Titel des Beitrags: Functional sodium iodide symporter expression in breast cancer xenografts in vivo after systemic treatment with retinoic acid and dexamethasone.

Abstract:
CONTEXT: The sodium iodide symporter (NIS) mediates iodide uptake in the thyroid gland as well as in lactating breast, and is also expressed in the majority of breast cancers. Recently, we have reported stimulation of all-trans retinoic acid (atRA)-induced NIS expression in the human breast cancer cell line MCF-7 by dexamethasone (Dex), resulting in an enhanced therapeutic effect of (131)I in vitro. OBJECTIVE: In the current study we examined the efficacy of Dex stimulation of atRA-induced NIS expression in vivo in MCF-7 xenotransplants in nude mice. DESIGN: After systemic treatment with atRA alone or in combination with Dex, iodide accumulation in the tumors was assessed by gamma camera imaging and gamma counter analysis. In addition, NIS expression was examined on RNA and protein level by RT-PCR and immunohistochemistry, respectively. RESULTS: Using gamma camera imaging after intraperitoneal injection of 18.5 MBq (123)I, no iodide accumulation was detected in tumors of untreated mice or mice treated with atRA only. After combined treatment with atRA/Dex significant (123)I accumulation was detected in MCF-7 xenografts, which, by ex vivo gamma counting revealed a 3.3-fold increase in iodide accumulation as compared to control.
tumors. Surprisingly, in a subset of mice treated with atRA or atRA/Dex iodide accumulation was also detected in the normal mammary glands. In a normal human mammary epithelial cell line HB-2, however, no functional NIS expression was induced after treatment with atRA and/or Dex in vitro. Further, NIS mRNA and protein expression was detected in atRA/Dex treated MCF-7 tumors by RT-PCR and immunohistochemistry, respectively. CONCLUSION: Treatment with Dex in the presence of atRA is able to induce significant amounts of iodide accumulation in breast cancer xenotransplants in vivo due to stimulation of functional NIS protein expression, which opens exciting perspectives for a possible diagnostic and therapeutic role of radioidine in the treatment of breast cancer.