA) analysis instead revealed activation of a cryptic splice site (Fig. 2B). The germ-line TP53 gene in the proband, her sister, and her mother contained an R282W deleterious missense mutation. Thus, the proband had inherited deleterious mutations in both TP53 and PTEN.

In tumors from patients with the Li–Fraumeni syndrome or Cowden’s syndrome, there is often somatic mutation or silencing of the second copy of the tumor-suppressor gene.3 The granulosa-cell tumor, xanthoastrocytoma, and multiple liposarcoma samples from our proband revealed no somatic mutations in TP53 or PTEN. Loss of heterozygosity was not detected in TP53, but it was detected in PTEN in the granulosa-cell tumor and the liposarcoma specimen after chemotherapy (but not in specimens from the initial resection and lung metastasis) (Fig. 2C). The finding that several of the patient’s tumors did not have loss of heterozygosity or somatic mutations was also reported for tumors from a mouse model that was doubly heterozygous for p53 and Pten mutations.4

The types and numbers of tumors that developed in the proband by 4 years of age are not typical of the Li–Fraumeni syndrome or Cowden’s syndrome, and four malignant conditions are expected to develop in only 2% of patients with the Li–Fraumeni syndrome.1,5 This tumor spectrum may reflect the intricate coregulation of the TP53 and PTEN proteins.4 Clinically, it may be useful to sequence in parallel multiple cancer-associated genes of patients with unusual cancer phenotypes.

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Cytomegalovirus Immunity after Vaccination with Autologous Glioblastoma Lysate

TO THE EDITOR: Glioblastoma is a malignant brain tumor with overall survival rates of less than 3.3% at 5 years.1 Few effective treatments are available. The durability of a radiographically defined response to treatment is limited, and median survival is less than 2 years.

We are conducting a phase 1 trial of autologous dendritic-cell vaccination as adjunctive therapy in glioma, a study that has been approved by the institutional review board at the University of California, Los Angeles. All patients are treated with surgery, standard radiotherapy, and temozolomide, followed by vaccination with dendritic cells that are pulsed with an autologous tumor lysate. To date, we have enrolled 14 patients with newly diagnosed glioblastoma (World Health Organization grade IV).

Here we describe Patient 4-908 with glioblastoma who was enrolled in the trial and in whom a robust CD8+ T-cell response to the pp65 immunodominant epitope of human cytomegalovirus (CMV) began immediately after one injection of
The patient's tumor appeared to be infected with CMV. Immunohistochemical staining of tumor tissue showed focal expression of human CMV pp65 in the tumor but not in a tumor from Patient 2-261 with an HLA-A0201–positive glioblastoma, in whom a CMV-specific immune response did not occur after vaccination. In Patient 4-908, serum cytokine measurements revealed increased levels of tumor necrosis factor α after one dendritic-cell vaccination, a response that peaked 2 weeks after the second vaccination (Fig. 1C).

An association has been discovered between human CMV and malignant gliomas.\(^3\)\(^-\)\(^5\) We found that a CMV-specific CD8+ T-cell response was induced in a patient with glioblastoma after therapeutic vaccination with dendritic cells pulsed with an autologous tumor lysate. Our results suggest that the presence of human CMV in glial cells could serve as an immunotherapeutic target in the vaccine (Fig. 1A and 1B). We found that after vaccination, 4.4% of the patient's CD8+ T cells were specific for pp65. The vaccination was not associated with any systemic symptoms. Local lymphadenopathy was observed at the time of the expansion of the human CMV–specific T cells.\(^2\)

The vaccine (Fig. 1A and 1B). We found that after vaccination, 4.4% of the patient's CD8+ T cells were specific for pp65. The vaccination was not associated with any systemic symptoms. Local lymphadenopathy was observed at the time of the expansion of the human CMV–specific T cells.\(^2\)
glioblastoma. The relative ease of eliciting an immune response against viral antigens contrasts with the difficulty of immunization against “self” tumor antigens. This case highlights the potential for targeted vaccination strategies with the use of dendritic cells as an adjunct to standard treatments for glioblastoma, although multicenter, randomized studies will be necessary to demonstrate clinical efficacy.

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