are a minority, there must be in humans at least one other gene involved in this pathway.

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References


**To the editor:**

**Down-modulation of the C/EBPα transcription factor in core binding factor acute myeloid leukemias**

Acute myeloid leukemia (AML) is characterized by abnormalities frequently affecting transcriptional control elements, leading to differentiation block.1 C/EBPα is one of the most frequently involved transcription factors, being disrupted by point mutations in 7% to 11% of cases.2,3 In the setting of the frequently involved transcription factors, being disrupted by the C/EBPα/H9251 fusion (35 644 vs 105 173 C/EBPα/H9251 copies/10⁴ ABL copies, P = .0001), which showed values similar to those found in healthy controls (77 865 and 56 845 C/EBPα copies/10⁴ ABL copies in normal BM and PB, respectively). Moreover, the comparison between the C/EBPα expression obtained in BM samples from patients with AML/ETO-positive FAB M2 AML compared with AML/ETO-negative FAB M2 cases demonstrated a highly significant difference (32 523 vs 71 983 C/EBPα copies/10⁴ ABL copies, P = .0001). Similar differences were detected by analyzing FAB M4 cases with and without the CBFB/MYH11 fusion (35 644 vs 105 173 C/EBPα copies/10⁴ ABL copies, P = .0002). The Western blot assays further confirmed these differences noted during follow-up; by contrast in the 4 CBF AML patients who relapsed (red lines), C/EBPα expression was downmodulated again. By contrast, no differences in C/EBPα expression were noted during follow-up in the 6 patients characterized by normal karyotype (green lines). Of these 6 patients, 4 persisted in CR and 2 relapsed.


Figure 1. C/EBPα expression in the different FAB subtypes of AML and during follow-up. (A) C/EBPα expression is significantly downmodulated in FAB M2 AML patients characterized by the (t(8;21)) and in FAB M4 characterized by inv(16) with respect to those with normal karyotype. The mean values are defined by horizontal bars. (B) C/EBPα expression is significantly downmodulated in CBF AML patients at diagnosis, and it is up-regulated during chemotherapy-induced complete remission (CR). In the 8 CBF AML patients who persisted in CR (blue lines), C/EBPα expression did not change during follow-up; by contrast in the 4 CBF AML patients who relapsed (red lines), C/EBPα expression was downmodulated again. By contrast, no differences in C/EBPα expression were noted during follow-up in the 6 patients characterized by normal karyotype (green lines). Of these 6 patients, 4 persisted in CR and 2 relapsed.
data by showing a reduction of the total amount of C/EBPα protein in AML cases with t(8;21) or inv(16) with respect to those lacking these abnormalities. A further demonstration that the down-regulation of C/EBPα is a characteristic feature of the CBF-disrupted AMLs derives from data obtained on follow-up samples (Figure 1B). In patients characterized by t(8;21) and inv(16) (7 and 5, respectively) who achieved a complete remission (CR), C/EBPα transcript amounts increased to values not significantly different from those obtained in normal samples (P = 0.4) or in the other subgroups of AML at onset (P = 2). Subsequently, these values remained stable in all of the samples collected during CR, and showed a significant decrease in 3 cases of t(8;21) and in 1 case of inv(16) who subsequently relapsed. By contrast, the 6 patients with normal karyotype did not show significant differences between the CEBPα expression level at onset, in CR, and at relapse.

Our data clearly show that decreased levels of C/EBPα expression are present also in the AML cases with inv(16) and, therefore, that down-modulation of C/EBPα is a common feature of both major subtypes of CBF AMLs (ie, t(8;21)-positive and inv(16)-positive AML).

Daniela Cilloni, Sonia Carturan, Enrico Gottardi, Francesca Messa, Emanuela Messa, Milena Fava, Daniela Diverio, Angelo Guerrasio, Francesco Lo-Coco, and Giuseppe Saglio

References


To the editor:

CMV seropositivity and mycosis fungoides—the Indian perspectives

I read with interest the paper by Herne et al1 showing significant cytomegalovirus (CMV) seropositivity in patients with mycosis fungoides (MF) and Sézary syndrome (SS).

The same authors have shown previously that patients with MF/SS had significant association with HLA-DR5 and HLA-DQB*03 alleles.2 Of these 2 HLA antigens, HLA-DR5 was shown to be exquisitely sensitive to stimulation by staphylococcal superantigens, which were associated with the erythrodermic phase of MF/SS.

In India, MF/SS is an extremely rare neoplasm.3 Tata Memorial Hospital in Mumbai, which is one of the biggest oncology centers in India, sees only a few patients with MF/SS out of several thousand patients with non-Hodgkin lymphoma (NHL) every year (T. Saikia, personal written communication, December 2002). Another busy tertiary care center from South India reported only 20 cases of MF/SS over 10 years, out of which 1 patient was serologically positive for human T-cell leukemia virus type 1.4 Another argument could be that we may be missing the diagnosis in many patients in our country because routine biopsy of the various skin lesions is usually not done, and modern immunophenotyping techniques are not widely available, although very expert histopathologists with special interest in lymphoma diagnosis are available in many tertiary centers. Other conditions like alopecia areata and vitiligo, in which T-cell infiltration into the dermis may occur, are also not uncommon in India. The most common cause of vitiligo in India used to be leprosy, which is almost on the verge of eradication; hence, in the future we may get more of those subtypes of vitiligo, which may be a premalignant stage of MF/SS. However, it is unlikely that a disease such as CTCL, which is progressive in many patients, will not eventually be diagnosed en masse.

It may not be out of place to mention here that there was not a single patient of Asian origin with MF/SS in the large series of this disease presented by the authors1 in Table 1, although several million Asians older than 30 years live in the United States (age ranges for MF/SS described in Table 1, 30-86 years). This disease, incidentally, is also rare in the whole of Asia.5 CMV infection might require association of some other viruses to drive CTCL in the same way as HIV1 infection needs help from Kaposi sarcoma herpesvirus to produce Kaposi sarcoma. Hence, a search for such helper viruses in these patients is important. The prevalence of infection with different CMV genotypes may vary in different parts of the world, and this variation may also partly explain the varying pathogenic potential of this virus. From India, very few studies on