Cellular density of low-grade transition zone prostate cancer: A limiting factor to correlate restricted diffusion with tumor aggressiveness.

Related Articles

Cellular density of low-grade transition zone prostate cancer: A limiting factor to correlate restricted diffusion with tumor aggressiveness.

Eur J Radiol. 2020 Aug 20;131:109230

Authors: Barral M, Jemal-Turki A, Beuvon F, Soyer P, Camparo P, Cornud F

Abstract

OBJECTIVE: To compare the mean apparent diffusion coefficient (ADCmean) and glandular density of Gleason score (GS) 3 + 3 transition zone prostate cancers (TZ-PCa) with those of the peripheral zone (PZ-PCa).

MATERIAL & METHODS: Seventy-nine men (mean age: 65 ± 6 [SD] years; range: 52–81 years) with 37 TZ-PCa (37÷79; 53 %) and 42 PZ-PCa (42÷79; 47 %) had prostate MRI before radical prostatectomy. Glandular cell density was semi-quantitatively evaluated in all tumors. ADCmean and glandular cell density of GS3 + 3 TZ-PCa were compared to those of PZ-PCa. ADCmean was correlated to GS in each zone.

RESULTS: ADCmean of GS 3 + 3 tumors was significantly lower in the TZ (728 × 10–6 ±52 [SD] mm²/s; range: 670-1060mm²/s) than in the PZ (865 × 10–6 ±121 [SD] mm²/s; range: 670-1120mm²/s) (p = 0.0007), related to a significantly higher glandular density involving more than 50 % of the tumor in 58 % (7÷12) of patients in GS3 + 3 TZ-PCa versus 7.6 % (1÷13) in PZ-PCa (p = 0.03). ADCmean of GS3 + 3 TZ-PCa was not significantly different from that of GS 3 + 4 (p = 0.14) or GS>3 + 4 Ca (p = 0.9), whatever the zone of origin. In the PZ, ADCmean of GS 3 + 3-PCa was higher than that of Gleason>3 + 4 PZ-PCa (p = 0.02) and similar to that of GS 3 + 4 PZ-PCa (p = 0.24). Correlation between ADCmean and GS was weak for TZ-PCa (r = 0.32; p = 0.04) and moderate for PZ-PCa (r = 0.45; p = 0.003).

CONCLUSION: ADCmean of GS 3 + 3 TZ-PCa is significantly lower than that of GS 3 + 3 PZ-PCa, related to a unique dense histological pattern and reaches that of higher-grade PCa, whatever the zone of origin.

PMID: 32866908 [PubMed — as supplied by publisher]

Facile fluorescent aptasensor using aggregation-induced emission luminogens for exosomal proteins profiling towards liquid biopsy.

Related Articles

Facile fluorescent aptasensor using aggregation-induced emission luminogens for exosomal proteins profiling towards liquid biopsy.

Biosens Bioelectron. 2020 Aug 16;168:112520


Abstract

Surface protein patterns of tumor-derived exosomes could be promising noninvasive diagnostic biomarkers for liquid biopsy. However, a convenient and cost-effective platform for exosomal protein profiling is still lacking. Herein, a facile fluorescent aptasensor is developed to assess exosomal tumor-associated proteins, combining aptamers, aggregation-induced emission luminogens (AIEgens), and graphene oxide (GO) as recognition elements, fluorescent dye, and the quencher, respectively. Specifically, numerous TPE-TAs could bind one aptamer and form aggregates rapidly, resulting in an amplified fluorescence signal. In the absence of tumor-derived exosomes, GO absorbs the TPE-TAs/aptamer complex, allowing fluorescence quenching. When the target exosomes are introduced, the aptamer preferentially binds with its target. Thus the TPE-TAs/aptamer complexes detach from GO surface, followed by the appearance of a “turn-on” fluorescent signal. Under the optimized conditions, the linear range of target exosomes is estimated to be 4.07 × 105 to 1.83 × 107 particles/μL (0.68−30.4 pM) with a detection limit of 3.43 × 105 particles/μL (0.57 pM). This strategy demonstrated great performance in differentiating prostate cancer from healthy individuals (AUC: 0.9790). Furthermore, by profiling three tumor-associated protein markers including epidermal growth factor receptor (EGFR), epithelial cell adhesion molecule (EpCAM), and human epidermal growth factor receptor 2 (HER2) on exosomes in a breast tumor cohort, this sensing platform diagnoses breast tumors with high efficiency (AUC: 0.9845) and exhibits a high sensitivity of 97.37% for distinguishing malignant breast cancers, where the stage I cases were detected with 92.31% sensitivity. Therefore, this aptasensor provides a promising strategy to profile tumor-derived exosomal proteins for early diagnosis in liquid biopsy.
Germline HSD3B1 Genetics and Prostate Cancer Outcomes.

Authors: Thomas L, Sharifi N

Abstract
Dihydrotestosterone synthesis in prostate cancer from adrenal DHEA/DHEA-sulfate requires enzymatic conversion in tumor tissues. 3β-hydroxysteroid dehydrogenase-1 (3β-HSD1) is an absolutely necessary enzyme for such dihydrotestosterone synthesis and is encoded by the gene HSD3B1 which comes in two functional inherited forms described in 2013. The adrenal-permissive HSD3B1(1245C) allele allows for rapid dihydrotestosterone synthesis. The adrenal-restrictive HSD3B1(1245A) allele limits androgen synthesis. Studies from multiple cohorts show that adrenal-permissive allele inheritance confers worse outcomes and shorter survival after castration in low-volume prostate cancer and poor outcomes after abiraterone or enzalutamide treatment for castration-resistant prostate cancer. Here, we review the clinical data and implications.

Related Articles

Author Reply: 3D Printing, Augmented Reality, and Virtual Reality for the Assessment and Management of Kidney and Prostate Cancer: A Systematic Review.

Authors: Wake N, Bjurlin MA

Abstract
3D Printing, Augmented Reality, and Virtual Reality for the Assessment and Management of Kidney and Prostate Cancer: A Systematic Review.

Urology. 2020 Aug 28;:

Authors: Wake N, Bjurlin MA

PMID: 32866508 [PubMed — as supplied by publisher]


Authors: Lu MT, Raghu VK, Mayrhofer T, Aerts HJWL, Hoffmann U

Abstract
BACKGROUND: Lung cancer screening with chest computed tomography (CT) reduces lung cancer death. Centers for Medicare & Medicaid Services (CMS) eligibility criteria for lung cancer screening with CT require detailed smoking information and miss many incident lung cancers. An automated deep-learning approach based on chest radiograph images may identify more smokers at high risk for lung cancer who could benefit from screening with CT.

OBJECTIVE: To develop and validate a convolutional neural network (CXR-LC) that predicts long-term incident lung cancer using data commonly available in the electronic medical record (EMR) (chest radiograph, age, sex, and whether currently smoking).

DESIGN: Risk prediction study.


PARTICIPANTS: The CXR-LC model was developed in the PLCO (Prostate, Lung, Colorectal, and Ovarian) Cancer Screening Trial (n = 41 856). The final CXR-LC model was validated in additional PLCO smokers (n = 5615, 12-year follow-up) and NLST (National Lung Screening Trial) heavy smokers (n = 5493, 6-year follow-up). Results are reported for validation data sets only.

MEASUREMENTS: Up to 12-year lung cancer incidence predicted by CXR-LC.

RESULTS: The CXR-LC model had better discrimination (area under the receiver-operating characteristic curve [AUC]) for incident lung cancer than CMS eligibility (PLCO AUC, 0.755 vs. 0.634; P LIMITATION: Validation in lung cancer screening trials and not a clinical setting.

CONCLUSION: The CXR-LC model identified smokers at high risk for incident lung cancer, beyond CMS eligibility and using information commonly available in the EMR.

PRIMARY FUNDING SOURCE: None.

PMID: 32866413 [PubMed — as supplied by publisher]
Metal-free Twofold Electrochemical C-H Amination of Activated Arenes: Application to Medicinally Relevant Precursor Synthesis.

Related Articles

Metal-free Twofold Electrochemical C-H Amination of Activated Arenes: Application to Medicinally Relevant Precursor Synthesis.

Chemistry. 2020 Aug 31;:


Abstract
The efficient production of many medicinally or synthetically important starting materials suffers from wasteful or toxic precursors for the synthesis. In particular, the aromatic non-protected primary amine function represents a versatile synthetic precursor, but its synthesis typically requires toxic oxidizing agents and transition metal catalysts. The twofold electrochemical amination of activated benzene derivatives via Zincke intermediates provides an alternative sustainable strategy for the formation of new C-N bonds of high synthetic value. As a proof of concept, we use our approach to generate a benzoxazinone scaffold that gained attention as a starting structure against castrate-resistance prostate cancer. Further improvement of the structure led to significantly increased cancer cell line toxicity. Thus, exploiting environmentally benign electrooxidation, we present a new versatile and powerful method based on direct C-H activation that is applicable for e.g. the production of medicinally relevant compounds.

PMID: 32866328 [PubMed — as supplied by publisher]

Incorporating MRI and biomarkers in active surveillance protocols — results from the prospective Stockholm3 Active Surveillance trial (STHLM3AS).

Related Articles

Incorporating MRI and biomarkers in active surveillance protocols — results from the prospective Stockholm3 Active Surveillance trial (STHLM3AS).

J Natl Cancer Inst. 2020 Aug 31;:


Abstract
BACKGROUND: Active surveillance (AS) for men with low-risk prostate cancer (PC) can lead to patient morbidity and healthcare overutilization. The aim of this study was to evaluate an AS-protocol using the Stockholm3 test and MRI to reduce biopsy intensity.

METHODS: We conducted a prospective multicenter study of 280 invited men from a contemporary screening study (STHLM3), with Gleason Score (GS) 3 + 3 PC on a current AS-protocol. Patients underwent prostate-MRI and blood sampling for analysis of the Stockholm3 test including protein biomarkers, genetic variants and clinical variables to predict risk of GS ≥ 3 + 4 PC, then followed by systematic biopsies and targeted biopsies (for PIRADS ≥3 lesions) in all men. Primary outcomes were reclassification to GS ≥ 3 + 4 PC and clinically significant PC (csPC) including unfavorable intermediate risk PC or higher based on NCCN-guidelines.

RESULTS: Adding MRI-targeted biopsies to systematic biopsies increased sensitivity of GS ≥ 3 + 4 PC compared to systematic biopsies alone (relative sensitivity (RS) = 1.52; 95% CI = 1.28 to 1.85). Performing biopsies in only MRI positive increased sensitivity of GS ≥ 3 + 4 PC (RS = 1.30; 95% CI = 1.04 to 1.67), reduced number of biopsy procedures by 49.3% while missing 7.2% GS ≥ 3 + 4 PC and 1.4% csPca. Excluding men with negative Stockholm3 test reduced number of MRI investigations at follow-up by 22.5%, biopsies by 56.8% while missing 6.9% GS ≥ 3 + 4 PC and 1.3% csPca.

CONCLUSION: During AS, including MRI and targeted/systematic biopsies increase sensitivity of PC reclassification. Incorporation of risk prediction models including biomarkers may reduce the need for MRI use in men with low risk PC.

PMID: 32866231 [PubMed — as supplied by publisher]

Gene panel screening for insight towards breast cancer susceptibility in different ethnicities.

Related Articles

Gene panel screening for insight towards breast cancer susceptibility in different ethnicities.


Authors: Bishop MR, Omeler-Fenaud SM, Huskey ALW, Merner ND

Abstract
African American breast cancer genetics is less understood compared to European American breast cancer susceptibility. Despite the many advantages of gene panel screening, studies investigating African American inherited breast cancer risk and comparing variant contributions between ethnicities are infrequent. Thus, 97 breast cancer-affected individuals of African and European descent from the Alabama Hereditary Cancer Cohort were screened using the research-based gene-panel, B.O.P.
(Breast, Ovarian, and Prostate cancer). Upon sequencing and bioinformatic processing, rare coding variants in 14 cancer susceptibility genes were categorized according to the American College of Medical Genetics guidelines and compared between ethnicities. Overall, 107 different variants were identified, the majority of which were benign/likely benign. A pathogenic/likely pathogenic variant was detected in 8.6% and 6.5% of African American and European American cases, respectively, which was not statistically significant. However, African Americans were more likely to have at least one variant of uncertain significance (VUS; p-value 0.006); they also had significantly more VUSs in BRCA1/2 compared to European Americans (p-value 0.015). Additionally, 51.4% of African Americans and 32.3% of European Americans harbored multiple rare variants, and African Americans were more likely to have at least one VUS and one benign/likely benign variant (p-value 0.032), as well as multiple benign/likely benign variants (p-value 0.089). Moreover, of the 15 variants detected in multiple breast cancer cases, ATM c.2289T>C (p.F763L), a VUS, along with two likely benign variants, BRCA2 c.2926_2927delinsAT (p.S976I) and RAD51D c.251T>A (p.L84H), were determined to be associated with African American breast cancer risk when compared to ethnic-specific controls. Ultimately, B.O.P. screening provides essential insight towards the variant contributions in clinically relevant cancer susceptibility genes and differences between ethnicities, stressing the need for future research to elucidate inherited breast cancer risk.

PMID: 32866190 [PubMed — as supplied by publisher]

Meeting report from the prostate cancer foundation PSMA theranostics state of the science meeting.

Related Articles

Meeting report from the prostate cancer foundation PSMA theranostics state of the science meeting.

Prostate. 2020 Aug 31:


Abstract

INTRODUCTION: The Prostate Cancer Foundation (PCF) convened a PCF prostate-specific membrane antigen (PSMA) Theranostics State of the Science Meeting on 18 November 2019, at Weill Cornell Medicine, New York, NY.

METHODS: The meeting was attended by 22 basic, translational, and clinical researchers from around the globe, with expertise in PSMA biology, development and use of PSMA theranostics agents, and clinical trials. The goal of this meeting was to discuss the current state of knowledge, the most important biological and clinical questions, and critical next steps for the clinical development of PSMA positron emission tomography (PET) imaging agents and PSMA-targeted radionuclide agents for patients with prostate cancer.

RESULTS: Several major topic areas were discussed including the biology of PSMA, the role of PSMA-targeted PET imaging in prostate cancer, the physics and performance of different PSMA-targeted PET imaging agents, the current state of clinical development of PSMA-targeted radionuclide therapy (RNT) agents, the role of dosimetry in PSMA RNT treatment planning, barriers and challenges in PSMA RNT clinical development, optimization of patient selection for PSMA RNT trials, and promising combination treatment approaches with PSMA RNT.

DISCUSSION: This article summarizes the presentations from the meeting for the purpose of globally disseminating this knowledge.
to advance the use of PSMA-targeted theranostic agents for imaging and treatment of patients with prostate cancer.

PMID: 32865839 [PubMed — as supplied by publisher]

Phototoxic eruption caused by enzalutamide (Xtandi®).

Related Articles
Phototoxic eruption caused by enzalutamide (Xtandi®).

Contact Dermatitis. 2020 Aug 31;:
Authors: Navarro-Triviño FJ, Ruiz-Villaverde R
PMID: 32865823 [PubMed — as supplied by publisher]

Knocking Down Long Noncoding RNAs Using Antisense Oligonucleotide Gapmers.

Related Articles
Knocking Down Long Noncoding RNAs Using Antisense Oligonucleotide Gapmers.

Methods Mol Biol. 2020;2176:49–56
Authors: Maruyama R, Yokota T

Abstract
Long noncoding RNAs (lncRNAs) are a class of RNA with 200 nucleotides or longer that are not translated into protein. lncRNAs are highly abundant; a study estimates that at least four times more lncRNAs are typically present than coding RNAs in humans. However, function of more than 95% of human lncRNAs are still unknown. Synthetic antisense oligonucleotides called gapmers are powerful tools for lncRNA loss-of-function studies. Gapmers contain a central DNA part, which activates RNase H-mediated RNA degradation, flanked by modified oligonucleotides, such as 2’-O-methyl RNA (2’OMe), 2’-O-methoxyethyl RNA (2’MOE), constrained ethyl nucleosides (cEt), and locked nucleic acids (LNAs). In contrast to siRNA or RNAi-based methods, antisense oligonucleotide gapmer-based knockdown is often more effective against nuclear-localized lncRNA targets, since RNase H is mainly localized in nuclei. As such, gapmers are also potentially a powerful tool for therapeutics targeting lncRNAs in various diseases, including cancer, cardiovascular diseases, lung fibrosis, and neurological/neuromuscular diseases. This chapter will discuss the development and applications of gapmers for lncRNA loss-of-function studies and tips to design effective antisense oligonucleotides.

PMID: 32865781 [PubMed — as supplied by publisher]

Type of Androgen Deprivation Therapy and Risk of Dementia Among Patients With Prostate Cancer in Taiwan.

Related Articles
Type of Androgen Deprivation Therapy and Risk of Dementia Among Patients With Prostate Cancer in Taiwan.

JAMA Netw Open. 2020 Aug 03;3(8):e2015189
Authors: Huang WK, Liu CH, Pang ST, Liu JR, Chang JW, Liaw CC, Hsu CL, Lin YC, See LC

Abstract
Importance: It remains unclear whether androgen deprivation therapy (ADT) is associated with subsequent dementia risk in patients with prostate cancer. There are limited data regarding dementia risk across ADT types.

Objective: To examine the association between all-cause dementia, including Alzheimer disease (AD), and different ADT types in patients with prostate cancer.

Design, Setting, and Participants: This cohort study used linked data from the Taiwan National Cancer Registry, the National Health Insurance Research Database, and the Taiwan National Death Registry. A cohort of 23 651 patients with newly diagnosed prostate cancer between January 1, 2008, and December 31, 2015, was identified and followed up from 1 year after diagnosis until December 31, 2017. Data analysis was performed between January 2019 and May 2020.

Exposures: Patients who received and did not receive ADT, including gonadotropin-releasing hormone (GnRH) agonists, orchiectomy, or antiandrogen monotherapy.

Main Outcomes and Measures: The primary outcomes were all-cause dementia or AD. Stabilized inverse probability of treatment weighting was used to balance baseline covariates. The association between dementia and various ADT types was examined using the Cox proportional hazards model. Furthermore, a multivariate Cox proportional model with age as the time scale was conducted for complementary comparison.

Results: In the cohort of 23 651 male patients (median [interquartile range] age, 73 [66–79] years), 6904 (29.2%) did not receive ADT, 11 817 (50.0%) received GnRH agonists, 876 (3.7%) received orchiectomy, and 4054 (17.1%) received antiandrogen monotherapy. Overall, 1525 patients were diagnosed with incident dementia (1.72 per 100 person-years) during a median (interquartile range) follow-up of 3.46 (1.92–5.51) years. Compared with those who did not receive ADT, those using antiandrogen monotherapy showed an increased risk of dementia (weighted hazard ratio [HR], 1.34; 95% CI, 1.16–1.55) and AD (weighted HR, 1.52; 95% CI, 1.13–2.04). The risk of dementia was similar between GnRH agonist use or orchiectomy and no ADT use (GnRH agonist: weighted HR, 1.13; 95% CI, 1.00–1.28; orchiectomy: 1.00; 95% CI, 0.74–1.37). Several sensitivity analyses revealed consistent findings for both outcomes.

Conclusions and Relevance: In this study, the use of antiandrogen monotherapy was associated with increased risk of dementia or
AD, while GnRH agonist use and orchiectomy had no significant difference compared with patients who did not receive ADT. Further prospective studies are warranted to confirm these findings.

PMID: 32865575 [PubMed — as supplied by publisher]

Trends in Diagnosis and Disparities in Initial Management of High-Risk Prostate Cancer in the US.

Related Articles
Trends in Diagnosis and Disparities in Initial Management of High-Risk Prostate Cancer in the US.
JAMA Netw Open. 2020 Aug 03;3(8):e2014674
Authors: Agrawal V, Ma X, Hu JC, Barbieri CE, Nagar H
PMID: 32865572 [PubMed — as supplied by publisher]

Macrophages Expedite Cell Proliferation of Prostate Intraepithelial Neoplasia through Their Downstream Target ERK.

Related Articles
Macrophages Expedite Cell Proliferation of Prostate Intraepithelial Neoplasia through Their Downstream Target ERK.
FEBS J. 2020 Aug 31;
Authors: Thomas MU, Messex JK, Dang T, Abdulkadir SA, Jorcyk CL, Liou GY
Abstract
The risk factors for prostate cancer include a high-fat diet and obesity, both of which are associated with an altered cell environment including increased inflammation. It has been shown that chronic inflammation due to a high-fat diet or bacterial infection has the potential to accelerate prostate cancer as well as its precursor, prostatic intraepithelial neoplasia (PIN), development. However, the underlying mechanism of how chronic inflammation promotes prostate cancer development, especially PIN, remains unclear. In this study, we showed that more macrophages were present in PIN areas as compared to the normal areas of human prostate. When co-culturing PIN cells with macrophages in 3D, more PIN cells had nuclear localized cyclin D1, indicating that macrophages enhanced PIN cell proliferation. We identified ICAM-1 and CCL2 as chemotactants expressed by PIN cells to recruit macrophages. Furthermore, we discovered that macrophage-secreted cytokines including C5a, CXCL1, and CCL2 were responsible for increased PIN cell proliferation. These three cytokines activated ERK and JNK signaling in PIN cells through a ligand-receptor interaction. However, only blockade of ERK abolished macrophage cytokines-induced cell proliferation of PIN.
Overall, our results provide a mechanistic view on how macrophages activated through chronic inflammation can expedite PIN progression during prostate cancer development. The information from our work can facilitate a comprehensive understanding of prostate cancer development which is required for improvement of current strategies for prostate cancer therapy.

PMID: 32865335 [PubMed — as supplied by publisher]


Related Articles
J Thromb Haemost. 2020 Aug 31;
Authors: Voigtlaender M, Beckmann L, Schulenkorf A, Sievers B, Rolling C, Bokemeyer C, Langer F
Abstract
BACKGROUND: Inflammation with leukocyte activation is a hallmark of cancer-associated thrombosis (CAT), and elevated leukocytes predict venous thromboembolism in cancer outpatients. In a recent trial, rivaroxaban was more efficacious than dalteparin in preventing CAT recurrence.
OBJECTIVES: In a proof-of-concept study, we aimed to provide a mechanistic basis for improved efficacy of rivaroxaban compared to low-molecular-weight heparin in CAT treatment.
METHODS: We studied the effects of rivaroxaban, dalteparin and tinzaparin at peak and trough levels on tumor cell-induced procoagulant activity and platelet aggregation in the presence or absence of the cationic leukocyte-derived enzyme, myeloperoxidase (MPO). Furthermore, pro-inflammatory conditions were generated by stimulating whole blood with lipopolysaccharide (LPS) or phorbol-myristate-acetate (PMA), before measuring thrombin generation in plasma supernatants.
RESULTS: All three anticoagulants inhibited thrombin generation, fibrin clot formation and platelet aggregation induced by the tissue factor-expressing prostate carcinoma cell line, 22Rv1. Pre-incubation with MPO partially attenuated the anticoagulant activity of dalteparin and tinzaparin at peak and trough levels on tumor cell-induced procoagulant activity and platelet aggregation in the presence or absence of the cationic leukocyte-derived enzyme, myeloperoxidase (MPO). Furthermore, pro-inflammatory conditions were generated by stimulating whole blood with lipopolysaccharide (LPS) or phorbol-myristate-acetate (PMA), before measuring thrombin generation in plasma supernatants.
RESULTS: All three anticoagulants inhibited thrombin generation, fibrin clot formation and platelet aggregation induced by the tissue factor-expressing prostate carcinoma cell line, 22Rv1. Pre-incubation with MPO partially attenuated the anticoagulant activity of dalteparin and tinzaparin, but not rivaroxaban, at trough levels. The effect of MPO did not involve the enzyme’s catalytic properties, but required its structural integrity, as indicated by heat denaturation. In plasma obtained from LPS- or PMA-stimulated whole blood, elevated MPO antigen levels inversely correlated with the ability of tinzaparin to inhibit 22Rv1-induced thrombin generation.
CONCLUSIONS: MPO release may partially attenuate the anticoagulant activity of trough levels of dalteparin and tinzaparin in the context of paraneoplastic leukocyte activation. However, this effect is likely not sufficient to explain the improved efficacy of
Cutaneous metastases of prostatic adenocarcinoma in two dogs.

Related Articles
Cutaneous metastases of prostatic adenocarcinoma in two dogs.

Vet Clin Pathol. 2020 Aug 31;:
Authors: Di Maria FM, Annoni M, Roccabianca P, Antoniazzi E, Bertazzolo W

Abstract
Canine prostatic adenocarcinoma is an aggressive malignancy characterized by rapid growth, local invasiveness, and early metastatic spread. Metastases of prostatic cancer are generally diffuse at the time of diagnosis due to hematogenous or lymphatic spread and by direct exfoliation of neoplastic cells into the peritoneal cavity. Here we describe two dogs with prostatic adenocarcinoma and skin metastases. The first was a 12-year-old intact male German Shepherd dog that was presented with a history of chronic prostatic disease and multiple skin nodules that recently appeared on the ventral abdomen. The second was an 8-year-old intact male mixed breed dog that was referred for a neurologic examination because of a 1-month history of back pain and kyphosis of undefined origin. Cutaneous cytology of the first case was suggestive of carcinoma, and at necropsy, prostatic adenocarcinoma with metastases to the skin, spleen, liver, pancreas, kidneys, and lungs were found. In the second case, a computed tomographic examination revealed a prostatic neoplasm with inguinal, subcutaneous, and cutaneous nodular metastases. Cytology and histopathology were suggestive of primary prostatic adenocarcinoma with cutaneous and subcutaneous metastases. To the authors’ knowledge, these are the first reported cases of prostatic adenocarcinoma skin metastases in dogs with cytologic descriptions.

PMID: 32865086 [PubMed — as supplied by publisher]

Polyphasic identification of three new species in Alternaria section Infectoriae causing human cutaneous infection.

Related Articles
Polyphasic identification of three new species in Alternaria section Infectoriae causing human cutaneous infection.

Mycoses. 2020 Feb;63(2):212–224

Abstract
BACKGROUND: Cutaneous phaeohyphomycosis is an emerging disease in immunocompromised patients, being Alternaria one of the most common genera reported as a causative agent. Species identification is not carried out mainly due to the complexity of the genus. Analysis of the ITS barcode has become standard for fungal identification, but in Alternaria it is only able to discriminate among species-groups or sections.

METHODS: We present three cases of cutaneous infection caused by Alternaria isolates morphologically identified as belonging to section Infectoriae. They have been morphologically characterised and phylogenetically delineated with five molecular markers (ITS, ATPase, gapdh, rpb2 and tef1).

RESULTS: Mycotic infections have been diagnosed by repeated
cultures and histopathological examination in two of the cases. The polyphasic approach has allowed to delineate three new species of Alternaria section Infectoriae, that is A anthropophila, A atrobrunnea and A guarroi. ATPase has been the only locus able to discriminate most of the species (29 out of 31) currently sequenced in this section, including A infectoria the commonest reported species causing alternariosis. Susceptibility test showed different antifungal patterns for the three species, although terbinafine was the most active in vitro drug against these fungi. CONCLUSIONS: The ATPase gene is recommended as an alternative barcode locus to identify Alternaria clinical isolates in section Infectoriae. Our results reinforce the relevance of identification of Alternaria isolates at the species level and the necessity to carry out antifungal susceptibility testing to determine the most adequate drug for treatment.

PMID: 31651065 [PubMed — indexed for MEDLINE]

Expansion of Luminal Progenitor Cells in the Aging Mouse and Human Prostate.

Related Articles

Expansion of Luminal Progenitor Cells in the Aging Mouse and Human Prostate.


Authors: Crowell PD, Fox JJ, Hashimoto T, Diaz JA, Navarro HI, Henry GH, Feldmar BA, Lowe MG, Garcia AJ, Wu YE, Sajed DP, Strand DW, Goldstein AS

Abstract

Aging is associated with loss of tissue mass and a decline in adult stem cell function in many tissues. In contrast, aging in the prostate is associated with growth-related diseases including benign prostatic hyperplasia (BPH). Surprisingly, the effects of aging on prostate epithelial cells have not been established. Here we find that organoid-forming progenitor activity of mouse prostate basal and luminal cells is maintained with age. This is caused by an age-related expansion of progenitor-like luminal cells that share features with human prostate luminal progenitor cells. The increase in luminal progenitor cells may contribute to greater risk for growth-related disease in the aging prostate. Importantly, we demonstrate expansion of human luminal progenitor cells in BPH. In summary, we define a Trop2+ luminal progenitor subset and identify an age-related shift in the luminal compartment of the mouse and human prostate epithelium.

PMID: 31390564 [PubMed — indexed for MEDLINE]

Quantification of Cell Death Using an Impedance-Based Microfluidic Device.

Related Articles

Quantification of Cell Death Using an Impedance-Based Microfluidic Device.

Anal Chem. 2019 03 19;91(6):4140–4148

Authors: Mansoorifar A, Koklu A, Beskok A

Abstract

Dielectric spectroscopy is a nondestructive method to characterize dielectric properties by measuring impedance data over a frequency spectrum. This method has been widely used for various applications such as counting, sizing, and monitoring biological cells and particles. Recently, utilization of this method has been suggested in various stages of the drug discovery process due to low sample consumption and fast analysis time. In this study, we used a previously developed microfluidic system to confine single PC-3 cells in microwells using dielectrophoretic forces and perform the impedance measurements. PC-3 cells are treated with 100 μM Enzalutamide drug, and their impedance response is recorded until the cells are totally dead as predicted with viability tests. Four different approaches are used to analyze the impedance spectrum. Equivalent circuit modeling is used to extract the cell electrical properties as a function of time. Principal component analysis (PCA) is used to quantify cellular response to drug as a function of time. Single frequency measurements are conducted to observe how the cells respond over time. Finally, opacity ratio is defined as an additional quantification method. This device is capable of quantitatively measuring drug effects on biological cells and detecting cell death. The results show that the proposed microfluidic system has the potential to be used in early stages of the drug discovery process.

PMID: 30793881 [PubMed — indexed for MEDLINE]