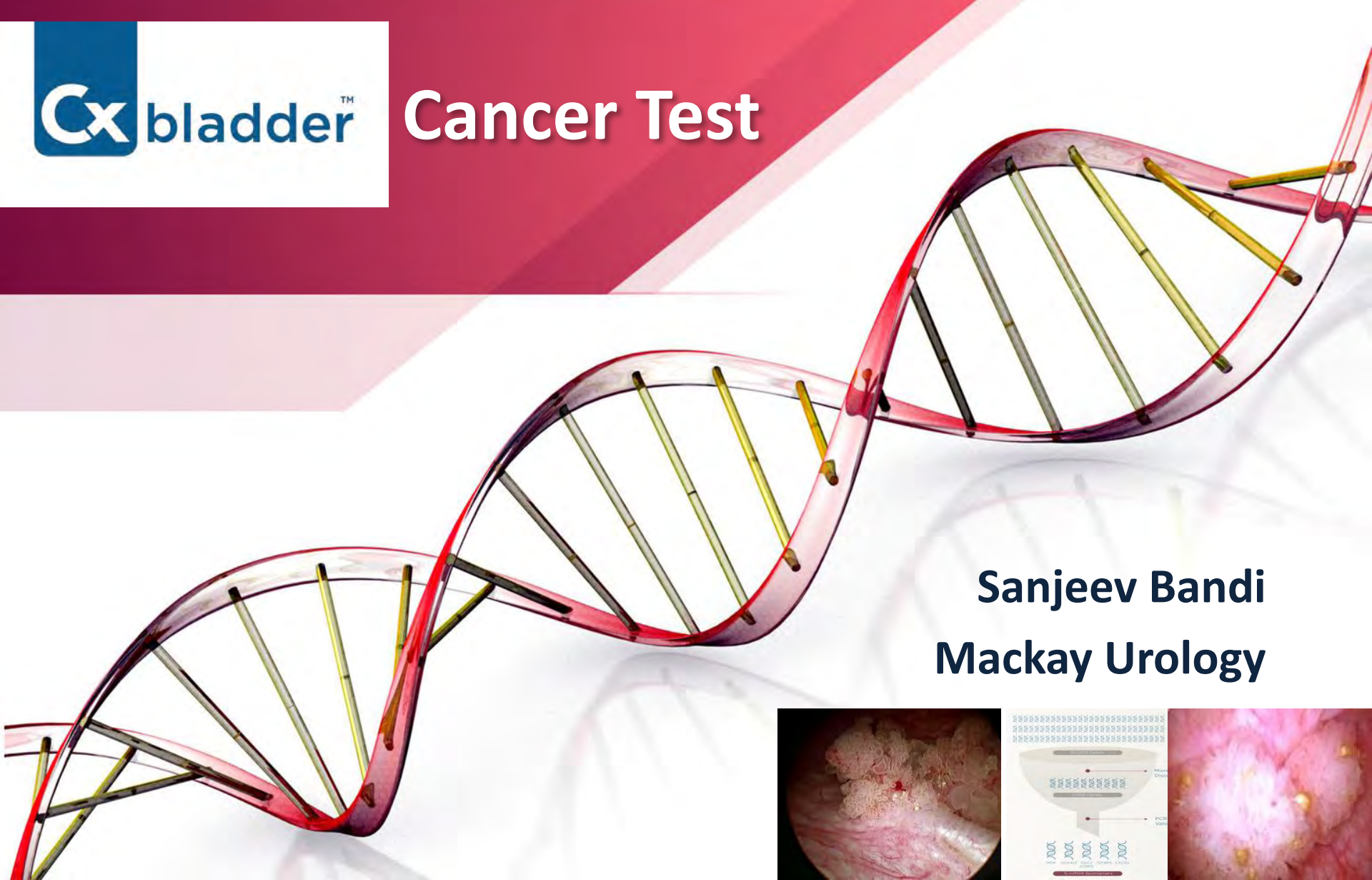
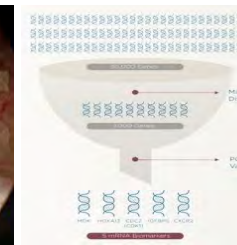


**Cx**bladder™

# Cancer Test



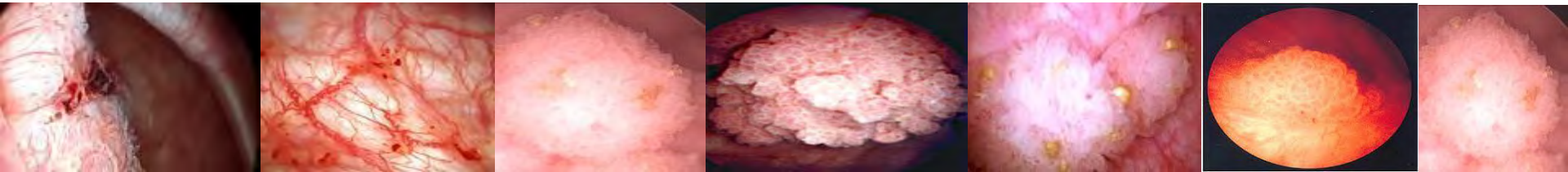
**Sanjeev Bandi**  
**Mackay Urology**





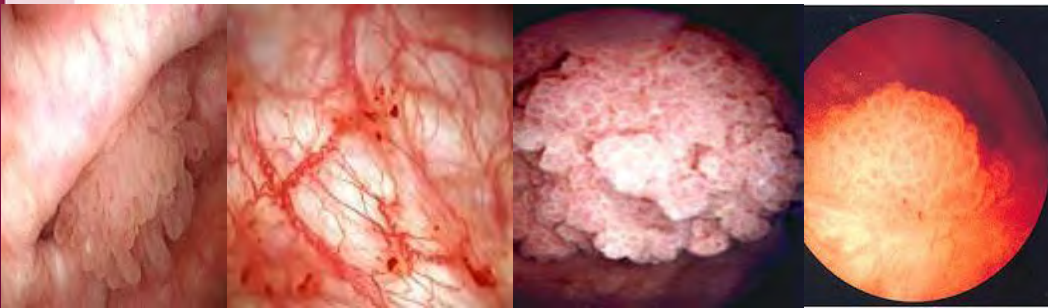
- Research from Pacific Edge<sup>1</sup> shows that messenger RNA (mRNA) levels of specific biomarkers are present at higher levels of concentration in patient urine samples that are positive for bladder cancer than in patients who are negative for the disease.

<sup>1</sup> Holyoake et al: Development of a multiplex RNA urine test for the detection and stratification of transitional cell carcinoma of the bladder, Clin Cancer Res 2008; 14(3): 742-749



# Cxbladder Biomarker Gene Descriptions

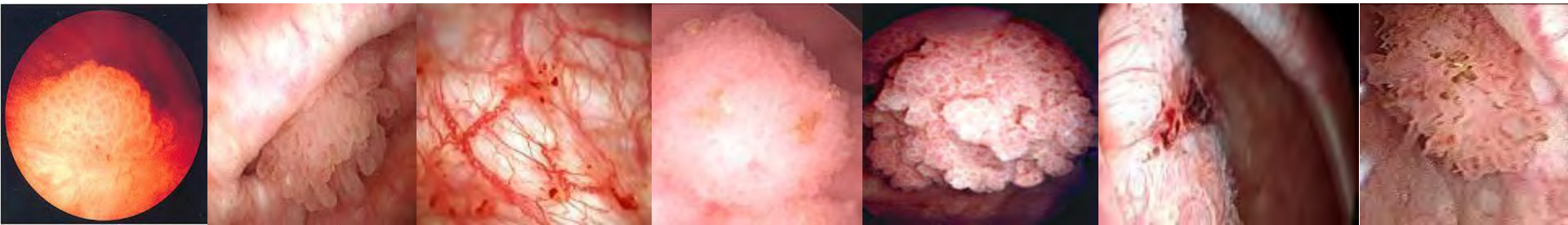
- **MDK: Blood vessel growth and cell migration**  
*Principally involved in cell proliferation, migration and angiogenesis in cancer cells.*
- **HOXA13: Cell differentiation**  
*Principally involved in cell differentiation and the morphogenesis and differentiation of the genitourinary tracts.*
- **CDC2 (CDK1): Cell division**  
*Cyclin dependent kinase. Essential to mitotic cell cycle: cell proliferation.*
- **IGFBP5: Programmed cell death**  
*Acts as an anti-apoptotic gene.*
- **CXCR2: Inflammation**  
*Mediates neutrophil migration to sites of inflammation. Moderates non-malignant inflammation(False Positives).*



# Cxbladder Cancer Test



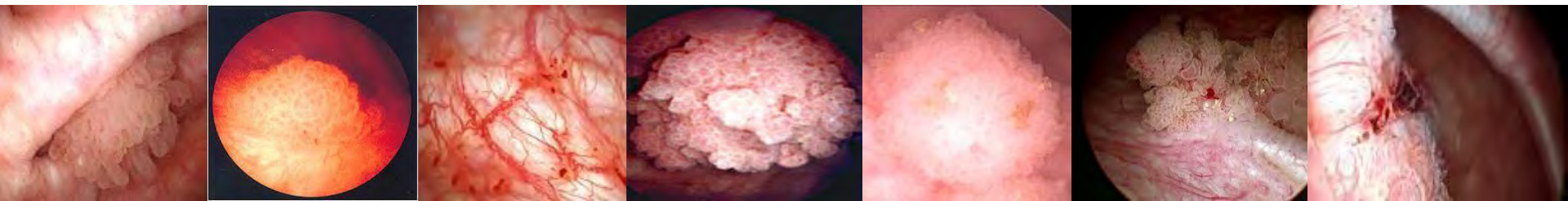
- A small sample (5 mL) of mid stream urine is required for the test. The sample undergoes a precise set of processes to extract and purify the mRNA present in the patient urine sample.



# Cxbladder Cancer Test



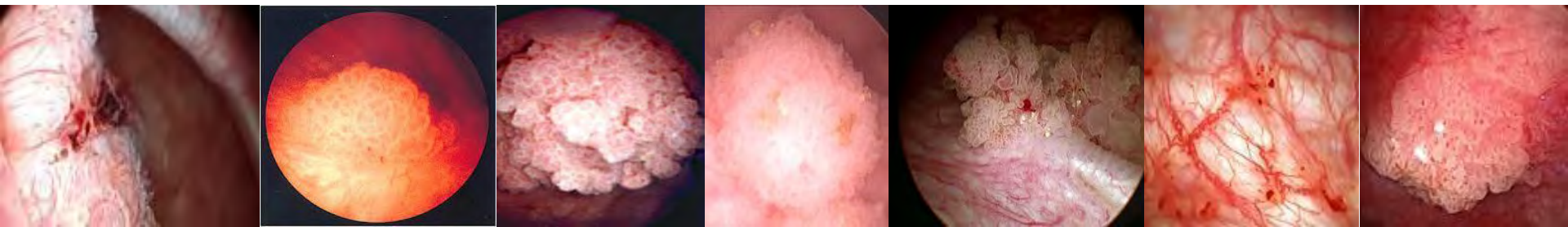
- The purified RNA is then quantified by a technique called Reverse Transcription quantitative Polymerase Chain Reaction or RT-qPCR. RT-qPCR first involves the conversion of RNA to DNA and then the amplification of that DNA by millions of fold, regulated by a repetitive cycle of temperature adjustment. The resulting millions of copies of DNA are detected by a probe whose fluorescence is directly proportional to the number of copies of DNA present.



# Cxbladder Cancer Test



- In the Cxbladder test, each of the five biomarkers of interest to us is quantified by a different probe and the relationship between the individual biomarkers is determined by a mathematical equation. The calculated outcome provides a measure of the probability of the presence of urothelial carcinoma (UC).



# Cxbladder Cancer Test



## **How Cxbladder can be used in your practice:**

Replace the need for other urine-based tests in primary workup.

Complement cystoscopy for bladder cancer detection.

Detect urothelial tumors not visible by cystoscopy.

Replace the need for CT / IVP in primary workup in some instances.

Improve patient compliance with accurate, non-invasive testing.

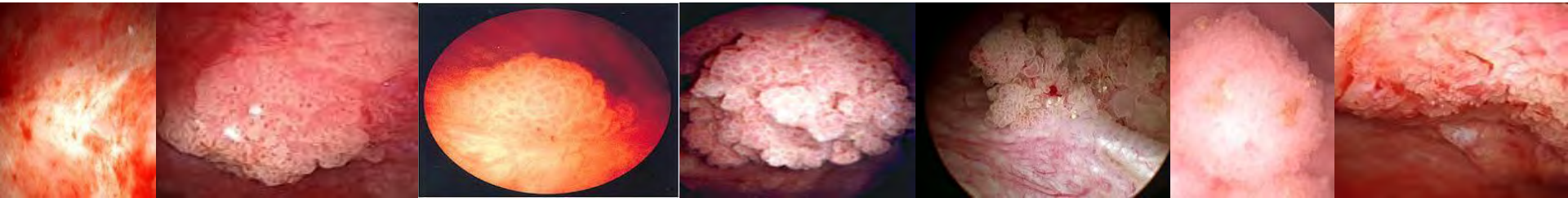


# Cxbladder Cancer Test



## Other applications may include:

- Complement cystoscopy for monitoring bladder cancer recurrence.
- Increase the interval between surveillance cystoscopies in certain circumstances.
- Triage patients presenting with micro-hematuria that do not need a full workup.
- Evaluate patients in 'at-risk' populations.



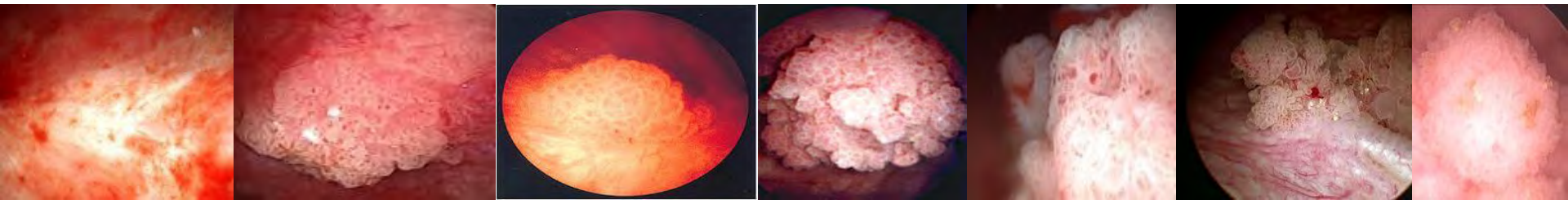


# Cxbladder Cancer Test



## Results Interpretation:

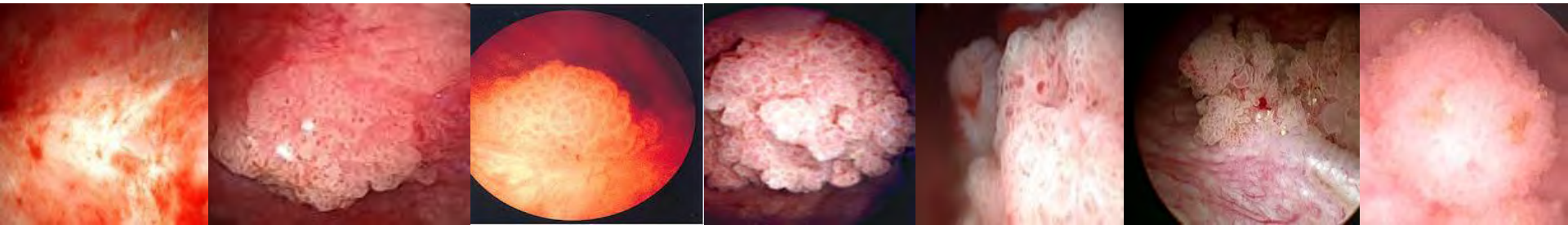
- **NORMAL Gene Expression Score ( $< 0.12$ ):** A score of  $< 0.12$  has a Negative Predictive Value (NPV) of 97%. High probability of NO UC.
- **ELEVATED Gene Expression Score ( $0.12 \leq \text{score} < 0.23$ ):** A score of  $0.12 \leq \text{score} < 0.23$  has an NPV of 94%. Low probability of UC, however a change in the pattern of gene expression of the biomarkers from what is normal suggests further clinical evaluation
- **HIGH Gene Expression Score ( $\geq 0.23$ ):** A score of  $\geq 0.23$  has a Positive Predictive Value (PPV) of 68%. High probability of UC.



# Cxbladder Cancer Test



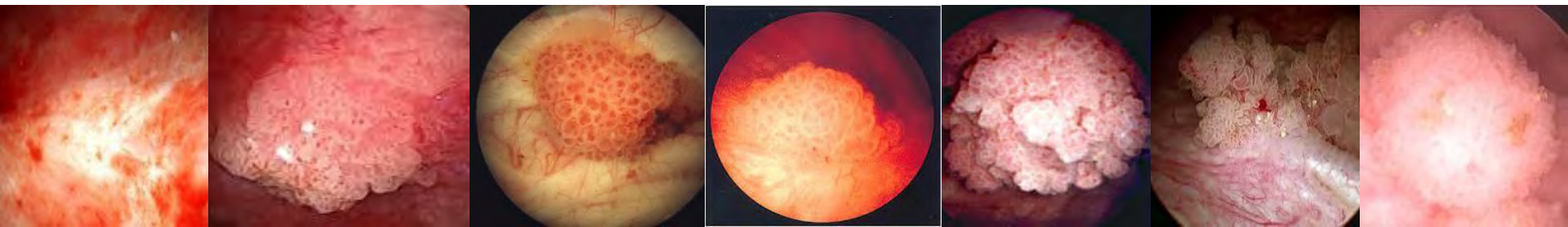
- **Publications**
- Holyoake et al: Development of a Multiplex RNA Urine Test for the Detection and Stratification of Transitional Cell Carcinoma of the Bladder, Clin Cancer Res 2008; 14(3): 742-749
- O'Sullivan et al: A multigene urine test for the detection and stratification of bladder cancer in patients presenting with hematuria, J Urol 2012; 188: 741-747



# Occupational risk factors.



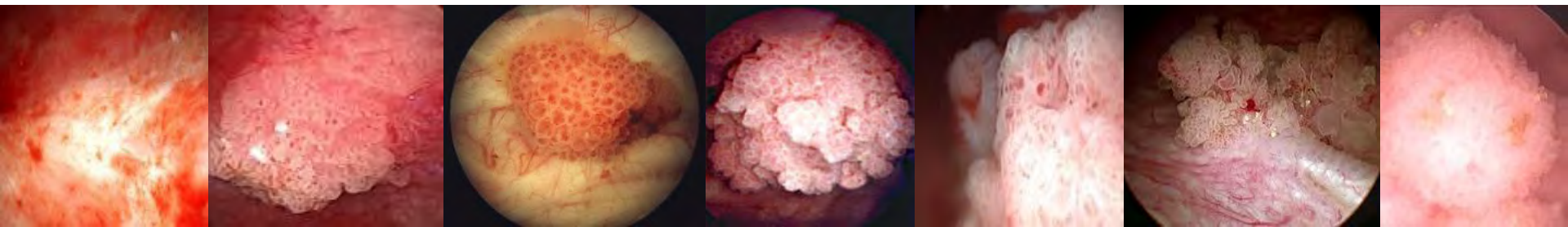
- [Scand J Urol Nephrol Suppl.](#) 2008 Sep;(218):58-63
- **Occupational risk factors.**
- [Delclos GL](#), [Lerner SP](#).
- **Abstract**
- The association between exposure to selected chemical carcinogens, occupations or industries and bladder cancer is well established, and it is estimated that 20-27% of bladder cancers are attributable to occupational exposures. The risk of bladder cancer stemming from an occupational exposure depends not only on compound carcinogenicity, exposure intensity and workplace characteristics, but also on individual susceptibility to these cancers. Regulatory controls in industrialized nations have resulted in a decreased burden of exposure to bladder carcinogens in the workplace. Unfortunately, the same is unlikely in many developing countries, where risky technologies may have been transferred from more developed countries, and where enforcement of regulations and worker protection are likely to be less stringent.



# Occupational exposure to carbon black and risk of cancer.



- [Puntoni R](#), [Ceppi M](#), [Gennaro V](#), [Ugolini D](#), [Puntoni M](#), [La Manna G](#), [Casella C](#), [Merlo DF](#).
- **Source**
- National Cancer Research Institute, Genova, Italy. [riccardo.puntoni@istge.it](mailto:riccardo.puntoni@istge.it)
- **Abstract**
- **OBJECTIVES:**
- To investigate cancer risk in dockyard workers exposed to carbon black.
- **METHODS:**
- Cancer incidence was ascertained among 2101 longshoremen employed at the dockyard of Genova, Italy They were categorized a priori as exposed to low, moderate, and high level of carbon black dust. Incidence rates for the male population of the City of Genova were used to compute standardized incidence ratios (SIR).
- **RESULTS:**
- A positive exposure-response relation with carbon black exposure was detected only for bladder cancer (SIR = 204, 95%CI = 112-343, in highly exposed workers). Increased incidence of pleural mesothelioma (SIR = 751, 95%CI = 302-1547) and melanoma (SIR = 288, 95%CI = 125-2168) were detected.
- **CONCLUSION:**
- Exposure to carbon black experienced by dockyard workers was associated with a two-fold increased risk of bladder cancer.

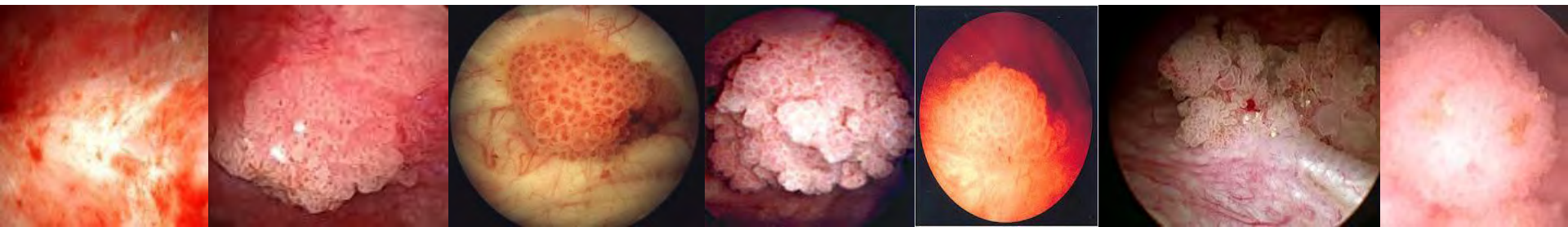


# Bowen Basin

## Operating Coal Mines:



- [Blackwater](#)
- [Burton](#)
- [Collinsville](#)
- [Coppabella](#)
- [Dawson Central](#)
- [Ensham](#)
- [German Creek](#)
- (includes Grasree, Central and Southern Colliery)
- [Gregory/Crinum](#) (2 mines)
- [Kestrel](#)
- [Moranbah North](#)
- [Newlands](#)
- [Norwich Park](#)
- [Peak Downs](#)
- [Yarrabee](#)
- [Blair Athol](#)
- [Callide](#)
- [Cook](#)
- [Curragh](#)
- [Foxleigh](#)
- [Goonyella/Riverside,](#)
- Broadmeadows
- [Hail Creek](#)
- [Jellinbah East](#)
- [Moorvale](#)
- [North Goonyella](#)
- [Oak Creek](#)
- [Rolleston - \*proposed\*](#)
- [South Walker Creek](#)
- [Saraji](#)



**Mining companies operating in the region include:**



**BHP Billiton Mitsubishi Alliance**

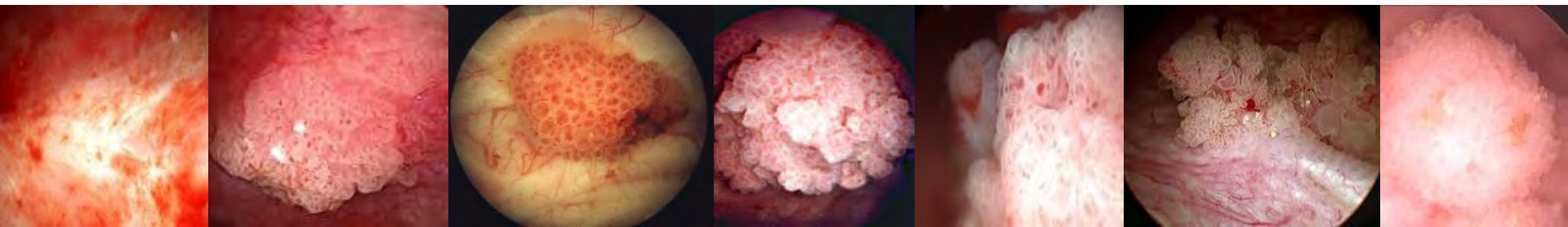
**Anglo Coal Australia Pty Ltd**

**Xstrata**

**Peabody Energy Australia Pty Ltd**

**Rio Tinto Coal Australia Pty Ltd**

**Macarthur Coal**

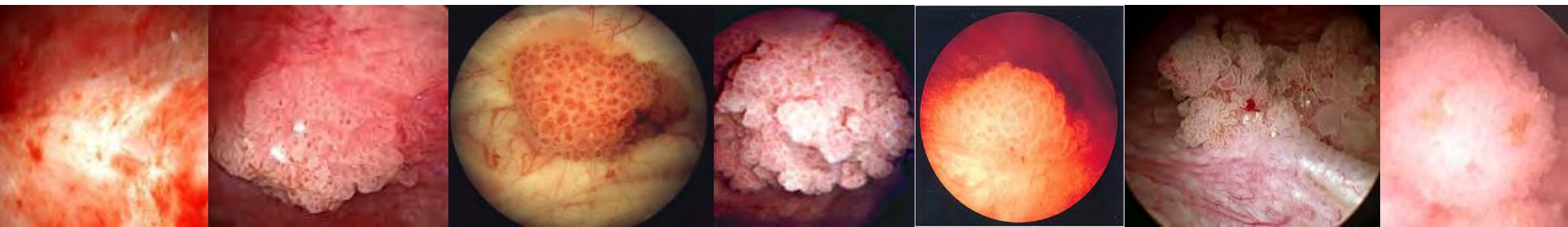


# Annual number of bladder cancer diagnoses with projections by sex, Queensland, 1982-2003

Data source: Queensland Cancer Registry.



Year	Males	Females	Persons		Year	Males	Females	Persons
1982	279	80	359	•	1993	362	129	491
1983	259	75	334	•	1994	409	141	550
1984	306	102	408	•	1995	393	130	523
1985	308	84	392	•	1996	393	133	526
1986	252	105	357	•	1997	427	140	567
1987	322	105	427	•	1998	459	139	598
1988	326	92	418	•	1999	408	138	546
1989	292	94	386	•	2000	467	151	618
1990	316	105	421	•	2001	455	129	584
1991	330	111	441	•	2002	419	151	570
1992	342	105	447	•	2003	431	129	560



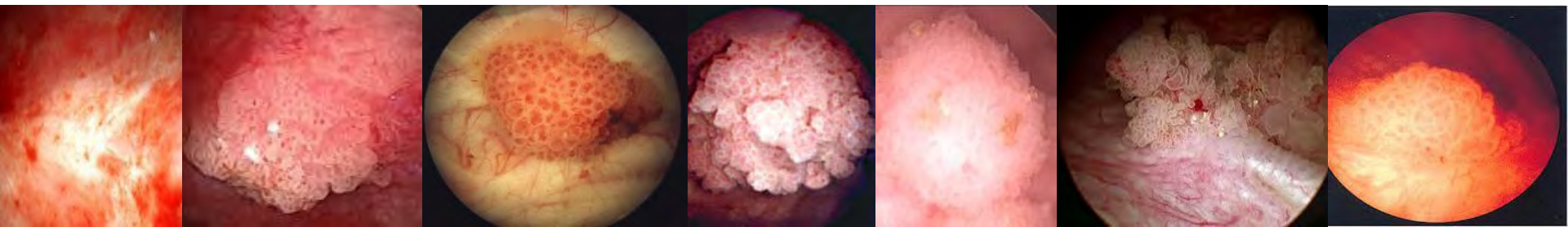
# Annual number of bladder cancer diagnoses with projections by sex, Queensland 2004-2020

Data source: Queensland Cancer Registry.



Year	Males	Females	Persons		Year	Males	Females	Persons
2004	425	149	574	•	2013	406 <sup>^</sup>	140 <sup>^</sup>	546 <sup>^</sup>
2005	433	120	553	•	2014	422 <sup>^</sup>	144 <sup>^</sup>	566 <sup>^</sup>
2006	443	130	573	•	2015	439 <sup>^</sup>	149 <sup>^</sup>	588 <sup>^</sup>
2007	328	122	450	•	2016	456 <sup>^</sup>	154 <sup>^</sup>	610 <sup>^</sup>
2008	329	111	440	•	2017	475 <sup>^</sup>	159 <sup>^</sup>	634 <sup>^</sup>
2009	334	132	466	•	2018	493 <sup>^</sup>	165 <sup>^</sup>	658 <sup>^</sup>
2010	353	116	469	•	2019	513 <sup>^</sup>	170 <sup>^</sup>	683 <sup>^</sup>
2011	375 <sup>^</sup>	130 <sup>^</sup>	506 <sup>^</sup>	•	2020	532 <sup>^</sup>	176 <sup>^</sup>	709 <sup>^</sup>
2012	391 <sup>^</sup>	135 <sup>^</sup>	526 <sup>^</sup>					

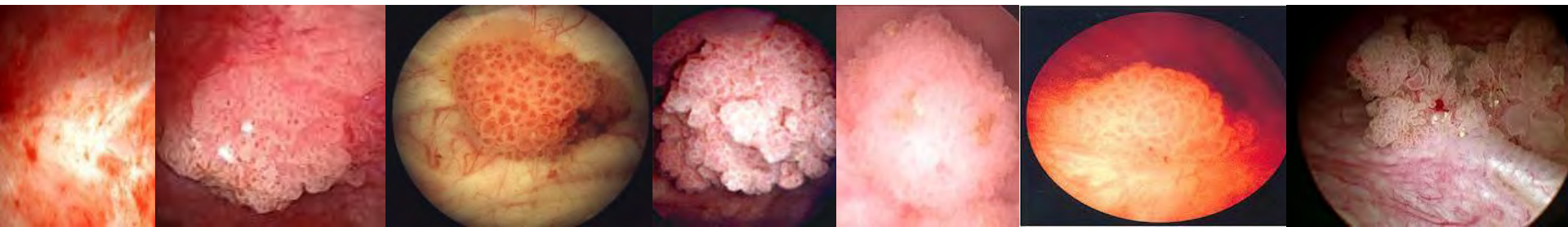
<sup>^</sup> Data for 2011-2020 are estimated projected counts.







- I have used the test in a variety of different situations and types of patients but this was not done as part of a formal protocol (on that basis I do not have data to present)
- Since mid July 2013 the tests have been carried out on voided urine as per protocol in 12 patients with very reliable results.
- I currently have more than 250 bladder cancer patients on my books and average 8-12 cystectomies a year in my solo practice with a dozen last year being the highest in 15 years in Mackay.



# Future Use for Cxbladder Cancer Test in Queensland



- Workplace Health and Safety in Mining Industry
- Monitoring of patients on long term surveillance
- Useful aid in screening at risk populations
- Useful adjunct in patients with upper tract TCC as an integral part of surveillance protocol thereby avoiding regular contrast studies and upper tract imaging in compromised renal function patients
- In screening of select patient groups such as analgesic nephropaths

