Prostate Field Cancerization – Thinking Outside the Tumor

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Prostate Field Cancerization – Thinking Outside the Tumor

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BACKGROUND

• Prostate cancer is the second most common cancer in American men with about 230,000 new diagnoses and 30,000 deaths annually. Diagnosis by biopsy is hampered by a 30-50% false-negative rate due to small and easily missed cancer foci.

• Field cancerization denotes genetic and/or biochemical molecular alterations in phenotypically normal cells residing in histologically normal tissues adjacent to prostate tumors and may represent a temporal record of pathways underlying oncogenesis.

Cancer Tissue Resource (CPCTR).

The present work is approved by Chapman University IRB protocol #1415H024

HYPOTHESIS and OBJECTIVE

• Hypothesis: EGR-1 protein expression will be similarly elevated in cancerous and histologically normal adjacent tissues, which will support the concept of field cancerization. We further hypothesize that markers of field cancerization, such as EGR-1, could serve as biomarkers of disease and improve early cancer detection (diagnosis) at the time of biopsy.

• Objective: Determine expression of EGR-1 protein in malignant and adjacent tissues.

EXPERIMENTAL METHODS

Tissue Samples: Human prostate tissues containing cancer cells (malignant) and matched adjacent tissues devoid of cancer cells (benign) from prostatesctomies and matched biopsies were obtained from the Cooperative Prostate Cancer Tissue Resource (CPCTR). The present work is approved by Chapman University IHS protocol #1415H024 under biosafety level 2 (BSL2) approved practices as per Institutional, State, and Federal laws.

Immuno-Fluorescence Microscopy: Immunofluorescence microscopy was performed using rabbit anti-human EGR-1 antibodies, unquenched control IgG, and goat anti-rabbit Alexa Fluor 488 (green) conjugated antibodies. Fluorescent DAPI dye (blue) was used to visualize cell nuclei.

Quantitative Fluorescence: Quantitative analysis (pixel densitometry) was performed using ImageJ (provided by the National Institutes of Health) and graphs were generated using Microsoft Excel and Jumpt software. Two signal acquisition modes were applied: Whole image analysis and region of interest analysis.

RESULTS

Prostatectomy (case 404) vs. Biopsy

Prostatectomy (case 476) vs. Biopsy

SIGNIFICANCE OF RESEARCH

• EGR-1 protein expression will be similarly elevated in cancerous and histologically normal adjacent (benign) tissues from both prostatectomy and biopsy tissues. This supports the concept of field cancerization and indicates a potential organ-wide molecular change.

• Future research includes improvements at the conceptual and technical level:
  ➢ Increasing the number of cases and including disease-free (age-matched) prostate tissues
  ➢ Overcoming the autofluorescence of prostate tissues by the use of Alexa Fluor 633-conjugated 2nd antibodies (for red) and increasing the resolution of detection by confocal microscopy
  ➢ Design studies towards the clinical exploitation of markers of field cancerization. In particular, we are interested in developing non-invasive assessment methods using novel and upcoming technologies, including targeted nanoparticle imaging modalities

CONCLUSIONS and FUTURE RESEARCH

EGR-1 protein expression is similar in cancerous (malignant) and in histologically normal adjacent (benign) tissues from both prostatectomy and biopsy tissues. This supports the concept of field cancerization and indicates a potential organ-wide molecular change.

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