ferent p53 status, including p53-null cells (NH32), cells with wild-type p53 (TK6) and cells with mutated p53 (WTK1). The results showed that at the *TK1* locus p53-null cells had equivalent background mutation frequencies and were approximately as mutable as TK6, whereas WTK1 were much more sensitive to spontaneously arising and radiation-induced mutation. These results indicated that the lack of wild-type p53 does not lead to increased mutability. In this study, to explore further how p53 is involved in regulating mutational processes, we used 7K complementary DNA microarrays to compare the patterns of gene expression between TK6 and NH32 cells following irradiation. Total RNA was extracted 3, 6, and 24 h after irradiation with 10-Gy X-rays. Our preliminary results indicated that irradiation resulted in more genes being upregulated than downregulated in human lymphoblast cells regardless of their p53 status. Furthermore, cluster analyses of gene expression profiles in TK6 and NH32 revealed different patterns. In TK6 radiation-induced p53-related responses showed a rapid induction (higher at 3 and 6 h after irradiation than at 24 h), whereas in NH32 radiation-induced p53-unrelated responses showed different kinetics (higher at 3 and 24 h after irradiation than at 6 h).

Chung, L. Ping. [39]

Allelic imbalance in lung cancers of nonsmokers in Hong Kong

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Lung cancer is a common malignancy in Hong Kong. The incidence in males is ranked medium, but that in females is among the highest in the world. More than 60% of female patients are lifelong nonsmokers, implying that carcinogenic mechanisms other than cigarette smoking may be involved in the development of lung cancers in female nonsmokers. To identify the candidate tumor suppressor genes involved, we screened 50 commonly deleted regions of all the chromosomal arms for loss of heterozygosity of microsatellite markers in 41 samples of cancerous lung tissue from nonsmokers. We found frequent allelic loss of 50–62.5% in the chromosomal regions 1q21–31, 3p14.2, 7q31, 8p21, 10q26, 13q12.3, 16q24, 17p13.1–13.3, 17q13.3, 18q23 and 19p13. Comparison with 40 lung cancers from smokers using the same markers showed a similar range of loss of heterozygosity frequency in the two populations. We found that some regions commonly deleted in smokers (for example, 4q32, 6q27, 9q21 and 11q23) were statistically less frequently deleted in nonsmokers, but we found no region frequently deleted in nonsmokers but not smokers. Our data on cancers from smokers indicate that smoking induces widespread genomic damage, leading to extensive chromosomal loss of long segments of DNA. Cancers from nonsmokers exhibit more targeted damage, with fewer and shorter segments of DNA loss. The deleted regions in cancers of nonsmokers might represent the essential complement of genetic material that must be lost for lung cancers to develop.

Collins, Colin [40]

Comprehensive sequence analysis of a human 20q13.2 cancer amplicon

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Amplification of 20q13.2 occurs in breast and other cancers and is associated with aggressive tumor behavior. We report the first sequence and comprehensive biological characterization of a tumor amplicon. Array-based comparative genomic hybridization resolved the 1.2-megabase amplicon into a pair of recurrent peaks. The proximal amplicon encodes the putative Zn-finger transcription factor ZNF217, a candidate oncogene recently shown to immortalize human mammary epithelial cells. Analysis of the genomic sequence for genes, repetitive elements, CpG islands, and gene expression revealed six previously discovered genes (*ZNF217, ZNF218, PIC1-like, NABC1, CYP24,* and *NABC2*) and four new genes (*PFDN4, NABC3, NABC4* and *NABC5*). *ZNF217* is the only protein-coding gene in the 160-Kb proximal amplicon peak. *CYP24* and *PFDN4* map in the distal amplicon. *PFDN4* is overexpressed in tumors in which it is amplified and in some in which it is not. Amplicon breakpoints cluster in regions of very high repeat content flanking *ZNF217* and *PFDN4.* A 14-Kb duplication, of a class associated with unstable chromosome regions, maps close to *ZNF217.* This duplicon is approximately 97% identical to a 14-Kb element on chromosome 22q13 and encodes one of three CpG islands in the amplicon and NABC3. We cloned and sequenced the syntenic region of mouse chromosome 2, revealing numerous homologies. These correspond to conserved exons and noncoding elements believed to be regulatory or structural in nature. We will report on these findings, which clearly demonstrate the power of comparative sequence analysis for cancer biology.

Coombes, K.R. [41]

Identifying and quantifying sources of variation in high-density cDNA microarray data using ^{33}P-labeled probes

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A microarray experiment involves several steps, including spotting complementary DNA, extracting RNA, labeling the probe, hybridizing, scanning and analyzing images. Each step introduces variability, confounding our ability to obtain accurate estimates of the biological differences between samples. We ran repeated experiments using high-density cDNA microarray membranes (Research Genetics