Retinoic acid enhances sensitivity of neuroblastoma cells for imatinib mesylate.

BACKGROUND: Retinoids can induce differentiation of neuroblastoma (NB) cells and are in clinical use for the treatment of patients with NB. Despite improvements of standard treatment during the last years, many patients with NB still relapse and new treatment options for these patients are required. PROCEDURE: We analyzed NB cells after incubation with retinoids by using Affymetrix HG_U133A microarrays, reverse transcription-polymerase chain reaction (RT-PCR), and flow cytometry. Sequencing of RT-PCR products was applied for determination of CD117 mRNA sequences from NB cell lines. In addition, we tested sensitivity of NB cells for the kinase inhibitor imatinib mesylate after treatment with retinoids. RESULTS: Treatment of NB cells with retinoids induced expression of several genes including the retinoid metabolizing enzymes CYP26A1 and CYP26B1. In addition, we observed up-regulation of CD117 (KIT), particularly after long-term treatment with retinoids. Sequencing of CD117 mRNA from NB cell lines revealed heterozygosity for a non-synonymous single nucleotide polymorphism in SH-SY5Y NB cells. Up-regulation of CD117 in NB cells correlated with increased sensitivity for the kinase inhibitor imatinib mesylate. CONCLUSIONS: The combination of retinoids with kinase inhibitors might be worth exploring further for the treatment of NB patients.