with data obtained from Northern blot- and array-analyses. A preliminary screen of four additional melanoma cell lines points to *IL1B*, *APOD*, and *CYR61* as interesting candidates for drug-resistance associated genes. First tests using an automated on-chip electrophoresis platform indicate the applicability of this approach for high throughput measurements.
Conclusion: mRT-PCR combined with on-chip electrophoresis reveals a rapid and easy-to-handle method for candidate gene set evaluation from limited amounts of mRNA. Using gene sets indicative for different tumor phenotypes, this procedure may represent an alternative for future cancer diagnostics.

1223 PUBLICATION

Antisense-mediated downregulation of ML-IAP sensitizes melanoma cells to chemotherapy

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Background: Advanced malignant melanoma is an aggressive form of skin cancer which is highly resistant to standard anticancer agents. ML-IAP(melanoma inhibitor of apoptosis) is a potent inhibitor of apoptosis which is strongly upregulated in melanoma, while being undetectable in most normal tissues including normal melanocytes. Targeted downregulation of ML-IAP thus has potential to sensitize refractory melanoma to chemotherapy.
Materials and methods: We designed 20-mer phosphorothioate antisense oligonucleotides(AS-ODNs) complementary to five single-stranded target sites on the ML-IAP mRNA using a computer-based secondary structure prediction program. G361 and SK-MEL28 melanoma cells were transfected with AS-ODNs in the presence of cationic lipids. Inhibition of ML-IAP mRNA and protein expression were measured by real-time PCR and immunoblotting, respectively. Sensitization of cells to chemotherapy was detected in cell growth assays using the anticancer agent cisplatin.
Results: M706 was identified as the most efficient AS-ODN, which downregulated ML-IAP mRNA by 68% and 54% in G361 and SK-MEL28 cells, respectively. The specificity of target downregulation was confirmed using scrambled and mismatch sequence controls, which only marginally decreased ML-IAP mRNA levels in the cell lines. In addition, compared to transfection with control oligonucleotides, downregulation of ML-IAP using AS-ODN M706 resulted in more than 2-fold increase in cytotoxic effect of cisplatin on melanoma cells.
Conclusion: We describe a new antisense oligonucleotide that effectively downregulates ML-IAP expression and sensitizes drug resistant melanoma cells to chemotherapy. Our data warrant further investigations to define the therapeutic potential of ML-IAP antisense in the treatment of chemoresistant melanoma.

Paediatric Oncology

Oral presentations (Wed, 2 Nov, 9.15–11.15) **Paediatric oncology**

1224 ORAL

Radiotherapy in pediatric atypical rhabdoid/teratoid tumours of the CNS (CNS-ATRT) – results from the German HIT-data base

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Background: Atypical teratoid/rhabdoid tumours of the central nervous system (CNS-ATRT) are an extremely rare and aggressive, embryonal tumour entity of early childhood. Due to their rarity there is yet no standard therapy, prognosis is poor. Published reports mainly focus on chemotherapy regimen (ChX). The role of radiotherapy (RT) has yet not been analysed in detail, recommendations for RT have not been defined so far.
Material and methods: We report on patients with CNS-ATRT enrolled in the German HIT-study data base (GPOH) between 1988–2004. Clinical records were reviewed retrospectively with special regard to RT data and survival times. Statistical analysis was performed for overall survival (OS) and progression free survival (PFS) concerning 1. the role of RT compared to chemotherapy (ChX-pat. vs. RT-pat.) 2. the sequence of RT in clinical course (RT in primary therapy (primRT) vs. RT in relapse therapy (relRT)) 3. the radiation field necessary for local tumour control (involved field RT (focRT) vs. craniospinal RT (CSA-RT)). Distributions were estimated using Kaplan-Meier plots and log-rank test for significance.
Results: 64 pat. were diagnosed during a 16-year-interval. 59/64 (92.2%) have been centrally reviewed for histology. 29/64 pat (45.3%) had ChX solely, 35 pat. (54.7%) received combined RT/ChX. 45/64 pat. (70.3%) were younger than 3 years at Dx with RT/CHX in 18/44 cases (40.9%). In the age group over 3 years at Dx (n = 19) RT was delivered in 17/19 pat. (89.5%). In 18/35 cases (51.4%) RT was part of primary therapy, in 17/35 part of relapse therapy. RT target volume: 12 × focRT, 21 × CSA-RT, 2 no inf.. RT fractionation/total tumour dose (TTD): conventional fract. RT (n = 31): 54.6 Gy (44.5–59.4), CSA-dose 24–35.2 Gy; hyperfractionated RT (n = 2): 68/71 Gy, CSA-dose 36 Gy; radiosurgery (n = 1): 16 Gy. Survival analysis: 2-year-OS of pat. with combined RT/ChX (56.2%) was significantly better than that for pat. receiving ChX solely (9.2%); p = 0.001. There was no significant difference in 2-year-PFS (from date of RT) concerning sequence of RT (primRT-pat. (42.8%)/relRT-pat. (36.2%)); p = 0.4230. No difference was found in median PFS (from date of RT) concerning radiation field (focRT vs. CSA-RT) in local disease.
Conclusions: 1. RT should be part of treatment in CNS-ATRT. 2. RT at relapse is probably equivalent to RT in initial therapy. 3. Focal RT is probably equivalent to CSA-RT concerning tumour control in local disease.

1225 ORAL

Radiochemotherapy of pediatric atypical teratoid/rhabdoid CNS-tumors: an interim analysis of the German ATRT-CNS pilot study

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Background: The atypical teratoid/rhabdoid tumor (AT/RT) is a very rare CNS-tumor of newborns and infants. The overall survival is exceptionally poor (median: 6–11 months). No controlled treatment study has been published. An anthracyclin-based chemotherapy (Ctx) was effective to shrink the tumors but not to cure. In most series radiotherapy (RT) improved the outcome. However, there was no advantage of neuroaxis or whole brain RT compared with local RT. Therefore, based on the German pediatric survival data (28 eligible children) in the years 1990–2004 and on a meta-analysis of the outcome of treated children (64 case reports) in the years 1986–2004, we developed a novel anthracyclin-based multi-modality therapy including a local RT.
Patients and methods: Children are enrolled in this study if the diagnosis of ATRT of the CNS was confirmed by the German Neuropathology Reference Center. After two induction Ctx cycles (doxorubicin 25 mg/m^2/d, 12 h i.v., d 1–3; dactinomycin 45 μg/kg/d, i.v. push, d 1; cisplatin 70 mg/m^2/d, 6 h i.v., d 4; vincristine 1.5 mg/m^2/d, i.v. push, d 8, 15; methotrexate 2.0 mg single dose intrathecal, d 1–4) a high conformal local RT (54 Gy, 5 x 1.8 Gy/w) with simultaneous Ctx (carboplatin: 80 mg/m^2/d, 6 h i.v., d 1–4) was given. Due to the youth of the patients we choose a safety margin of only 0.5–1 cm around the GTV to define the PTV). Thereafter a reinduction Ctx cycle (same as 1st and 2nd cycle) was implemented. Next, a consolidation Ctx (6 cycles/9 months: CCNU 75 mg/m^2/d, d 1; cisplatin 70 mg/m^2/d, d 1; vincristine 1.5 mg/m^2/d, d 1, 8, 15; methotrexate 2.0 mg single dose intrathecal, d 1–4) was started.
Results: In 10 of 14 children (11 m., 3 f.; median age 11 months) data were available. Primary surgery: 1 SR, 7 PR, 2 biopsy. After induction Ctx, in 9 of 10 children (one died) a response was observed (1 CR, 7 PR, 1 SD). Two children completed the study and showed NED since 22 respectively 33 months after diagnosis. One child (12 month at RT) developed (4 month after RT) a radionecrosis within the PTV. However, he had no clinical symptoms and the MRT's showed no progression of the necrosis 21 month after RT.
Conclusion: The treatment results are encouraging. The induction Ctx is effective but toxic. High doses of RT+intrathecal MTX in infants can cause necrosis. However, this concept is firstly justified by the high risk