The only region of amplification that differed significantly between MEC and NMEC was 8q24. It was amplified in 2/5 (40%) of MEC versus none (0%) of 20 NMEC tumours (P = 0.03). The region started at 8q24.12, upstream of *EIF3H*, and ended at 8q24.13, downstream of *MYC*. It encompassed the *DEPDC6* (upstream) to *HAS2* (downstream) and contained *COL14A1* (collagen, type XIV), *MTBP* (Mdm2-binding protein, which stabilizes MDM2 and in this way increases p53 degradation) and *SNTB1* (syntrophin, beta 1, which is a dystrophin binding protein).
Of the putative targets of 8q24 amplification identified, the *HAS2* gene merits particular attention. It encodes hyaluronan synthase, and has been found overexpressed in many tumour types. The resulting high concentration of hyaluronan has been used as a tumour marker as its direct measurement in urine and serum samples has shown very good predictive values for cancer detection and grading. Also, in vitro silencing of the *HAS2* gene has reversed the aggressive potential of cancer cells and is hoped to entice pharmacological potential. The gene also encodes for a *cis*-antisense mRNA (HAS2AS gene), which regulates HAS2 transcription. Thus, if confirmed as a target of 8q24 amplification, the mechanism by which this increases cancer growth should also be elucidated. Further investigation of the significance of the 8q24 genes for EC aggressiveness is warranted. If confirmed, their amplification could reveal new knowledge on the mechanism behind the metastatic process.

812 Transcriptional profiling of early onset colorectal cancer identifies CLC as a potential cancer susceptibility gene

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Background: Genetic predisposition is estimated to be the cause of colorectal cancer (CRC) in up to 30% of all cases, including the known inherited CRC syndromes (*e.g.* Lynch syndrome and familial adenomatous polyposis) that accounts for only about 5%. The incidence of CRC increases with age and an early onset of disease is an indication of genetic predisposition. In an attempt to identify cancer susceptibility genes, whole genome transcriptional differences between samples from patients diagnose with CRC at an early age and samples from sporadic/late onset CRC were compared.
Material and Methods: CRC samples were obtained from hospitals in the South-East region of Norway. In total, 24 primary tumours from patients diagnosed at an early age (mean 43 years), 17 sporadic tumours from elderly patients (mean 79 years) and four normal mucosa samples were included. All tumours were microsatellite stable, and samples from both genders and from the different Dukes' stages were represented equally. Applied Biosystems AB1700 microarrays were used, which enables measurements of gene expression using 32,878 unique probes.
Results: Principle component and cluster analysis showed an equal overall expression profile when comparing the early and late onset tumours. Nevertheless, although not all reaching statistical significance, we identified 20 protein coding genes differentially expressed in the early onset tumours compared to those with a late onset. *CLC* was the overall most significant gene with an increased expression in the early onset samples. Gene Set Enrichment Analysis identified chromosome band 19q13 as the most significant region with an enrichment of genes with an increased expression in the early onset samples, a region that includes *CLC*. Supporting these findings, the expression data has in parallel been integrated with corresponding DNA copy number data and chromosome band 19q13.2 was one of the loci identified with concomitantly DNA copy number gain and increased mRNA expression (Berg *et al.*, unpublished).
Conclusions: Minor differences were found when comparing the overall transcriptome profiles of early and late onset CRC. Nevertheless, we have identified several genes which serve as potential cancer susceptibility genes warranting further investigation in the continuing search for inherited genetic alteration in CRC.

813 The scaffolding adaptor GAB2 promotes anchorage independence and drives a transcriptional program associated to metastatic progression of breast cancer

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Background: The ability to grow in the absence of anchorage to the extracellular matrix represents a key oncogenic property of cancer cells. To screen for genes conferring anchorage independence, we exploited a novel functional genomics approach recently developed in our laboratory.
Material and Methods: The screening was based on transduction of MCF10A human breast cells with a murine retroviral expression library. Transduced cells were then selected for anchorage independence by culturing them on polyhema-coated dishes. Exogenous cDNAs enriched after selection were identified by one-shot, species-specific quantitative tracing with murine DNA microarray analysis before and after selection.
Results: Independent infection-selection experiments highlighted significant and reproducible enrichment for murine cDNAs encoding the Gab2 protein, suggesting a role for this scaffolding adaptor in anchorage-independent growth. Gab2 was confirmed to strongly promote anchorage-independent growth when overexpressed. Such effect did not involve protection from detachment-induced apoptosis, but rather the maintenance of a proliferative status also in the absence of the consensus provided by integrin engagement. Interestingly, downregulation by RNA interference of endogenous Gab2 in neoplastic cells did not affect their adherent growth, but abrogated their growth in soft agar. Gab2-driven anchorage independence was found to specifically involve activation of the Src-Stat3 signaling axis. A transcriptional "signature" of 205 genes was obtained from GAB2-transduced, anchorage-independent MCF10A cells, and found to contain two main functional modules, respectively controlling proliferation and cell adhesion/migration/invasion. Notably, the signature was enriched in genes discriminating responsiveness of breast cancer cell lines to Dasatininb, a Src-family kinase inhibitor. Extensive validation on breast cancer datasets showed that the Gab2-signature provides a robust prognostic classifier for breast cancer metastatic relapse, largely independent from existing clinical and genomic indicators and from estrogen receptor status.
Conclusions: This work highlights a pivotal role for GAB2 and its transcriptional targets in anchorage-independent growth and breast cancer metastatic progression. Moreover, it delivers a transcriptional signature capturing metastatic propensity of breast cancer with high sensitivity and accuracy.

814 Men genotyped for BRCA1/2 mutations: how does it affect them?

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Background: Men who undergo genetic testing for harboring germline mutations in breast/ovarian cancer associated genes (*BRCA1*/*BRCA2*) represent an interesting and under investigated population. The reasons for testing are often a family history of either neoplasm or finding a mutation in a female relative. Testing for a "feminine" disease may have significant effects on men who are mutation carriers. The purpose of the study was to examine the cognitive, emotional and behavioral impacts that BRCA1/2 testing has on those tested men, by comparing carriers to non-carriers in a follow-up study.
Material and Methods: Fifty-one male carriers of a mutation in either the BRCA1 or BRCA2 genes were compared to a similar group of ethnically matched non-carriers on a questionnaire that measured changes in health behaviors since testing, within family communication about test results, risk perceptions, cognitive representations of breast cancer, and emotional reactions to test results. Participants filled-out the questionnaire in a telephone interview a few months after receiving test results and counseling in an oncogenetic clinic.
Results and Conclusions: Comparisons between carriers and non-carriers will be presented. Undergoing genetic testing for BRCA1/2 mutations may be experienced by some men as a threat to their manhood. Men found to be carriers may need support in adjusting to their genetic status and the impact that it has on their own health and that of their female offspring.

815 Fast statistical analysis of high density CGH and SNP arrays

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Background: Array-based Comparative Genomic Hybridization (array-CGH) and Single Nucleotide Polymorphism (SNP) arrays are used for studying the genetics of cancer. Their bioinformatical and statistical analysis is a critical step to identify gained and lost regions containing potential oncogenes or tumour suppressor genes.
Material and Methods: The CGHseg method (Picard et al 2005), which uses a dynamic programming algorithm, was shown to be one of the best methods (Lai et al 2006) to analyze CGH arrays and detect DNA copy number alterations. However, its application to very high density CGH and SNP arrays measuring the DNA copy number on more than 1 million loci per patient was limited due to algorithm complexity.
Results: We have found shortcuts in the dynamic programming algorithm and have implemented an improved version of the CGHseg method. The new algorithm recovers exactly the same result as the previous one in a drastically