(median, 6 cm). Thirty-seven patients were treated with surgery. Surgical margins were negative in 19 patients, microscopically positive in 9 patients, and grossly positive in 9 patients. One patient received definitive radiation therapy. The Ki-67 expression was positive (>5%) in 9 among 38 cases (24%).
Results: The median follow-up period was 34 months (range, 7−75). Five patients developed local progressions and 9 experienced local recurrences. The 3-year disease-free survival rate and the 3-year progression-free survival rate were 54% and 55%, respectively. Positive Ki-67 expression ($p = 0.036$), tumor size more than 5 cm ($p = 0.021$), debulking surgery ($p = 0.021$), and extra-abdominal location of tumor ($p = 0.004$) were associated with poor disease-free survival with significance.
Conclusions: The current data suggests that patterns of Ki-67 expression are also a prognostic factor in addition to the gross anatomy in the sporadic desmoid tumors. Thus patterns of Ki-67 expression can be used as criteria for adjuvant therapy after surgery.

Table. Prognostic factors for disease-free survival

Variables		No. of patient	3Y DFS[a]	p-value
Location	Extra-abdominal	23	27%	0.004[b]
	Abdominal wall	11	100%	
	Intra-abdominal	4	50%	
Tumor size	<5 cm	10	90%	0.021[c]
	⩾5cm	28	37%	
Surgery	Wide excision	26	67%	0.021[c]
	Debulking	11	33%	
Surgical margin	Negative	19	69%	0.181[c]
	Positive	18	44%	
Ki-67 expression	Negative	29	66%	0.036[c]
	Positive	9	0%	

[a]disease free survival; [b]One-way ANOVA. Extra-abdominal vs abdominal wall; [c]Log-rank test

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Association of genetic polymorphisms with survival in Japanese pancreatic cancer patients treated with gemcitabine

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Background: Gemcitabine (Gem) is an anti-cancer drug effective against solid tumors. Nucleoside transporters including SLC29A1, cytidine deaminase (CDA), and deoxycytidine kinase (DCK) are involved in the transportation, detoxication or activation of Gem. We previously reported that a non-synonymous single nucleotide polymorphism (SNP), CDA 208G>A (A70T), affected the pharmacokinetics and toxicity of Gem [1]. Therefore, we investigated the effects of genetic polymorphisms and background factors on survival in pancreatic cancer patients treated with Gem.
Materials and Methods: The study involved 76 Japanese patients with stage IV pancreatic cancer, a subset of the patients reported previously [1], receiving Gem monotherapy and no previous radiation therapy. Plasma CDA activity was measured using Gem or cytidine as a substrate. Polymorphisms of the CDA, DCK and SLC29A1 genes were detected by dideoxy sequencing using genomic DNA obtained from peripheral blood leukocytes. The log-rank test or Cox proportional hazard models were applied for survival analyses. The ethics committees of the National Cancer Center and the National Institute of Health Sciences approved this study, and written informed consent was obtained from each patient.
Results: CDA 208G>A, which was previously reported to lead to reduced Gem clearance [1], was associated with prolonged survival (median for GG and GA; 165 and 606 days, $P = 0.042$), while an intron SNP of CDA, IVS1+37G>A, was associated with reduced survival (median for GG+GA and AA; 178 and 86 days, $P = 0.012$). A non-synonymous SNP of DCK, 364C>T (P122S), showed strong association with reduced survival (survival for CC and CT; 178 and 60 days, $P = 0.0028$). The allele frequency of DCK 364C>T was 0.061 in our study. No genetic polymorphisms of SLC29A1 showed any significant association with survival. Performance status, CA19−9, CRP, and plasma CDA activity also showed significant effects on survival ($P < 0.05$ for all). A multivariate Cox proportional hazard model suggested that CA19−9, CRP, the intron SNP of CDA, and DCK 364C>T are major factors determining the prognosis of pancreatic cancer patients receiving Gem monotherapy.
Conclusions: These observations suggest that genetic polymorphisms involved in the activation and detoxication of Gem, as well as some tumor markers, can be useful indicators of prognosis in patients with pancreatic cancer receiving Gem monotherapy.

References

[1] E. Sugiyama et al., J Clin Oncol 2007; 26: 32−42.

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Epidermal growth factor (EGF) +61 A/G functional genetic polymorphism influences disease-free interval in androgen blockade treated prostate cancer patients

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Background: Most patients with Prostate Cancer (PCa) will evidence sometime along the course of their disease resistance to androgen-blockade therapy (ABT), emerging an androgen-independent state. EGF activates several intracellular pathways after binding to homo- (EGFR1) or hetero-dimmer receptors (EGFR1-HER2), ultimately leading to proliferation, differentiation and tumorigenesis of epithelial cells.
The EGF-EGFR/HER2 pathway seems to assume special relevance in androgen-independent Prostate Cancer state (AIPCa). EGF role in PCa oncobiology and the high frequency of AIPCa support the rationale for studying its potential as a molecular marker in prognosis and further evaluate pharmacogenomic application in ABT. Recently, a single nucleotide polymorphism (SNP) A/G in +61 locus of EGF gene was described, in which peripheral-blood mononuclear cells from A homozygous carriers expressed significantly less EGF mRNA compared to G allele carriers (AG/GG).
Materials and Methods: In the present study, EGF+61 A/G polymorphism detection was performed through Polymerase Chain Reaction – Restriction Fragment Length Polymorphism procedures in PCa patients submitted to ABT ($N = 124$), and in healthy controls without cancer evidence ($N = 152$).
Results: In the recessive model, genotype frequencies were similar between both groups (PCa group, AA = 27.4%, AG/GG = 72.6%; Control group, AA = 37.5%, AG/GG = 62.5%), without significant risk for being diagnosed with PCa in G-allele carriers (Odds Ratio, $OR = 1.59$, $P = 0.076$). Furthermore, there is an increased risk in AG/GG carriers for being diagnosed with a high grade PCa (Gleason ⩾7), compared to the control group ($OR = 2.49$, $P = 0.008$).
Disease free interval is significantly lower in AG/GG carriers compared with AA (mean±SEM, 32.1±7.1 and 71.3±13.2, respectively, $P = 0.008$). Kaplan Meier survival curves analysis and Log Rank test (Mantel-Cox) further support the influence of EGF+61 A/G polymorphism in disease free interval cumulative probability ($P = 0.018$).
Conclusions: In this sample, G-allele carriers have an increased risk for being diagnosed with high-grade disease and for developing precociously resistance to ABT. The results suggest that this EGF functional polymorphism may contribute to the establishment of a prognostic and predictive molecular profile in AIPCa patients submitted to ABT and support the involvement of EGF in an alternative pathway for tumor progression in androgen-independent prostatic tumors.

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An alternative splice variant of PIK3CD is common in neuroblastoma, colorectal and ovarian cancer

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Background: Alterations of the PI3K-Akt pathway in human cancers are very common. PIK3CD encodes p110δ, a catalytic subunit of type I phosphatidyl-inositol-3′ kinase (PI3K). The gene PIK3CD resides in chromosome region 1p36.2, a region commonly deleted in a variety of human cancers indicating that there is a gene in this region with a tumour suppressor function.
Material, methods & results: We have discovered an alternative splicesite in intron 5 of PIK3CD, resulting in an extra 163 bp insertion in the mature mRNA causing a frame shift and an early termination of the protein (302 aa compared to 1045 aa in p110δ). This splice variant encodes a protein that comprises a regulatory p85-binding domain but no catalytic domain. We can by cotransfection show that the protein resulting from the splice variant of PIK3CD colocalises with p85 in aggregates in the cytoplasm, whereas p110δ colocalises with p85 evenly distributed in the cytoplasm.