New Prostate Tumour Marker
LSD1 determines the Degree of Invasiveness

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Technology

Here we show that the expression level of the Lysine Specific Demethylase 1 (LSD1) is a marker to determine the degree of invasiveness during prostate cancer development.

Innovation

- Aids in decision between aggressive therapy and watchful waiting-strategy
- Provides a surrogate marker for systemic tumour progression
- Predicts benefit from aggressive therapy

Application

Direct clinical application: LSD1 is a strong marker to determine the degree of invasiveness during prostate cancer development.

Market Potential

Prostate cancer represents the most frequent malignant disease in men worldwide and the second leading cause of death from malignant tumors.

Proof of Concept

Please contact us for further information.

Patent Status

- Filed (PRD): February 18th, 2005
- International Patent Application (PCT)
Androgen Receptor Coactivators Lysine-Specific Histone Demethylase 1 and Four and a Half LIM Domain Protein 2 Predict Risk of Prostate Cancer Recurrence

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Abstract

Prostate cancer biology varies from locally confined tumors with low risk for relapse to tumors with high risk for progression even after radical prostatectomy. Currently, there are no reliable biomarkers to predict tumor relapse and poor clinical outcome. In this study, we correlated expression patterns of the androgen receptor (AR) coactivators lysine-specific histone demethylase 1 (LSD1) and four and a half LIM-domain protein 2 (FHL2), AR, Gleason score, Gleason grade, and p53 expression in clinically organ confined prostate cancers with relapse after radical prostatectomy. Our data showed that high levels of LSD1, nuclear FHL2, and very strong staining of nuclear p53 correlate significantly with relapse during follow-up. No correlation exists with relapse and the expression of AR and cytoplasmic expression of FHL2. To confirm these data, we did quantitative reverse transcription-PCR and Western blot analyses in a subset of tumor specimens. Consistently, both LSD1 mRNA and protein levels were significantly up-regulated in high-risk tumors. We previously identified LSD1 and FHL2 as nuclear cofactors interacting specifically with the AR in prostate cells and showed that both stimulate androgen-dependent gene transcription. Our present study suggests that LSD1 and nuclear FHL2 may serve as novel biomarkers predictive for prostate cancer with aggressive biology and point to a role of LSD1 and FHL2 in constitutive activation of AR-mediated growth signals.

Figure 1. Representative immunohistochemical staining of LSD1 and FHL2 in normal prostate glands and tumors from patients without relapse (group 1, Gleason score 6) or with relapse (group 2, Gleason score 9). H&E staining shows standard morphology (magnification, x400). Arrows, nuclear LSD1 staining in luminal cells of normal prostate glands and in prostate carcinoma cells. Also, strong cytoplasmic signals in basal cells of normal glands and weak signals in group 1 carcinomas are depicted. Group 2 carcinoma cells show both strong nuclear signals and a combined plasmalemmal and cytoplasmic staining pattern.

Figure 2. A, Kaplan-Meier plot showing cumulative relapse-free survival in cases with LSD1 scores of ≤8 (top) or >8. Log-rank (Mantel-Cox) analysis reveals significant difference between the curves (P = 0.002). B, box-plot showing arbitrary values of LSD1 mRNA expression (normalized to internal 18S RNA values) measured by quantitative RT-PCR (qRT-PCR). Mean values of group 1 and 2 are 84.1 (81.2-87.0) versus 87.7 (84.6-90.8), respectively.

Figure 3. Western blot analysis of four different tumors from patients with no relapse (group 1, A) and patients with relapse (group 2, B). Blot probed with (α)-LSD1 and (α)-5-actin antibodies. Normal (N) and carcinoma (T) tissue recovered from the same prostate. Bottom, expression levels of LSD1 (normalized to 5-actin) in the tumor sample relative to the corresponding adjacent normal tissue. Coomassie-stained gels used for Western blots are shown as control.

Figure 4. Nuclear stabilization of p53 in three representative prostate carcinomas. Sequencing genomic DNA recovered from the tumors revealed pathogenic p53 mutations in all three cases. Tumor morphology is shown as H&E staining (magnification, ×400). Arrows, intense nuclear immunostains.