

Infant Leukemia: Finding the Needle in the Haystack

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Historically, the study of rare malignancies, including retinoblastoma, angiosarcoma, and vaginal clear cell carcinoma, has led to major findings in our understanding of cancer etiology. Leukemias that occur in children less than 1 year of age likely represent another rare group that could potentially lead to further understanding of carcinogenesis. The vast majority of infants present with a genetic abnormality in their leukemia cells that affects the *MLL* gene on chromosome band 11q23, and a substantial body of evidence supports the contention that these *MLL* abnormalities (mostly rearrangements) occur *in utero* (1). Thus, the window of exposure is very brief. We and others have shown that specific environmental exposures (2, 3) and genotypes (4-7) may be unique to these *MLL* abnormalities in infant leukemias. Here, Pombo-de-Oliveira et al. (8) demonstrate an association between infant leukemia and maternal hormone use before and during pregnancy, which appeared to vary by timing of exposure and *MLL* status. The authors further show an association of *MLL*-positive infant leukemia with quinolones, which, although imprecise, is interesting given these drugs that interact with DNA topoisomerase II (9). These results support differing etiologies for molecularly defined subtypes of infant leukemia. Rarity is the major obstacle to elucidating translocation-specific risk factors but may be overcome by cooperative group participation (10) and international collaboration. Epidemiologic investigations may also be informed by mechanistic studies, which have sought to correlate prenatal exposures with the frequency of *MLL* transcripts or chromosome breakage at the 11q23 locus in cord blood (11, 12). Thus, we expect big developments from this small cancer.

References

1. Greaves MF, Maia AT, Wiemels JL, Ford AM. Leukemia in twins: lessons in natural history. *Blood* 2003;102:2321–33.
2. Ross JA, Potter JD, Reaman GH, Pendergrass TW, Robison LL. Maternal exposure to potential inhibitors of DNA topoisomerase II and infant leukemia (United States): a report from the Children's Cancer Group. *Cancer Causes Control* 1996;7:581–90.
3. Spector LG, Xie Y, Robison LL, et al. Maternal diet and infant leukemia: the DNA topoisomerase II inhibitor hypothesis: a report from the children's oncology group. *Cancer Epidemiol Biomarkers Prev* 2005;14:651–5.
4. Eguchi-Ishimae M, Eguchi M, Ishii E, et al. The association of a distinctive allele of NAD(P)H:quinone oxidoreductase with pediatric acute lymphoblastic leukemias with *MLL* fusion genes in Japan. *Haematologica* 2005;90:1511–5.
5. Kracht T, Schrappe M, Strehl S, et al. NQO1 C609T polymorphism in distinct entities of pediatric hematologic neoplasms. *Haematologica* 2004;89:1492–7.
6. Ma X, Buffler PA, Gunier RB, et al. Critical windows of exposure to household pesticides and risk of childhood leukemia. *Environ Health Perspect* 2002;110:955–60.
7. Wiemels JL, Smith RN, Taylor GM, Eden OB, Alexander FE, Greaves MF. Methylene tetrahydrofolate reductase (MTHFR) polymorphisms and risk of molecularly defined subtypes of childhood acute leukemia. *Proc Natl Acad Sci U S A* 2001;98:4004–9.
8. Pombo-de-Oliveira MS, Koifman S, Brazilian Collaborative Study Group of Infant Acute Leukemia. Infant acute leukemia and maternal exposures during pregnancy. *Cancer Epidemiol Biomarkers Prev* 2006;15:2336–41.
9. Elsea SH, Westergaard M, Burden DA, Lomenick JP, Osheroff N. Quinolones share a common interaction domain on topoisomerase II with other DNA cleavage-enhancing antineoplastic drugs. *Biochemistry* 1997;36:2919–24.
10. Steele JR, Wellemeyer AS, Hansen MJ, Reaman GH, Ross JA. Childhood cancer research network: a North American Pediatric Cancer Registry. *Cancer Epidemiol Biomarkers Prev* 2006;15:1241–2.
11. de la Chica RA, Ribas I, Giraldo J, Egozcue J, Fuster C. Chromosomal instability in amniocytes from fetuses of mothers who smoke. *JAMA* 2005; 293:1212–22.
12. Ravetto PF, Agarwal R, Chiswick ML, D'Souza SW, Eden OB, Taylor GM. Absence of leukaemic fusion gene transcripts in preterm infants exposed to diagnostic x rays. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F237–44.

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BLOOD CANCER DISCOVERY

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