

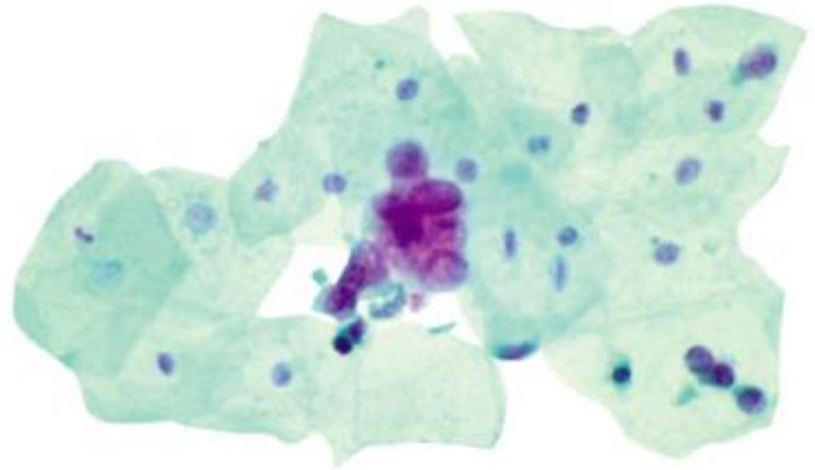
Combining Color and Morphology Improves Identification of Low-Grade Urothelial Cancer Cells

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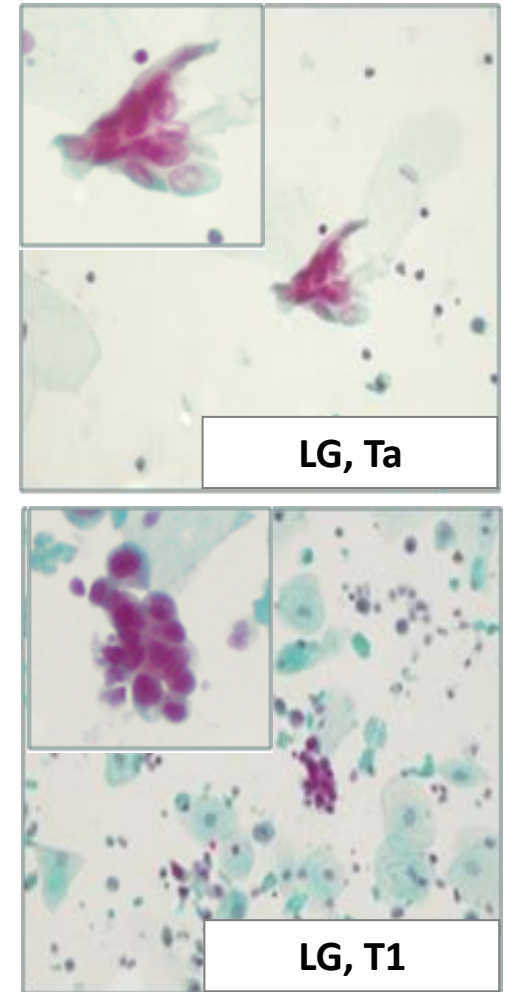
Technology Principles

- CellDetect® histochemical stain has been demonstrated to differentiate between normal and neoplastic cells by color alongside morphological features
- Using a proprietary plant extract and generic dyes, the stain colors the nuclei of neoplastic cells in reddish-purple, while normal cell nuclei are stained in green or blue

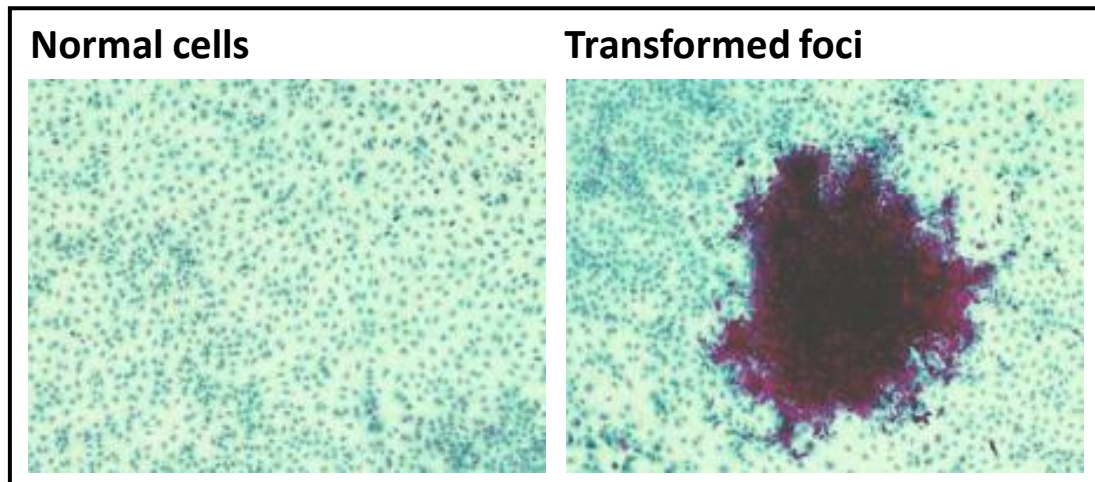
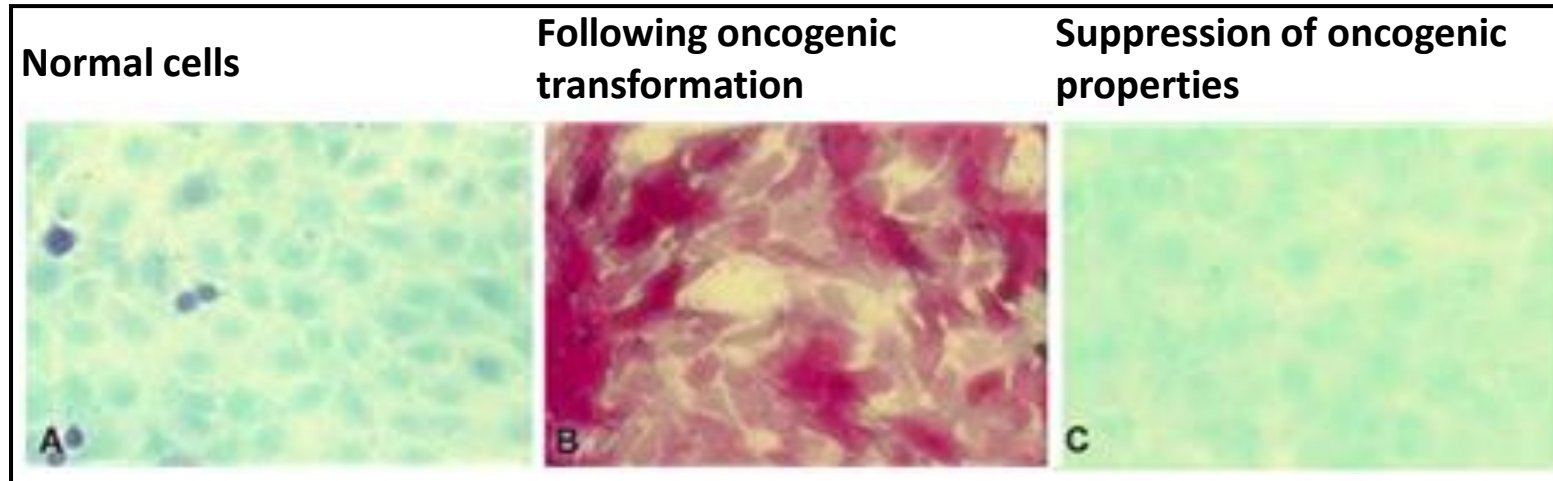


Assumed Mechanism of Action

- The discriminative capacity of the stain is most likely related to the increased metabolic activity observed in cancer cells
- Based on differential pH affinity, the combination of dyes enables color discrimination, which is accentuated and stabilized by the plant extract
- The CellDetect® stain is applicable to different specimens including histological tissues and cytological smears



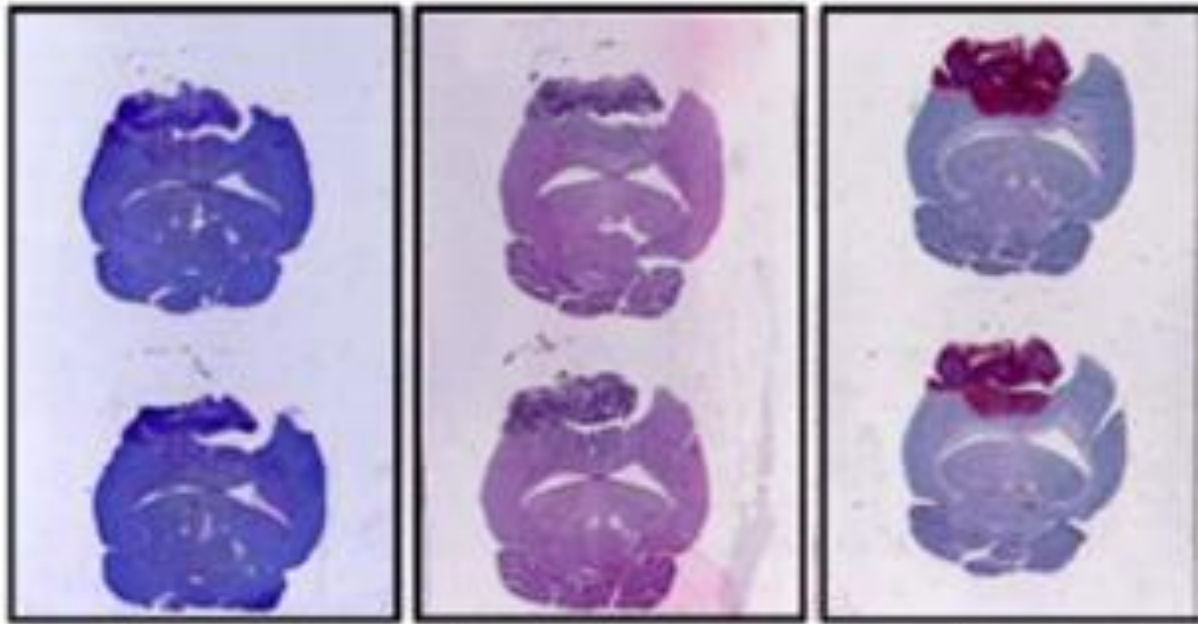
Cell Transformation in Tissue Culture



The staining technology is able to pick up early transformation events

Rat Brain Glioblastoma in Frozen Sections

Gross morphological detection of Rat brain Glioblastoma in frozen sections



Giemsa

H&E

CellDetect[®]

Open Label Clinical Study

- 58 archived bladder biopsies and 44 urine samples stained with CellDetect®
- 100% concordance between H&E and CellDetect®
- The sensitivity of detecting urothelial carcinoma in urine smears was 94% and the specificity 89%

A Novel Urine Cytology Stain for the Detection and Monitoring of Bladder Cancer

Noa Davis,^{*,†} Yoram Mor, Pavel Idelevich, Dov Terkieltaub,[†] Vivi Ziv,[‡] Adi Elkeles,[†] Sylvia Lew, Elimelech Okon,[§] Menachem Laufer, Jacob Ramon, Daniel Kedar, Jack Baniel and Ofer Yossepowitch[†]

From ZetiQ Technologies Ltd. (ND, PI, DT, VZ, AE), Tel Aviv, Patho-Lab Diagnostics Ltd. (SL) and LEM Pathology Laboratory (EO), Ness Ziona, Department of Urology, Chaim Sheba Medical Center (YM, ML, JR), Ramat-Gan and Institute of Urology, Rabin Medical Center (DK, JB, OY), Petach-Tikva, Israel

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Prospective Blinded Multicenter Study

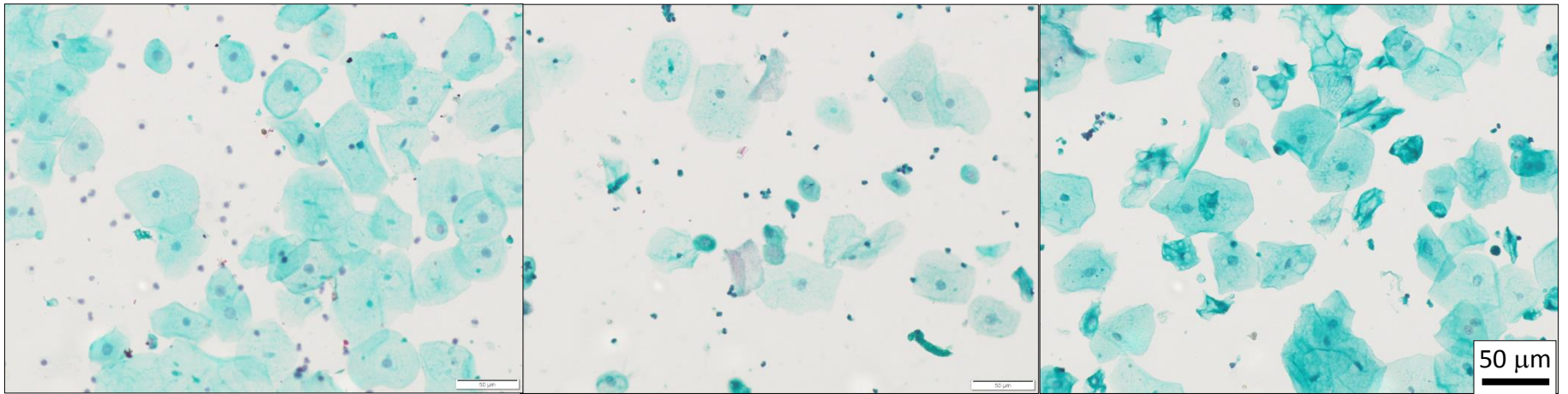
Objective

To further explore the performance of CellDetect® in urine specimens

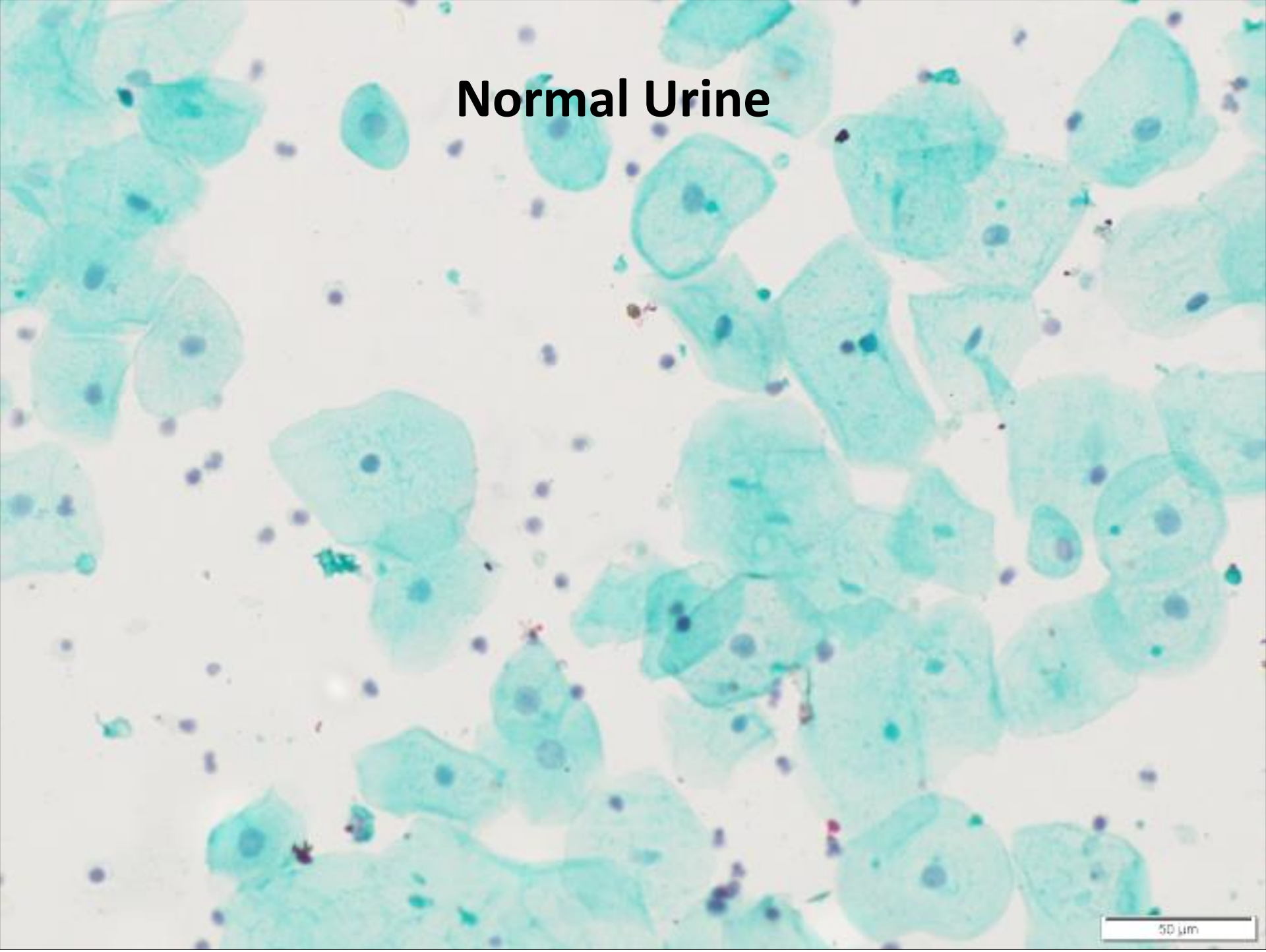
Methods

- The study was conducted in nine hospitals enrolling patients monitored for history of urothelial carcinoma
- Voided urine samples collected prior to routine cystoscopic surveillance or TURP/cystectomy
- The cytospin smears were blindly observed by at least two cytology experts
- The findings were compared to the histological diagnoses in positive cases and to cystoscopy and/or histology in negative cases

Normal Urine

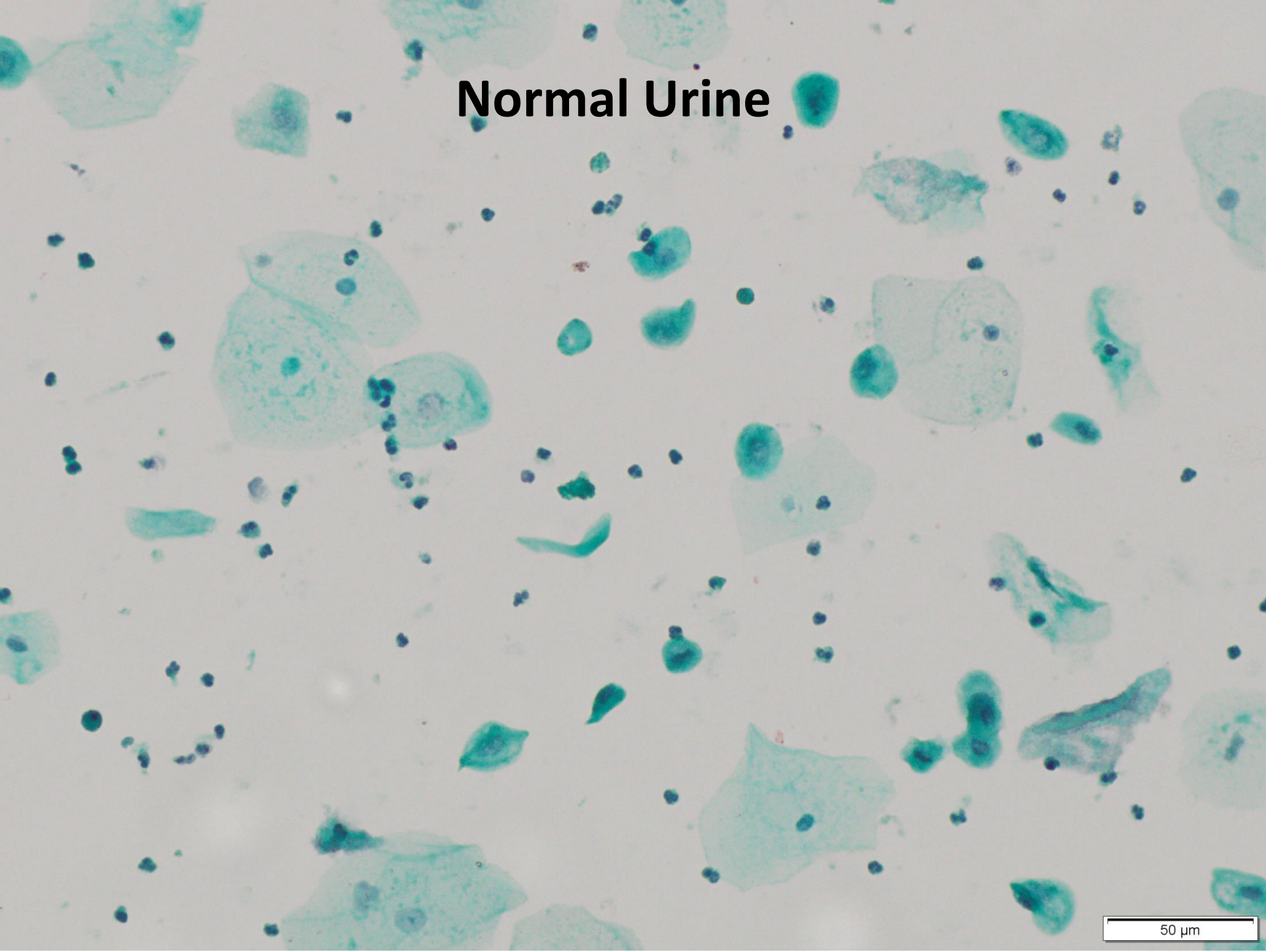


Normal Urine



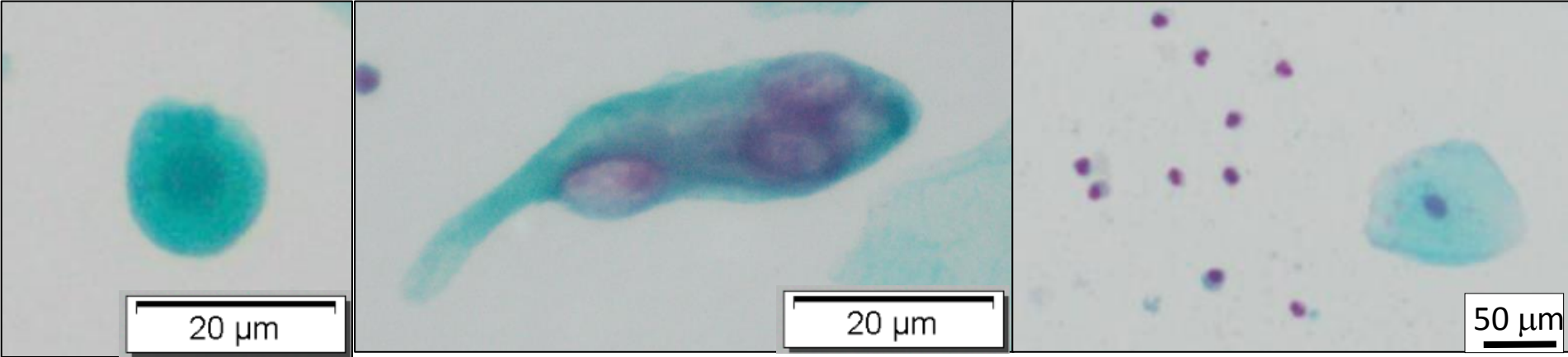
50 μ m

Normal Urine

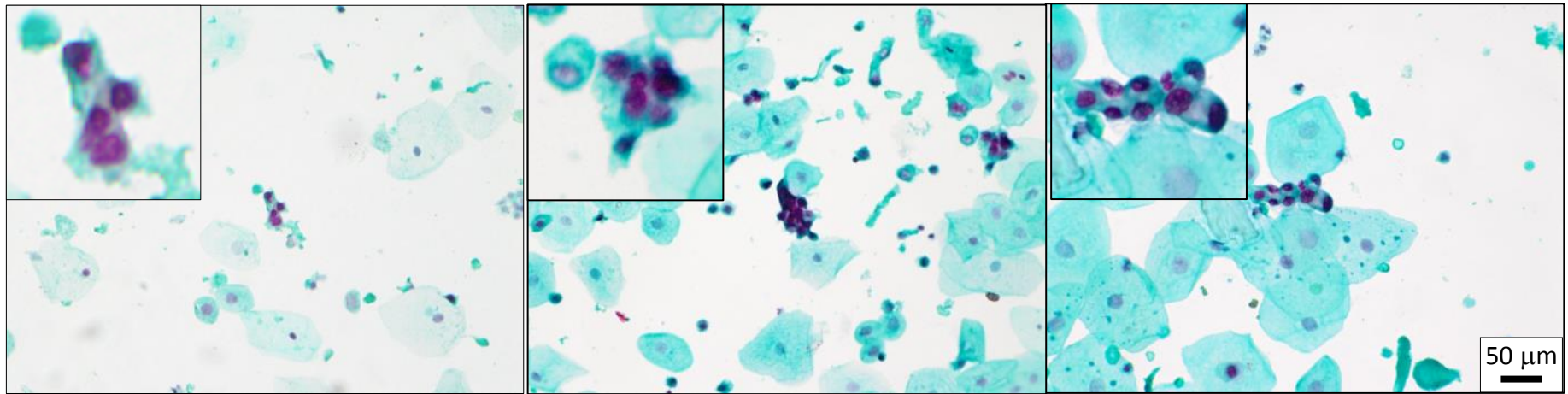


50 μ m

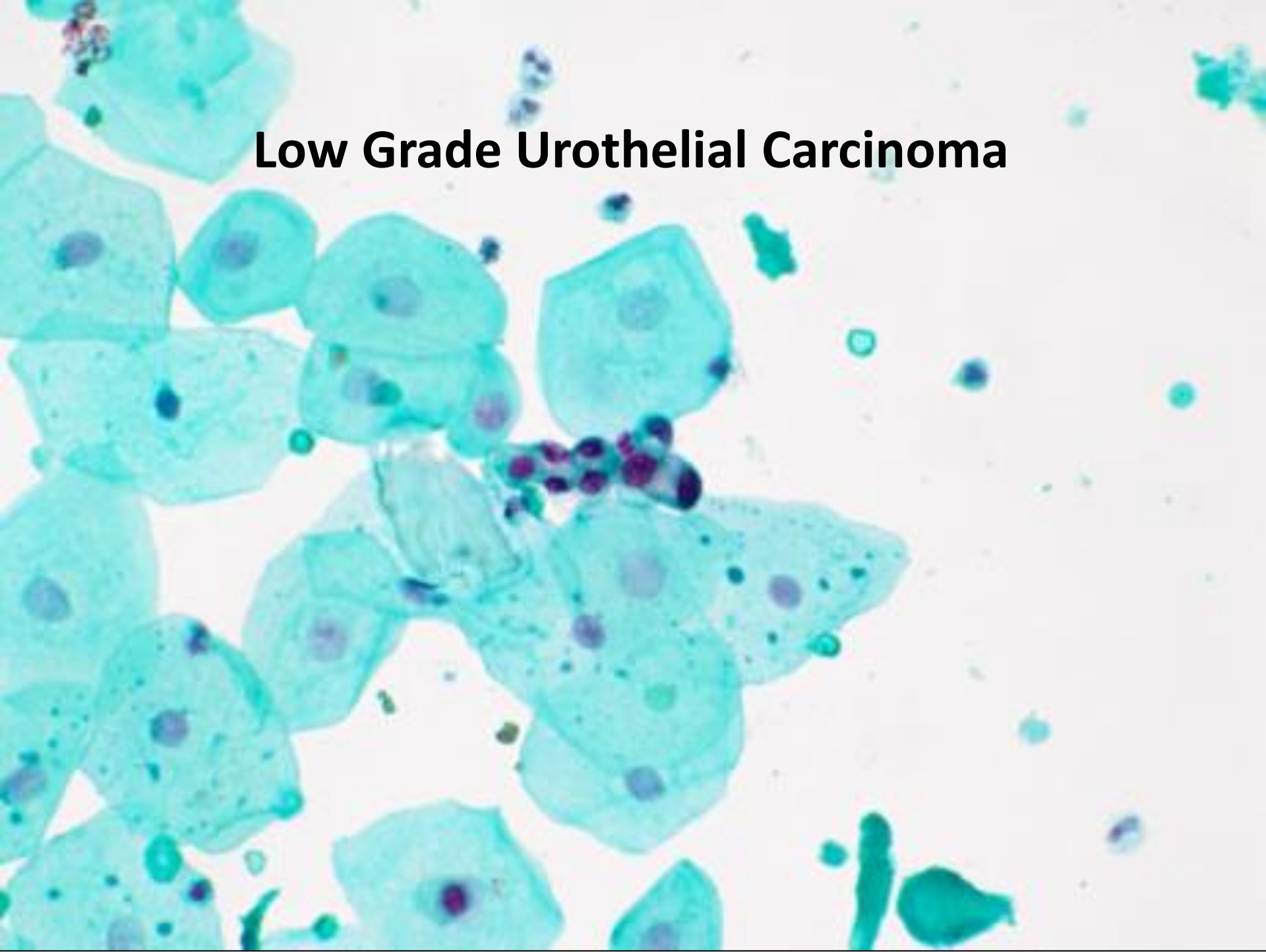
Benign Urothelial, Squamous & Inflammatory Cells



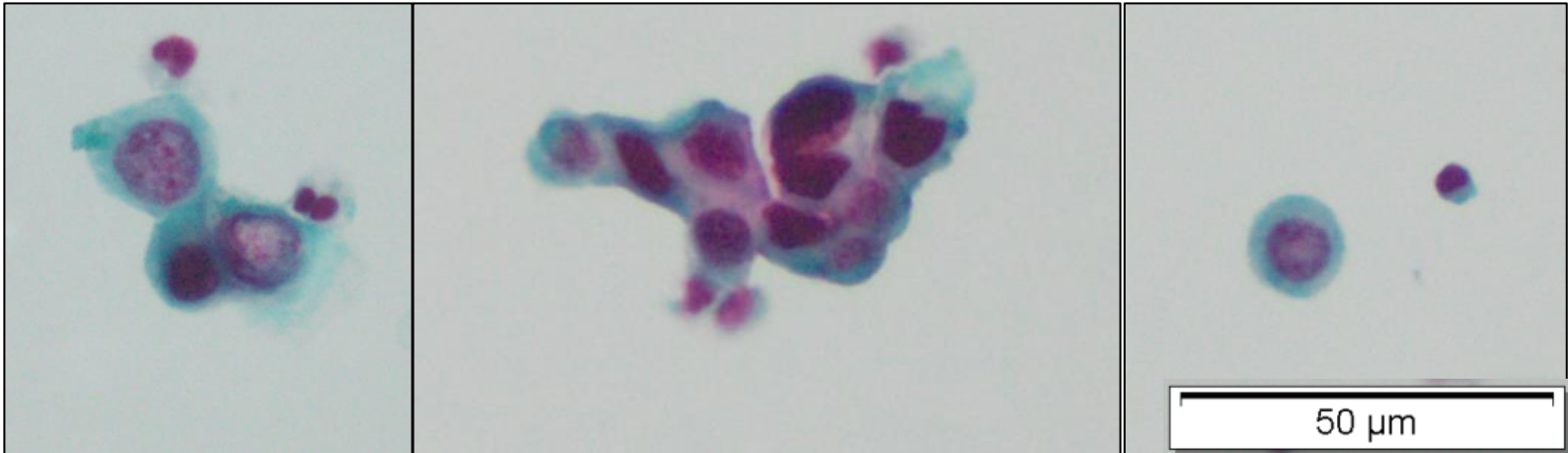
Low Grade Urothelial Carcinoma



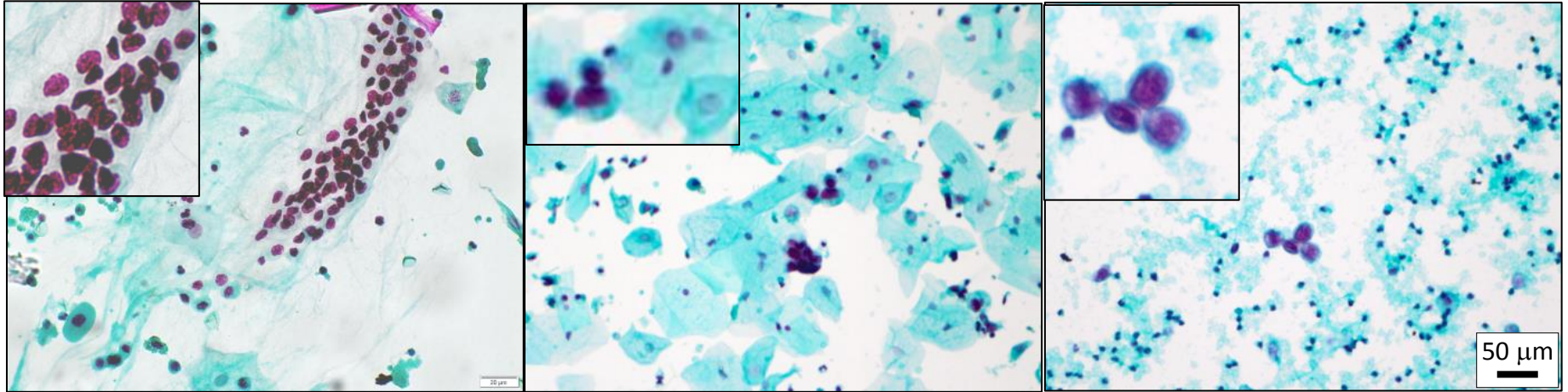
Low Grade Urothelial Carcinoma



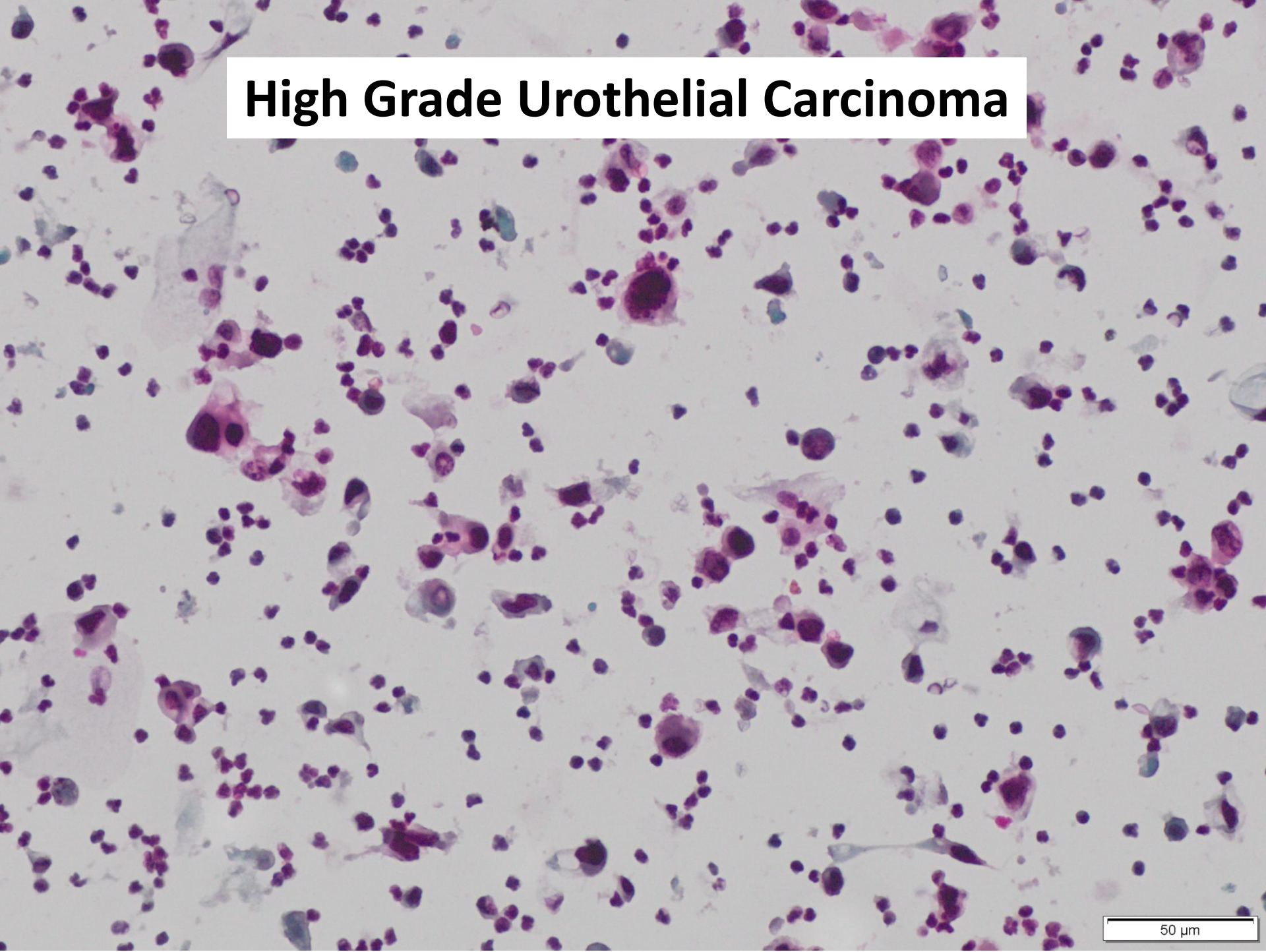
Low Grade Urothelial Carcinoma



High Grade Urothelial Carcinoma



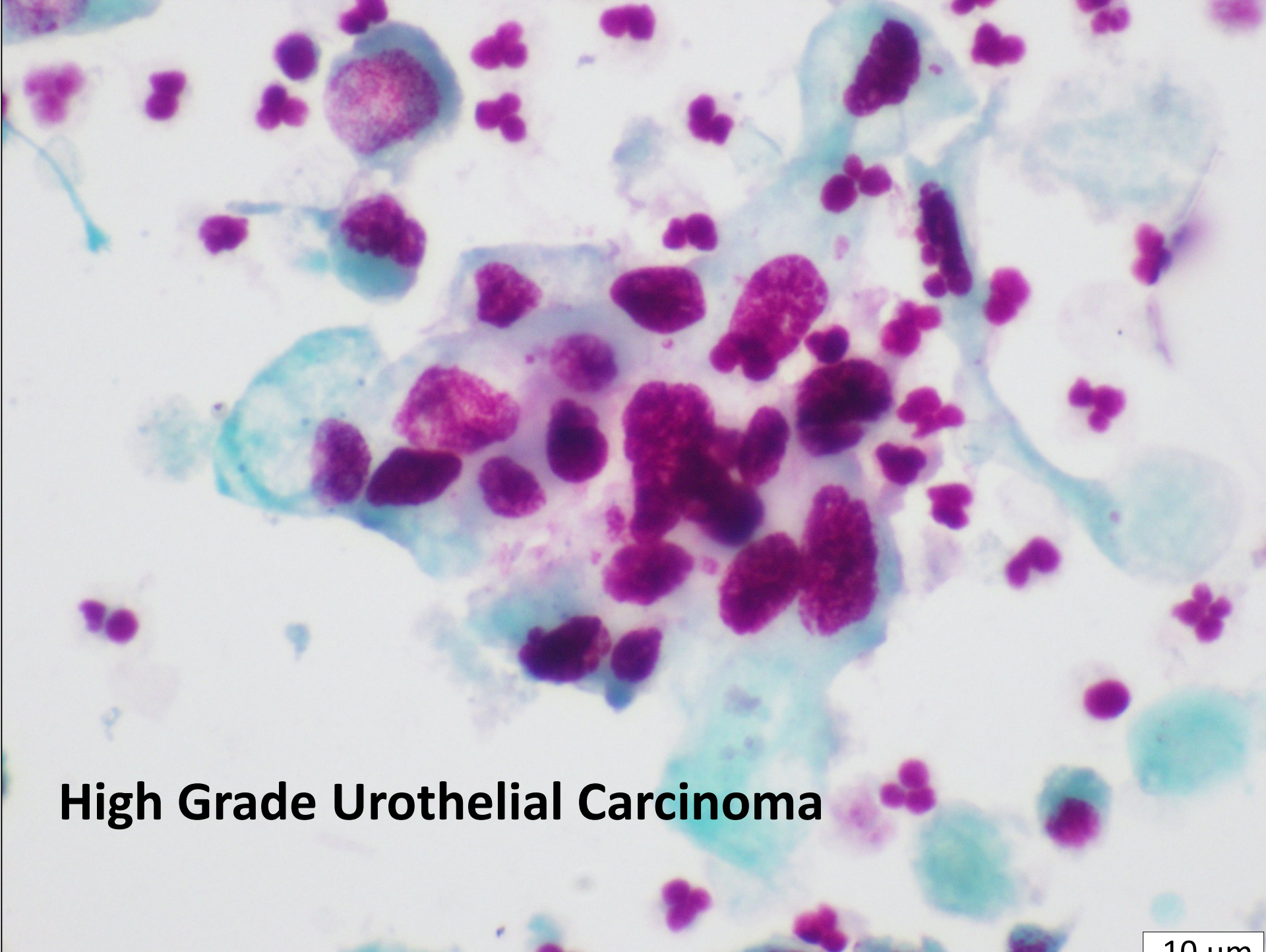
High Grade Urothelial Carcinoma



50 μm

High Grade Urothelial Carcinoma





High Grade Urothelial Carcinoma

10 μ m

Results of Blinded Multicenter Study

Study population - 217 subjects :

- 121 negative (normal appearing bladder / negative histology)
- 96 cancer cases (positive histology)

Cancer Grade	Nº of cases
LG	41
HG	54
Undetermined	1
Total	96

Cancer Stage	Nº of cases
Ta	50
T1, TIS	22
≥T2	22
Undetermined	2
Total	96

- Each slide was analyzed by at least two independent cytology experts who were blinded to patient true diagnosis
- Categories for diagnosis were: Negative, Reactive/Inflammatory, Suspicious, Highly suspicious and Positive
- Based on statistical analysis, cutoff for positive was Suspicious and up

Results of Blinded Multicenter Study

	Nº of cases	CellDetect® (n=217)
Sensitivity	96	84%
Specificity*	121	83%

* Adjusted to disease prevalence of 10% among monitoring population

Sensitivity stratified by tumor stage

	Nº of cases	Sensitivity
Ta	50	80%
T1, CIS	21	85%
≥T2	22	82%

Sensitivity stratified by tumor grade

	Nº of cases	Sensitivity
LG	41	78%
HG	54	89%

Conclusions

- CellDetect[®] stain demonstrates high sensitivity for both low & high grade bladder cancer tumors, which is of particular importance for the former
- The findings suggest that CellDetect[®] can be further developed to provide a non-invasive alternative to cystoscopic surveillance for the early detection of bladder cancer recurrence
- Further investigation is warranted to evaluate the performance of CellDetect[®] for the diagnosis of bladder cancer in suspected patients with hematuria and in instrumentation specimens
- Reactive atypia in nephrolithiasis, chemotherapy-induced changes, BK (polyoma virus) nephropathy, papillary urothelial neoplasm of low malignant potential and some other clinical cases are subject of further investigation

Publications

- Davis et al. A novel urine cytology stain for the detection and monitoring of bladder cancer. *The Journal of Urology* **2014**; 192:1628-1632
- He et al. Application of the CellDetect® staining technique in diagnosis of human cervical cancer. *Gynecologic Oncology* **2014**; 132:383-388
- Idelevich et al. Screening for cervical neoplasia: a community-based trial comparing Pap staining, human papilloma virus testing, and the new bi-functional CellDetect® stain. *Diagnostic Cytopathology* **2012**; 40:1054-61
- Idelevich et al. Novel dual-function CellDetect® staining technology: wedding morphology and tinctorial discrimination to detect cervical neoplasia; *Diagnostic Pathology* **2010**; 5:70
- Sagiv et al. A color discriminating broad range cell staining technology for early detection of cell transformation. *Journal of Carcinogenesis* **2009**; 8:16-23
- Idelevich et al. Novel Histochemical Stain for Tinctorial Detection of Cancer and Neoplastic Cells. *The Journal of Histotechnology* **2009**; 32:97-105

Thank you