

Correlation of Canary Histological Patterns at Radical Prostatectomy with Decipher GRID Basal and Luminal Signature Score

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Background

Basal and luminal phenotypes have been extensively studied in the context of breast carcinoma and more recently across other carcinomas. Similar to breast carcinoma, prostate carcinoma has been classified into basal and luminal subtypes based on gene expression studies that differ in their mutational profile, prognostic significance, and response to therapy (PMID: 28494073, 34554200). Across different studies, non-luminal/basal subtypes were associated with the worst prognosis, and luminal B prostate carcinomas were more likely to benefit from androgen deprivation therapy. Recent work evaluating the clinical significance of morphological patterns in prostate carcinoma from the Canary Consortium has identified patterns associated with favorable, borderline, and unfavorable outcomes (PMID: 38828674). In this study, we hypothesize that histological patterns of prostate carcinoma correlate with basal and luminal signatures.

Methods

Canary histological patterns were reviewed and recorded on 394 radical prostatectomy slides that underwent Decipher testing. Patterns were classified as unfavorable (Gleason pattern 5 (GP5), large cribriform (diameter >0.25 mm), intraductal carcinoma, complex intraluminal papillary architecture, anastomosing cords), borderline (glomerulations, small cribriform (diameter $\leq$ 0.25 mm), small nests, mucin, stromogenic grades 1-2), and favorable (absence of unfavorable and borderline features). The presence or absence of each of the Canary patterns was correlated with basal and luminal signature score from the Decipher GRID database using the student T-test. Statistical significance was defined by p-value <0.05. The basal luminal score is a continuous variable with basal subtypes having higher scores and luminal subtypes having lower scores.

Results

The mean basal/luminal score across the entire cohort was -0.31 (range -0.66 to 0.06, median -0.32, IQR -0.40, -0.22). Small nests, GP5 and single cell/single file ($p = <0.001$, 0.042, <0.001 respectively), were associated with higher scores consistent with a basal subtype. Glomerulations, complex intraluminal papillary and large cribriform ($p = 0.001$, 0.017, 0.005 respectively) were associated with lower scores, consistent with a luminal subtype (Table-1). Aggressive histological patterns were present in both basal (GP5, single cell/files) and luminal subtypes (complex intraluminal papillary and large cribriform). Basal and luminal subtypes correlate with distinct morphological features of large cribriform and complex papillary in the luminal subtype whereas the basal subtype showed lack of these features.

Conclusions

Histomorphological features of prostate carcinoma may be helpful in distinguishing basal and luminal subtypes of prostate carcinoma through a distinct separation of large cribriform and complex papillary phenotypes in the two subsets that in turn may be of prognostic relevance. These findings provide interesting questions for future research in prostate carcinoma to look at morphological and molecular overlap between basal and luminal subtypes through spatial genomics and better understand their relationship with regards to tumor evolution and progression.

Funding: None.

Acknowledgements: UCSF Department of Pathology and Urology.

Conflict of Interest Disclosure Statement: Dr. Matthew Cooperberg is a consultant for Veracyte, the maker of the Decipher test. The remaining authors have no relevant disclosures.

Table-1: Mean Basal Luminal Scores in Canary Patterns. The mean basal/luminal score across the entire cohort was -0.31 (range -0.66 to 0.06, median -0.32, IQR -0.40, -0.22). Higher scores correlate with basal subtype and lower scores with luminal subtype.

	Overall Mean (SD)	Pattern absent Mean (SD)	Pattern present Mean (SD)	p	
Glomerulations	-0.31 (0.14)	-0.29 (0.14)	-0.34 (0.14)	0.001	Consistent with luminal scores
Complex intraluminal papillary	-0.31 (0.14)	-0.30 (0.14)	-0.34 (0.13)	0.017	
Large cribriform	-0.31 (0.14)	-0.28 (0.14)	-0.32 (0.14)	0.005	
Small nests	-0.31 (0.14)	-0.33 (0.13)	-0.25 (0.14)	<0.001	Consistent with basal scores
Single cells/files	-0.31 (0.14)	-0.32 (0.14)	-0.21 (0.16)	<0.001	
Gleason pattern 5	-0.31 (0.14)	-0.32 (0.14)	-0.28 (0.15)	0.042	
Favorable	-0.31 (0.14)	-0.30 (0.20)	-0.31 (0.14)	0.756	
Borderline features	-0.31 (0.14)	-0.33 (0.17)	-0.30 (0.14)	0.325	
Stromogenic grades 1-2	-0.31 (0.14)	-0.31 (0.14)	-0.30 (0.12)	0.8	
Mucinous	-0.31 (0.14)	-0.30 (0.14)	-0.34 (0.12)	0.266	
Small cribriform	-0.31 (0.14)	-0.30 (0.16)	-0.31 (0.14)	0.482	
Unfavorable	-0.31 (0.14)	-0.29 (0.15)	-0.31 (0.14)	0.219	
Anastomosing cords	-0.31 (0.14)	-0.32 (0.13)	-0.30 (0.15)	0.211	
Comedonecrosis	-0.31 (0.14)	-0.31 (0.14)	-0.31 (0.12)	0.805	
Solid	-0.31 (0.14)	-0.30 (0.14)	-0.32 (0.14)	0.37	