*Lau, Ching* [35]

## Identification of a new fusion of *ETV6/TEL* and *NTRK3/TRKC* in a primitive neuroectodermal tumor

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*ETV6/TEL,* a member of the ETS family of transcription factors, has been involved in a variety of gene fusions in various neoplasms. One of its fusion partners is *NTRK3/TRKC,* which encodes the receptor for neurotrophin-3. Although *NTRK3* is expressed broadly in neural tissues during the growth and development of the central nervous system, its fusion with *TEL* has never been reported in central nervous system tumors. We report here a new *TEL–NTRK3* fusion in a primitive neuroectodermal tumor (PNET). The patient was five months old when she underwent a resection of a left frontal tumor that was diagnosed as a benign desmoplastic infantile ganglioglioma. Three months later she had another resection for the recurrent tumor, which was diagnosed as a highly malignant PNET. G-banding karyotype analysis showed 46, XX in both tumors, but spectral karyotyping revealed a single near-tetraploid cell in the first tumor with a t(12; 15)(p13; q25) translocation and the same translocation in all metaphases in the PNET. Subsequent fluorescence *in situ* hybridization analysis using a *TEL* probe revealed the translocation of the *TEL* gene to the der(15) chromosome. Based on a similar translocation previously described in infantile fibrosarcoma, congenital mesoblastic nephroma and acute myeloid leukemia involving the *TEL* and *NTRK3* genes, we used the polymerase chain reaction with reverse transcription, with primers flanking the coding sequences of *TEL* and *NTRK3,* to detect a chimeric message of 1.6 kilobases. We located the breakpoint at the end of exon 4 of *TEL* in frame with exon 12 of *NTRK3.* This results in a unique *TEL–NTRK3* fusion transcript with the helix–loop–helix dimerization domain of *TEL* fused to the protein tyrosine kinase domain of *NTRK3.* Since t(12; 15) is the only structural chromosome aberration in this case and a similar *TEL–NTRK3* fusion product has been used to transform NIH 3T3 cells, we propose that the *TEL–NTRK3* fusion may have contributed to the cellular transformation and progression of this tumor.

*Lee, Ann* [36]

## Identification of genes differentially expressed in breast cancer cells treated with tamoxifen, using microarray-based expression profiling

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Adjuvant tamoxifen therapy is effective in reducing the risk of recurrence and death in patients with estrogen-receptor-positive breast cancer. However, the development of acquired resistance to tamoxifen limits its clinical effectiveness. To determine the effects of tamoxifen on breast cancer cells, long-term cultures of the breast cancer MCF-7 cell line, treated with tamoxifen, were established. Gene expression profiles of tamoxifen-treated and untreated MCF-7 cells were characterized using the Clontech Atlas human cancer 1.2 array, representing 1,176 genes. RNA was extracted from tamoxifen-sensitive cells 4 days and 6 weeks after commencement of treatment with tamoxifen, as well as from untreated MCF-7 cells at the same time points. Only gene expression differences greater than twofold were considered. At 4 days, 13 genes were found to be overexpressed and 2 genes were underexpressed in the tamoxifen-treated MCF-7 cells compared with the untreated MCF-7 cells. In the tamoxifen-treated MCF-7 cells harvested at 6 weeks, 16 genes were overexpressed and 5 genes were underexpressed compared with the treated cells harvested at 4 days. Wnt-5a, disheveled homologue 1, cyclin kinase inhibitor p19INK4D and the signaling lymphocytic activation molecule were overexpressed in both of the comparisons. Gene expression profiling is useful for the rapid identification of genes differentially expressed during tamoxifen treatment.

*Leszczynski, Dariusz* [37]

## Proteomics: new way to to determine possible biological effects of mobile phone radiation

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Despite years of research, the question of whether exposure to radiofrequency-modulated electromagnetic fields (RF-EMF) generated by mobile phones affects human health remains unsolved. We obtained a comprehensive overview of the possible extent of cellular response to RF-EMF irradiation by determining the total cellular changes in protein expression and in protein phosphorylation that occur in response to RF-EMF exposure under athermal conditions. As a model we used human endothelial cell line EA.hy926. Cells were exposed for one hour to a 900-MHz GSM signal. Immediately following exposure we harvested cells and extracted and separated proteins using two-dimensional electrophoresis. To determine changes in protein phosphorylation, $^{32}P$ was present in the cultures during the exposure period. Using Bio-Rad's PDQUEST 6.1.0 software we identified over 1,200 proteins in two-dimensional gels ($10 \times 20$ cm). A large number of protein spots changed expression following irradiation. In control cells we detected over 180 phosphoproteins. RF-EMF exposure has generated a large number of newly phosphorylated proteins that were not present in controls. Among the proteins with altered phosphorylation levels were shock proteins, such as hsp27. Thus the expression and phosphorylation of a large number of proteins isolated from EA.hy926 cells seems to be altered by short RF-EMF exposure, suggesting that cells mount a vigorous response to RF-EMF stress. However, whether the observed stress can cause long-lasting physiological effects remains to be determined.

*Lin, Lin* [38]

## Identification and characterization of a 19q12 amplicon in esophageal adenocarcinomas using two-dimensional genomic scanning and amplification mapping of sequence tagged sites

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Amplification of genomic DNA can confer a selective advantage in tumors by increasing the dosage of gene(s) involved in tumor development or progression.