**XPD Lys751Gln polymorphism in the etiology and outcome of childhood acute myeloid leukemia: a Children’s Oncology Group report**

Parinda A. Mehta, Todd A. Alonzo, Robert B. Gerbing, James S. Elliott, Tiffany A. Wilke, Rebekah J. Kennedy, Julie A. Ross, John P. Perentesis, Beverly J. Lange, and Stella M. Davies

Genetic polymorphisms result in interindividual variation in DNA repair capacity and may, in part, account for susceptibility of a cell to genotoxic agents and to malignancy. Polymorphisms in XPD, a member of the nucleotide excision repair pathway, have been associated with development of treatment-related acute myeloid leukemia (AML) and with poor outcome of AML in elderly patients. We hypothesized that XPD Lys751Gln polymorphism may play a role in causation of AML in children and, as shown in adults, may affect the outcome of childhood AML therapy. Genotyping of 456 children treated for de novo AML was performed at XPD exon 23. Genotype frequencies in patients were compared with healthy control subject frequencies, and patient outcomes were analyzed according to genotype. Gene frequencies in AML patients and healthy controls were similar. There were no significant differences in overall survival (P = .82), event-free survival (P = .78), treatment-related mortality (P = .43), or relapse rate (RR) (P = .92) between patients with XPD751AA versus 751AC versus 751CC genotypes, in contrast to reports in adult AML. These data, representing the only data in pediatric AML, suggest that XPD genotype does not affect the etiology or outcome of childhood AML. (Blood. 2006;107:39-45)

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**Introduction**

DNA is continuously damaged by endogenous and exogenous mutagens. Repair of DNA damage is a complex process carried out by an array of DNA repair pathways, including nucleotide excision and base excision repair pathways. The nucleotide excision repair (NER) pathway eliminates the widest variety of damage to the human genome, including UV-induced photoproducts, bulky monoadducts, cross-links, and oxidative damage.

Hereditary genetic defects in DNA repair lead to increased risk of cancer. Individuals with xeroderma pigmentosum (XP), a rare autosomal recessive disease resulting from a defect in NER of UV-damaged DNA, have a 1000-fold increased risk of skin cancer. Cell-fusion analyses have identified 7 genetic complementation groups (XPA to XPG) that encode for proteins participating in different steps of the NER pathway.

Xeroderma pigmentosum complementation group D (XPD) is a major participant in NER pathway and is also involved in transcription initiation, control of cell cycle, and apoptosis.

**XPD** functions as an evolutionarily conserved ATP-dependent helicase within the multisubunit transcription repair factor complex, TFIH. TFIH has 2 distinct roles, first in basal transcription carried out by RNA polymerase II and second in NER of DNA damage. It appears that XPD protein needs to be present to maintain the stability of the TFIH complex. XPD possesses both single-strand DNA-dependent ATPase and 5'→3' DNA helicase activities and is thought to participate in DNA unwinding during NER and transcription. Mutations in the XPD gene can completely prevent DNA opening and dual incision, steps that lead to the repair of DNA adducts.

Genetic polymorphisms result in interindividual variation in DNA repair capacity and may, in part, account for differences in susceptibility of a cell to genotoxic agents and to malignancy. Several single nucleotide polymorphisms, including an adenine (A) to cytosine (C) (A → C) transition, which leads to Lys751Gln in exon 23 of the XPD gene, have been shown to be associated with elevated frequency of chromosomal aberrations and a variety of environmentally induced cancers in adults. There is also evidence that dysregulation of DNA repair proteins and NER pathways may be involved in pathogenesis and prognosis of some myeloid leukemia.

Recent data from elderly acute myeloid leukemia (AML) patients treated on MRC11 trial showed reduced event-free survival (EFS) and overall survival (OS) along with increased risk of developing treatment-related leukemia in XPD751 glutamine homoygotes (CC), suggesting that the glutamine variant confers greater protection against chemotherapy-induced leukemic blast-cell death, leading to earlier disease relapse and ultimately shorter overall survival. In this study we show that, in contrast to the adult data, XPD751 does not influence outcome of therapy in children with AML.
Patients, materials, and methods

Patients

The study population included 456 children with de novo AML treated on Children’s Cancer Group (CCG) therapeutic studies CCG-2941 (n = 37) and CCG-2961 (n = 419) between 1995 and 2002. Clinical data, including age, sex, white blood cell (WBC) count at diagnosis, race, presence of chloroma, presence of central nervous system (CNS) disease, and immunophenotype were collected prospectively (Table 1). Cases were classified on the basis of criteria established and revised by the French-American-British (FAB) Cooperative Study Group by central pathology review. All FAB categories except acute promyelocytic leukemia (APL–AML M3) were eligible for enrollment and were treated with the same chemotherapy regimens.

Chemotherapy treatment regimen

CCG-2961 study was a randomized phase 3 trial of intensively timed induction, consolidation, and intensification therapy for pediatric patients with previously untreated AML or myelodysplastic syndrome (MDS). The study was conducted between August 1996 and December 2002. CCG-2941 was a feasibility pilot of the same chemotherapy regimen that preceded the randomized study. Induction included 5 drugs: idarubicin, etoposide, dexamethasone, cytarabine, and 6-thioguanine (IDA DCTER) given on days 0 to 3 followed by 5 drugs (daunorubicin, etoposide, dexamethasone, Ara-C, and 6-thioguanine) (DCTER) given on days 10 to 13. Upon recovery of white blood cell and platelet counts, patients were

<table>
<thead>
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<th>Characteristic</th>
<th>AA; N = 193</th>
<th>AC; N = 202</th>
<th>CC; N = 61</th>
<th>AA vs AC</th>
<th>AC vs CC</th>
<th>AA vs CC</th>
</tr>
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<td>Age, y, median (range)</td>
<td>10.2 (0.15-19.5)</td>
<td>9.6 (0.01-19.8)</td>
<td>11.0 (0.13-20.9)</td>
<td>.43</td>
<td>.57</td>
<td>.98</td>
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<td>WBC count, × 10⁹/L, median (range)</td>
<td>22.8 (1-373.3)</td>
<td>18.65 (1-860)</td>
<td>18.8 (0.3-684)</td>
<td>.36</td>
<td>.53</td>
<td>.22</td>
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<td>Bone marrow blasts, %, median (range)</td>
<td>70.5 (0-100)</td>
<td>70 (1-100)</td>
<td>67 (15-98)</td>
<td>.73</td>
<td>.65</td>
<td>.48</td>
</tr>
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<td>Study, no. (%)</td>
<td></td>
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<td></td>
<td></td>
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<td>CCG-2941</td>
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<td>18 (9)</td>
<td>8 (13)</td>
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<tr>
<td>CCG-2961</td>
<td>182 (94)</td>
<td>184 (91)</td>
<td>53 (87)</td>
<td></td>
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<td>Sex, no. (%)</td>
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<td></td>
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<tr>
<td>Male</td>
<td>109 (56)</td>
<td>105 (52)</td>
<td>36 (59)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>84 (44)</td>
<td>97 (48)</td>
<td>25 (41)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race, no. (%)</td>
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<td>White</td>
<td>116 (60)</td>
<td>142 (70)</td>
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<td>&lt; .01</td>
<td>&lt; .001</td>
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<td>Black</td>
<td>20 (10)</td>
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<td>0 (0)</td>
<td>.74</td>
<td>.02</td>
<td>.01</td>
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<td>Hispanic</td>
<td>40 (21)</td>
<td>26 (13)</td>
<td>5 (8)</td>
<td>.05</td>
<td>.44</td>
<td>.04</td>
</tr>
<tr>
<td>Asian</td>
<td>7 (4)</td>
<td>7 (3)</td>
<td>0 (0)</td>
<td>.86</td>
<td>.36</td>
<td>.20</td>
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<tr>
<td>Other</td>
<td>9 (5)</td>
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<td>1 (2)</td>
<td>.90</td>
<td>.46</td>
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<td>0 (—)</td>
<td>0 (—)</td>
<td>—</td>
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<td>—</td>
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<td>FAB, no. (%)</td>
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</tr>
<tr>
<td>M0</td>
<td>17 (9)</td>
<td>7 (3)</td>
<td>2 (3)</td>
<td>.04</td>
<td>&gt; .99</td>
<td>.26</td>
</tr>
<tr>
<td>M1</td>
<td>30 (16)</td>
<td>31 (15)</td>
<td>9 (15)</td>
<td>.95</td>
<td>.93</td>
<td>.97</td>
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<tr>
<td>M2</td>
<td>61 (32)</td>
<td>53 (26)</td>
<td>18 (30)</td>
<td>.27</td>
<td>.73</td>
<td>.86</td>
</tr>
<tr>
<td>M4</td>
<td>39 (20)</td>
<td>60 (30)</td>
<td>19 (31)</td>
<td>.04</td>
<td>.96</td>
<td>.11</td>
</tr>
<tr>
<td>M5</td>
<td>31 (16)</td>
<td>37 (18)</td>
<td>9 (15)</td>
<td>.66</td>
<td>.65</td>
<td>.95</td>
</tr>
<tr>
<td>M6</td>
<td>5 (3)</td>
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<td>1 (2)</td>
<td>.75</td>
<td>&gt; .99</td>
<td>1.00</td>
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<td>8 (4)</td>
<td>3 (5)</td>
<td>.64</td>
<td>.72</td>
<td>.40</td>
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<tr>
<td>Other</td>
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<td>2 (1)</td>
<td>0 (0)</td>
<td>.44</td>
<td>&gt; .99</td>
<td>.58</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (—)</td>
<td>0 (—)</td>
<td>0 (—)</td>
<td>—</td>
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<td>Cytogenetics, no. (%)</td>
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<tr>
<td>Normal</td>
<td>28 (23)</td>
<td>27 (23)</td>
<td>11 (31)</td>
<td>.94</td>
<td>.48</td>
<td>.51</td>
</tr>
<tr>
<td>t(8;21)</td>
<td>18 (15)</td>
<td>18 (15)</td>
<td>10 (28)</td>
<td>.90</td>
<td>.14</td>
<td>.13</td>
</tr>
<tr>
<td>Abn 16</td>
<td>15 (13)</td>
<td>10 (8)</td>
<td>2 (6)</td>
<td>.42</td>
<td>.73</td>
<td>.36</td>
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<td>Abn 11</td>
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<td>26 (22)</td>
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<td>.84</td>
<td>.87</td>
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<td>t(6;9)</td>
<td>1 (1)</td>
<td>3 (3)</td>
<td>1 (3)</td>
<td>.37</td>
<td>&gt; .99</td>
<td>.41</td>
</tr>
<tr>
<td>−7/7q⁻</td>
<td>6 (5)</td>
<td>2 (2)</td>
<td>0 (0)</td>
<td>.28</td>
<td>&gt; .99</td>
<td>.34</td>
</tr>
<tr>
<td>−5/5q⁻</td>
<td>2 (2)</td>
<td>2 (2)</td>
<td>0 (0)</td>
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<td>&gt; .99</td>
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<tr>
<td>+8</td>
<td>11 (9)</td>
<td>7 (6)</td>
<td>0 (0)</td>
<td>.48</td>
<td>.20</td>
<td>.07</td>
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<tr>
<td>Pseudodiploid</td>
<td>10 (8)</td>
<td>15 (13)</td>
<td>3 (8)</td>
<td>.37</td>
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<td>&gt; .99</td>
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<tr>
<td>Hypodiploid</td>
<td>4 (3)</td>
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<td>.37</td>
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<td>.57</td>
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<tr>
<td>Unknown</td>
<td>73 (—)</td>
<td>84 (—)</td>
<td>25 (—)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>CNS at on-study</td>
<td>8 (4)</td>
<td>10 (5)</td>
<td>5 (8)</td>
<td>.89</td>
<td>.35</td>
<td>.31</td>
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<tr>
<td>Chloroma at on-study</td>
<td>15 (8)</td>
<td>26 (13)</td>
<td>8 (13)</td>
<td>.13</td>
<td>.67</td>
<td>.31</td>
</tr>
<tr>
<td>Response at end of first course, no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>REM</td>
<td>170 (90)</td>
<td>165 (86)</td>
<td>51 (84)</td>
<td>.30</td>
<td>.81</td>
<td>.26</td>
</tr>
<tr>
<td>PD</td>
<td>9 (5)</td>
<td>15 (8)</td>
<td>8 (13)</td>
<td>.31</td>
<td>.32</td>
<td>.04</td>
</tr>
<tr>
<td>Die</td>
<td>10 (5)</td>
<td>12 (6)</td>
<td>2 (3)</td>
<td>.86</td>
<td>.53</td>
<td>.74</td>
</tr>
<tr>
<td>W/D or unevaluable</td>
<td>4 (—)</td>
<td>10 (—)</td>
<td>0 (—)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

— indicates not applicable.

We randomly selected 578 healthy blood donors to determine control genotype frequencies: 432 were white and 146 were black controls.
randomly assigned to consolidation therapy consisting of the same sequence of drugs or to fludarabine/ cytarabine/idarubicin. Intrathecal cytarabine was used for CNS prophylaxis. Patients with matched-related donors were assigned to allogeneic marrow transplant intensification. Pretransplant cytoreduction was busulfan and cyclophosphamide. Patients without a related donor received high-dose cytarabine/L-asparaginase (Capozzi II) and additional intrathecal cytarabine. After recovery from chemotherapy, patients were randomized again to either receive interleukin-2 or standard follow-up care. Patients who received transplants were not eligible for randomization to interleukin-2.

**XPD genotyping**

DNA extracted from diagnostic marrow samples using standard methods was normalized to 10 ng/μL. Genotyping was performed using a fluorescence-based allelic discrimination assay (TaqMan; Applied Biosystems, Foster City, CA). Gene-specific polymerase chain reaction (PCR) primers and fluorescent probes for allelic discrimination are described in Table 2.

PCR cycling reactions were performed in 96-well microtiter plates in a GeneAmp PCR System 9600 (Perkin-Elmer). For each 25-μL reaction, 10 ng DNA template was added to the reaction mixture containing wild-type VIC and variant FAM probe, PCR mastermix (Applied Biosystems), and forward and reverse primers (final concentration 0.3 μM). Thermocycling was performed with an initial 50°C incubation for 2 minutes followed by a 10-minute incubation at 95°C. A 2-step cycling reaction was performed for 40 cycles with denaturation at 95°C for 15 seconds, and annealing and extension at 62°C for 1 minute. Results were analyzed by the automated TaqMan allelic discrimination assay using sequence detection system 2.1 software (ABI TaqMan 7700, Applied Biosystems).

DNA from healthy controls was extracted using standard techniques and genotyped as described for cases. Genotyping results were duplicated in 10% of samples; concordance between repeats was 100%. Furthermore, 10% of the samples also were genotyped using direct sequencing; concordance with TaqMan genotyping was 100%.

**Statistical analysis**

Data were analyzed from CCG-2941 and CCG-2961 through April 2005 for both studies. The significance of observed differences in proportions was tested using the Chi-square test and Fisher exact test when data were sparse. Differences in cumulative incidence estimates were tested for significance using Gray decompeting events. Differences in nonprogressive disease where failures at the end of 2 courses, relapses and deaths from nonprogressive disease were competing events. Differences between polymorphism subgroups; 57% to 13% in CC patients at 5 years (log-rank P = .239).

**Table 2. Allele-specific primers and probes**

<table>
<thead>
<tr>
<th>Primers</th>
<th>Probes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forward primer-CCT TCT CCC TTT CCT CTG TTC T</td>
<td>VIC (wild-type)-ATC CTC TTC AGC GTC T</td>
</tr>
<tr>
<td>Reverse primer-CAC TCA GAG CTG CTG AGC AAT C</td>
<td>FAM (variant)-TCC TCT GCA GGC TC</td>
</tr>
</tbody>
</table>

**Results**

**Genotype frequencies**

Allele and genotype frequencies for cases and controls are shown in Table 3. XPD genotype frequencies for black and white controls were significantly different (P < .001). Genotype frequencies did not differ by sex (data not shown). Comparison of genotype frequencies was therefore performed separately for white cases versus white controls and black cases versus black controls. Genotype frequencies were similar in white cases and controls (Table 3; P = .125) and black patients and black controls (P = .239). The distribution of XPD genotypes was consistent with the Hardy-Weinberg equilibrium. Stratification of cases by age at diagnosis (0-2 y vs > 2-10 y vs > 10 y), WBC count at diagnosis (< 50 000 vs ≥ 50 000), AML subtype, or cytogenetics revealed no difference in genotype frequencies. There were more XPD751AC patients compared to AA in hyperdiploid cases; however, this difference should be interpreted cautiously due to the very small total number of patients with hyperdiploidy.

**XPD genotype and outcome**

There were no significant differences in OS from study entry between patients with XPD751AA versus 751AC versus 751CC genotypes (53% ± 8% vs 50% ± 8% vs 45% ± 13% respectively at 5 years; log-rank P = .82; Figure 1). In addition, induction of remission did not vary by genotype (Table 1). When OS from end of one course of therapy for patients in remission was compared between different genotypes, there was no statistical difference between polymorphism subgroups; 57% ± 8% in XPD751AA versus 58% ± 8% in AC versus 52% ± 15% in CC patients at 5 years (log-rank P = .96).

Analysis of EFS from study entry in different genotypes also showed similar estimates: 41% ± 7% in XPD751AA versus 38% ± 7% in AC versus 41% ± 13% in CC patients at 5 years (log-rank P = .78) (Figure 2). DFS from the end of one course of therapy for patients in remission also was similar among the 3
significant frequencies in the population. Spitz et al. studied the polymorphisms that likely change protein function and occur at consequences of human polymorphism, it is important to target suggestions that functionality of the codon 751 polymorphism may be exposure—and pathway—specific, affecting both DNA repair and cell death. Consistent with a role for \textit{XPD} in cell death, P53-mediated apoptosis is attenuated in \textit{XPD} mutated fibroblasts. Furthermore, P53 interacts directly with the carboxy terminus of \textit{XPD}, which includes the polymorphic codon 751 residue.

A previous report of adult subjects showed that \textit{XPD}751 genotype influenced susceptibility to therapy-related leukemia, but not de novo AML. In agreement with this, in this pediatric study we found no influence of \textit{XPD}751 genotype on susceptibility to de novo AML in children. It should be noted that the present pediatric study focused on de novo and not therapy-related AML.

There is evidence that DNA repair (NER) protects against mutagenicity and toxicity by removing deleterious DNA lesions from the genome, including those induced by chemotherapy. Because increased DNA repair plays an important role in resistance to platinum-based compounds, Park et al evaluated the effect of \textit{XPD} Lys751Gln polymorphism on outcome of 73 patients treated with 5-fluorouracil (5-FU)/oxaloplatin for metastatic colorectal cancer. Their results showed a significant association between response to 5-FU/oxaloplatin and the \textit{XPD} Lys751Gln polymorphism. Patients with Lys/Lys genotype had the longest median survival, and those with Gln/Gln genotype were 6 to 12 times more likely to have progressive disease.

Allan et al evaluated the association of \textit{XPD} Lys751Gln polymorphism with outcome following chemotherapy for AML in 341 elderly patients (> 60 years of age) entered into the United Kingdom Medical Research Council (MRC) AML 11 trial. In this study \textit{XPD}751 glutamine homozygotes had significantly inferior DFS at 1 year compared with patients with other genotypes. The authors postulated 2 general mechanisms by which the \textit{XPD} codon 751 variant may modulate myeloid-cell death in response to chemotherapy: either via a direct role for \textit{XPD} in signaling cell death or indirectly via \textit{XPD} repair of protoxic DNA lesions.

In contrast to the findings of Allan et al., our study did not demonstrate any differences in outcome of AML therapy in children with different \textit{XPD}751 genotypes. It is possible that children with AML differ from adults in terms of the biology of their disease, for example, studies show that older adults have increased frequency of adverse cytogenetic features compared to children. Also, over time adult patients have more opportunity to accumulate additional genetic insults (secondary hits), with perhaps increased susceptibility to develop cancers that are more resistant to therapy. Outcomes for treatment of adult AML are commonly inferior to those reported in pediatric series. Also, association studies involving genetic polymorphisms need to be interpreted cautiously in the context of differences in study or population variables. For example, compared to children, older...
adults have poorer tolerance of combination chemotherapy regi-
mens, leading to the use of less-intensive treatment protocols, as
well as increased levels of primary drug resistance associated with
overexpression of P-glycoprotein (P-gp). Adults in the study by
Allan et al received chemotherapy agents (daunomycin, cytosine
arabinoside, thioguanine, etoposide) broadly similar to those
received by the children in our study, but it is possible that the
effect of XPD polymorphism is regimen specific. A subset of
patients in the adult study received an alkylating agent (cyclophos-
phamide) in postremission therapy in contrast to our pediatric
study, and half were randomized to interferon-α, either of which
may have influenced the results. Progress in AML therapy in children
has largely been made by aggressive intensification of chemotherapy. It
is also possible that intensification of chemotherapy in children can
overcome a marginal modulating effect of XPD genotype. Additionally,
this XPD variant may be of functional importance in children with AML
when combined with other XPD variants or polymorphic alleles of other
DNA repair genes. Mechanistic studies further defining the functionality
of XPD polymorphisms will help clarify the importance of variants at
this site.

Appendix

COG Active Institutions, listed alphabetically, are as follows: A.B. Chan-
dler Medical Ctr, University of Kentucky, Lexington, KY; Advocate Hope
Children’s Hospital, Oak Lawn, IL; Albany Medical Center, Albany, NY;
Alberta Children’s Hospital, Calgary, AB, Canada; All Children’s Hospital,
St. Petersburg, FL; Allan Blair Cancer Centre, Regina, SK, Canada; Atlantic
Health System, Morristown, NJ; Backus Children’s Hospital at MHUMC,
Savannah, GA; Baptist Children’s Hospital, Miami, FL; Baystate Medical
Center, Springfield, MA; Boston Floating Hospital for Infants & Children,
Boston, MA; British Columbia’s Children’s Hospital, Vancouver, BC,
Canada; Brookdale Hospital Medical Center, Brooklyn, NY; Brooklyn
Hospital Center, Brooklyn, NY; Broward General Medical Center, Ft.
Lauderdale, FL; C.S. Mott Children’s Hospital, Ann Arbor, MI; Cabell
Huntington Hospital, Huntington, WV; Cancer Research Center of Hawaii,
Honolulu, HI; CancerCare Manitoba, Winnipeg, MB, Canada; Cardinal
Glennon Children’s Hospital, St. Louis, MO; Carilion Medical Center for
Children at Roanoke Community Hospital, Roanoke, VA; Carolinas
Medical Center, Charlotte, NC; Cedars-Sinai Medical Center, Los Angeles,
CA; Centre Hospitalier Universitaire de Quebec, Ste-Foy, QC, Canada;
Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, QC, Canada;
Children’s Healthcare of Atlanta, Emory University, Atlanta, GA; Chil-
dren’s Hem/Onc Team at Covenant Children’s Hosp, Lubbock, TX;
Children’s Hospital and Regional Medical Center, Seattle, WA; Children’s
Hospital Central California, Madera, CA; Children’s Hospital of Austin,
Austin, TX; Children’s Hospital of Eastern Ontario, Ottawa, ON, Canada;
Children’s Hospital of Michigan, Detroit, MI; Children’s Hospital of
Pittsburgh, Pittsburgh, PA; Children’s Hospital of the Greenville
Hospital System, Greenville, SC; Children’s Hospital San Diego, San Diego, CA;
Children’s Medical Center Dayton, Dayton, OH; Children’s Memorial
Medical Center at Chicago, Chicago, IL; Children’s National Medical
Center—D.C., Washington, DC; Children’s of New Orleans/LUSMC
CCOP, New Orleans, LA; Children’s Hospital & Clinics Minneapolis & St
Paul, Minneapolis, MN; Children’s Hospital Los Angeles, Los Angeles, CA;
Children’s Hospital Medical Center Cincinnati, Cincinnati, OH; Children’s
Hospital Medical Center-Akron, Ohio, Akron, OH; Children’s Hospital
Oakland, Oakland, CA; Children’s Hospital of Orange County, Orange, CA;
Children’s Hospital of Philadelphia, Philadelphia, PA; Children’s Hospital
of Western Ontario, London, ON, Canada; Childrens Hospital-King’s Daugh-
ters, Norfolk, VA; Childrens Memorial Hospital of Omaha, Omaha, NE;
Christiana Care Health Services/A.I. duPont Inst., Wilmington, DE; City of
Hope National Medical Center, Duarte, CA; Columbia Presbyterian Col-
lege of Phys & Surgeons, New York, NY; Columbus Children’s Hospital,
Columbus, OH; Connecticut Children’s Medical Center, Hartford, CT;
Cook Children’s Medical Center, Fort Worth, TX; Dana-Farber Cancer
Institute and Children’s Hosp, Boston, MA; Dartmouth-Hitchcock Medical
Center, Lebanon, NH; DeVos Children’s Hospital, Grand Rapids, MI;
Doernbecher Childrens Hospital—OHSU, Portland, OR; Driscoll Chil-
dren’s Hospital, Corpus Christi, TX; Duke University Medical Center,
Durham, NC; East Carolina University School of Medicine, Greenville,
NC; East Tennessee Childrens Hospital, Knoxville, TN; East Tennessee
State University, Johnson City, TN; Eastern Maine Medical Center, Bangor,
ME; Emanuel Hospital-Health Center, Portland, OR; Florida Hospital
Cancer Institute, Orlando, FL; Geisinger Medical Center, Danville, PA;
Georgetown University Medical Center, Washington, DC; Gundersen
Lutheran, La Crosse, WI; Hackensack University Medical Center, Hacken-
sack, NJ; Hospital Sainte-Justine, Montreal, QC, Canada; Hospital for Sick
Children, Toronto, ON, Canada; Hurley Medical Center, Flint, MI; Indiana
University—Riley Childrens Hospital, Indianapolis, IN; Inova Fairfax
Hospital, Fairfax, VA; IWK Health Centre, Halifax, NS, Canada; Janeway
Child Health Center, St. John’s, NF, Canada; Joe DiMaggio Children’s
Hospital at Memorial, Hollywood, FL; John Hunter Children’s Hospital,
Newcastle, NSW, Australia; Johns Hopkins Hospital, Baltimore, MD;
Kaiser Permanente Medical Group, Inc., Northern CA, Sacramento, CA;
Kalamazoo Center for Medical Studies, Kalamazoo, MI; Kingston General
Hosp/Kingston Regional Cancer, Kingston, ON, Canada; Kosair Childrens
Hospital, Louisville, KY; Loma Linda University Medical Center, Loma
Linda, CA; Loyola University Medical Center, Maywood, IL; Lutheran
General Childrens Medical Center, Park Ridge, IL; M.D. Anderson Cancer
Center, Houston, TX; Madigan Army Medical Center (USOC), Tacoma,
WA; Maimonides Medical Center, Brooklyn, NY; Maine Children’s Cancer
Program, Scarborough, ME; Marshall Field Clinic, Marshallfield, WI; Mary
Bridge Hospital, Tacoma, WA; Massachusetts General Hospital, Boston,
MA; Mayo Clinic and Foundation, Rochester, MN; McGill Univ Health Ctr
- Montreal Children’s Hosp, Montreal, QC, Canada; McMaster University,
Hamilton, ON, Canada; Medical College of Georgia Childrens Medical Ctr,
Augusta, GA; Medical University of South Carolina, Charleston, SC;
Memorial Sloan Kettering Cancer Center, New York, NY; Mercy Children’s
Hospital, Toledo, OH; MericCare Medical Group DBA Roger Maris Cancer
Ctr, Fargo, ND; Methodist Children’s Hospital of South Texas, San
Antonio, TX; Miami Children’s Hospital, Miami, FL; Michigan State
University, East Lansing, MI; Midwest Children’s Cancer Center, Milwau-
kee, WI; Miller Children’s Hospital/Harbor-UCLA, Long Beach, CA;
Mission Hospitals, Asheville, NC; Montefiore Medical Center, Bronx, NY;
Mount Sinai Medical Center, New York, NY; Mountain States Tumor
Institute, Boise, ID; Naval Medical Center/Portsmouth (USOC), Ports-
mouth, VA; Nemours Children’s Clinic-Jacksonville, Jacksonville, FL;
Nemours Children’s Clinic-Orlando, Orlando, FL; Nevada Cancer Re-
search Foundation—CCOP, Las Vegas, NV; New York Hospital-Cornell
Univ Medical Center, New York, NY; New York Medical College, Valhalla,
NY; New York University Medical Center, New York, NY; New York
Beth Israel Medical Center, Newark, NJ; North Texas Hosp for Children at Med
City Dallas, Dallas, TX; Ochsner Clinic, New Orleans, LA; Penn State
Children’s Hospital, Hershey Med Ctr, Hershey, PA; Phoenix Childrens
Hospital, Phoenix, AZ; Presbyterian Hospital, Charlotte, NC, Presbyte-
rian/St Lukes Medical Center and CHOA, Denver, CO; Primary Childrens
Medical Center, Salt Lake City, UT; Princess Margaret Hospital for
Children, Perth, WA, Australia; Rainbow Babies and Childrens Hospital,
Cleveland, OH; Raymond Blank Children’s Hospital, Des Moines, IA;
Rhode Island Hospital, Providence, RI; Roswell Park Cancer Institute,
Buffalo, NY; Royal Children’s Hospital, Brisbane, Herston, Brisbane,
QLD, Australia; Royal Children’s Hospital, University of Melbourne,
Parkville, VI, Australia; Rush-Presbyterian St. Luke’s Medical Center,
Chicago, IL; Sacred Heart Children’s Hospital, Spokane, WA; Sacred Heart
Hospital, Pensacola, FL; Saint Barnabas Medical Center, Livingston, NJ;
Saint Peter’s University Hospital, New Brunswick, NJ; Saint Jorge
Children’s Hospital, Santurce, PR; Santa Barbara Cottage Children’s Hospital,
Santa Barbara, CA; Saskatoon Cancer Center, Saskatoon, SK, Canada;
Schneider Children’s Hospital, New Hyde Park, NY; Scott & White
Memorial Hospital, Temple, TX; Sinai Hospital of Baltimore, Baltimore,
MD; Sioux Valley Children’s Specialty Clinics, Sioux Falls, SD; South
Carolina Cancer Center, Columbia, SC; South Island Child Cancer Service,
Christchurch, New Zealand; Southern California Permanente Medical
Group, Downey, CA; Southern Illinois University School of Medicine,
References


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Erratum

In the article by Airoldi et al entitled “Lack of Il12rb2 signaling predisposes to spontaneous autoimmunity and malignancy,” which appeared in the December 1, 2005, issue of Blood (Volume 106:3846-3853), an author name was misspelled. The eighth author’s name should have been Mario Paolo Colombo.

This byline error was corrected online in departure from print.
XPD Lys751Gln polymorphism in the etiology and outcome of childhood acute myeloid leukemia: a Children's Oncology Group report

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