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Growth restraint and differentiation by LPS/TNF-alpha/IFN-gamma reorganization of the microtubule network in human leukemia cell lines.

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The microtubule (MT) network of the cytoskeleton has been implicated as a mediator of cellular signal transduction; disorganization of this network may allow for mitogenesis. In previous work, loss of MT network organization in human MOLT4 and HUT78 T-cell leukemias was demonstrated in contrast to an organized "spoke-wheel-like arrangement" in normal human T-lymphocytes. In this study, loss of MT network organization was shown in several representative acute myeloid leukemia (AML) cell lines: KG1 myeloblastic, HL60 promyelocytic, and U937 myelomonocytic cells. Re-organization of the MT network was observed in HL60 and U937 AML cells treated with combined lipopolysaccharide (LPS), tumor necrosis factor-alpha (TNF-alpha) and interferon-gamma (IFN-gamma). This re-organization paralleled earlier work which showed this combination was effective in inducing monocytic pathway differentiation and growth restraint in HL60 cells, and growth restraint in U937 cells. In contrast, KG1 cells exhibited growth restraint, but did not re-organize with LPS/TNF-alpha/IFN-gamma treatment. These results are consistent with a role for the MT network in mitogenesis. Loss of MT network organization appeared to parallel the neoplastic phenotype in three AML cell lines, whereas MT network re-organization accompanied recovery of growth control in 2 of 3 AML cell lines.