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RESEARCH ARTICLE

# Clinical significance of the increased expression of the WT1 gene in peripheral blood of patients with acquired aplastic anemia

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## Abstract

To determine the significance of increased *Wilms tumor 1* (WT1) gene expression in the peripheral blood of patients with acquired aplastic anemia (AA), we analyzed serial changes in *WT1* mRNA copy number (WT1cn) in 63 patients with AA as well as in five patients with myelodysplastic syndromes (MDS) and seven patients with paroxysmal nocturnal hemoglobinuria (PNH). WT1cn was higher than the cut-off (≥50 copies/$\mu$g RNA) at the time of the first measurement in 41% of untreated (60–190 copies/$\mu$g RNA [median 130]) and 59% of treated (59–520 copies/$\mu$g RNA [median 150]) AA patients. Although WT1cns gradually increased in most AA patients during the 2–105 months follow-up period, they did not lead to clonal evolution except in three patients in whom the maximum change ratio of WT1cn (WT1cn-change max), defined as the ratio of WT1cn at the first examination to that of the maximum value, exceeded 20.0 and who developed MDS at 2, 46, and 105 months. Increased WT1 gene expression was enriched in granulocytes rather than in mononuclear cells in most WT1-positive AA patients and did not correlate with mutations of genes associated with myeloid malignancy. WT1cns were high at 690–5700 (median 2000) in MDS patients and remained high thereafter, while WT1cns in PNH patients (77–200; median 96) were similar to those in AA. Thus, moderate increases in WT1cns up to 600 are common in AA patients in stable remission. An increase in the WT1cn-change max over 20.0 may portend transformation from AA to MDS.

KEYWORDS
aplastic anemia, myelodysplastic syndrome, *WT1* mRNA copy number

Ken Ishiyama and Tran Cao Dung contributed equally to this work.