Rapid screening assays can help to define aptamers inhibiting desired cellular features. Further work scrutinizing the nature and mechanisms of the activity of functional aptamers in detail will contribute to increase the basic knowledge of the molecular determinants of metastasis and, in the future, may help to create new agents for prognostic or therapeutic purposes.

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Increased expression of VEGF in a prostate intraepithelial neoplasia (PIN)-like cell line leads to Epithelial-to-Mesenchymal transition (EMT)

O. Gonzalez-Moreno[1], J. Lecanda[2], V. Segura[3], D. Serrano[1], R. Catena[1], J.E. Green[4], A. Calvo[1]
[1]Center for Applied Medical Research, Division of Oncology, Pamplona, Spain; [2] Center for Applied Medical Research, Division of Hepatology and Gene Therapy, Pamplona, Spain; [3] CEIT & TECNUM, University of Navarra, Pamplona, Spain [4] NIH, Laboratory of Cancer Biology and Genetics, Bethesda, USA

Prostate intraepithelial neoplasia (PIN) is thought to be the precursor lesion leading to invasive carcinoma. During this transition, several growth factors are overexpressed, including the vascular endothelial growth factor (VEGF), which plays a role in recruiting blood vessels. We have mimicked such a process in vitro using the PIN-like C3(1)/Tag-derived Pr-111 cell line. These cells are poorly angiogenic and exhibit very low tumorigenicity in vivo. Increased expression of VEGF164 in Pr-111 cells led to a significant increase in tumorigenicity as shown when inyected subcutaneously in nude mice, invasiveness when performed Boyden chamber assays, proliferation rates and angiogenesis. Moreover, VEGF164 induced strong changes in cell morphology and in the cell transcriptome, through an autocrine mechanism. Gene expression of 398 genes was significantly altered in VEGF164-overexpressing Pr-111 cells. These included genes related to modification of the actin filaments, cell adhesion, signal transduction, and proliferation. Pr-111-overexpressing cells also displayed features of epithelial-to-mesenchymal transition (EMT), with an increased expression of mesenchymal markers, such as N-cadherin and Vimentin. Levels of E-cadherin and B-catenin were not changed in these cells. Our results strongly suggest that increased expression of VEGF in malignant cells during the transition from PIN to invasive carcinoma leads to EMT through an autocrine loop, thus promoting tumor cell invasion and motility. Blockade of VEGF in PIN lesions would likely impair not only tumor angiogenesis, but also spread of malignant cells.

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The promoting effect of dietary lipids on experimental mammary cancer is accompanied by changes in the expression of differentiation-related genes

M. Solanas[1], R. Moral[1], L. Grau[1], E. Vela[1], R. Escrich[1], G. Garcia[1], I. Costa[1], E. Escrich[1]
[1]Universitat Autonoma de Barcelona, Cell Biology Physiology and Immunology, Cerdanyola del Valles, Barcelona, Spain

Breast cancer is a significant cause of mortality in women worldwide. Environmental factors, specially diet and lifestyle, have an important role in its etiology. In this study we have investigated the effects of a high corn oil and a high virgin olive oil diets on tumour clinical, anatomopathological and molecular parameters related to differentiation. Female Sprague-Dawley rats were induced with DMBA and fed a low fat (LF, 3% corn oil), a high corn oil (HF-C, 20% corn oil) or a high olive oil (HF-O, 3% corn oil plus 17% olive oil) diet. The results showed that the HF-C diet reduced the latency time and increased the mammary tumour incidence, content and volume. On the other hand, the HF-O diet led to the opposite effects (higher latency time and lower tumour incidence, content and volume). Moreover, the HF-C diet increased the tumour morphological aggressiveness, whereas the HF-O diet led to adenocarcinomas displaying features of low morphological malignancy. These results showed a clear stimulating effect of the high corn oil diet on breast cancer and a negative modulator role for high virgin olive oil diet. We also analysed the effect of these diets on the expression of differentiation related genes. We studied the classical breast differentiation markers alpha- and beta-casein, finding that their expression was deregulated in the mammary tumours. We also investigated the protooncogene PCPH, observing that its expression pattern was associated to the cell differentiation degree of the mammary gland. Furthermore, this protein was down-modulated by effect of the HF-C. Finally, using cDNA microarrays we identified 3 genes down-modulated by the HF-C diet, but not by the HF-O diet: submaxilar alpha-2u globulin, VDUP1 and H19. These genes have also been related to differentiation. Our results suggest that changes in the modulation of genes with a role in differentiation can be one of the mechanisms by which the high corn oil and the high olive oil exert their differential modulatory effects on experimental breast cancer.

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Relationship between the methylation status of deleted in liver cancer-1 gene and invasiveness and metastasis of hepatocellular carcinoma

Y. Zhang[1], J. Liu[2], S. Zhang[1], M. Shi[1]
[1]Nantong University, Surgical Oncology, Nantong, China; [2] Nantong University, Oncology, Nantong, China

Objective: To study the relationship between the expression level of the methylation Status of Deleted in Liver Cancer(DLC-1(gene and invasiveness and metastasis of hepatocellular carcinoma(HCC). Methods:76 surgical specimens and blood samples of patients with HCC were divided into high invasive and low invasive groups according to their clinical and pathological features. A methylation-specific PCR(MSP) was performed for the detection of hypermethylation of DLC-1 gene. Results: the expression level of the methylation Status of DLC-1 gene in surgical specimens of patients of HCC with high invasive group (n=40) was significantly higher than those with low invasive group(n=36)(÷2=4.3567, P < 0. 05), So was it in blood samples (÷2=4.4652, P < 0. 05)); Methylation Status of DLC-1 gene in HCC surgical specimens correlated with the clinical stages of patients with HCC((÷2=10.8478, P < 0. 05); Methylation Status of DLC-1 gene in blood samples from HCC patients correlated with their clinical stages(P < 0. 05), and with serum AFP level; The Median Survival Time were significantly different between HCC patients with the expression of the Methylated DLC-1gene and that without the expression of the Methylated DLC-1gene by follow-up (P < 0. 05). Conclusion: The expression level of the methylation Status of DLC-1 gene may play an important role in invasiveness and metastasis of HCC. Detection of the abnormal methylation of DLC-1 gene from HCC patients might not only offer an effective method for the auxiliary earlier diagnosis of the invasiveness and metastasis, but also serve as an objective target for HCC therapies.

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LMP1 gene variants of Russian origin from patients with EBV-associated pathologies and healthy individuals

V. Gurtsevitch[1], K. Smirnova[1], S. Diduk[1], E. Goncharova[1], L. Scherback[1], V. Stepina[1], L. Yakovleva[1]
[1]Cancer Research Center, Laboratory of viral carcinogenesis, Moscow, Russian Federation

Background. Molecular analysis of Epstein-Barr virus (EBV) LMP1gene of different clinical and geographical origin allowed discovering two variants of gene (designated as LMP1-Cao and LMP1-C1510) possessing significantly higher transforming potential in comparison with their prototype LMP1-B95.8. Proteins encoded by these genes showed structural variations, consisting of multiple single base mutations, a C-terminal 30-base pair (bp) deletion and deletion of 15-bp unique sequence with insertion of three 33-bp repeats in the repeat region. On the basis of primary nucleotide structure and geographic origin LMP1 samples were classified as specific sequence variants.

As far as information concerning the strain differences of LMP1 EBV persisting in Russia was absent the main goal of present investigation was to carry out sequence analysis of LMP1 samples amplified from biological materials of Russian patients with EBV-associated diseases of lymphoid and epithelial origin, as well as healthy individuals.

Materials and methods. The DNA sequencing of tested LMP1 samples was carried out by means of reagents ABI PRISM® BigDye™ Terminator v. 3.1 with the subsequent analysis of the reaction products on automatic sequenator SEQDNA ABI PRISM 3100-Avant. The data processing was carried out with help of Chromas 230 and Vector NTI programs.

Results obtained allowed us to come to following conclusions: among point mutations detected in tested LMP1 samples the mutations I85L, F106Y, E328Q and S366T are predominant and possibly playing key role in modification of numerous signaling pathways as well as having important influence on transforming potential of the gene; individual variant of LMP1 for specific disease under investigations has not been detected; Cao-like deletions in LMP1 samples of Russian origin were detected occasionally in different studied groups; different genetic variants of LMP1 detected in different biological materials of the same patients possibly indicate both the of simultaneous persistence of genetically different variants of LMP1 as well as genetic drift of the original variant of gene as a result of mutations occurred de novo.

Conclusion. LMP1 samples amplified from Russian patients with HL, NHLs, IM, NPC and GC, as well as blood donors represent genetically heterogeneous group consisting of both earlier described in literature and possibly new variants of the gene.

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