



# ***TERT* promoter mutation in non-malignant urothelium of bladder is associated with recurrence in patients with non-muscle invasive bladder carcinoma.**

**Yujiro Hayashi<sup>1</sup>, Kazutoshi Fujita<sup>1,2</sup>, Satoshi Nojima<sup>3</sup>, Eisuke Tomiyama<sup>1</sup>, Yoko Koh<sup>1</sup>, Makoto Matsushita<sup>1</sup>, Kosuke Nakano<sup>1</sup>, Taigo Kato<sup>1,4</sup>, Koji Hatano<sup>1</sup>, Atsunari Kawashima<sup>1</sup>, Takeshi Ujike<sup>1</sup>, Motohide Uemura<sup>1,4</sup>, Eiichi Morii<sup>3</sup>, George J Netto<sup>5</sup>, and Norio Nonomura<sup>1</sup>**

1. Department of Urology, Osaka University Graduate School of Medicine
2. Department of Urology, Kindai University Faculty of Medicine
3. Department of Pathology, Osaka University Graduate School of Medicine
4. Department of Urological Immuno-oncology, Osaka University Graduate School of Medicine
5. Department of Pathology, The University of Alabama at Birmingham

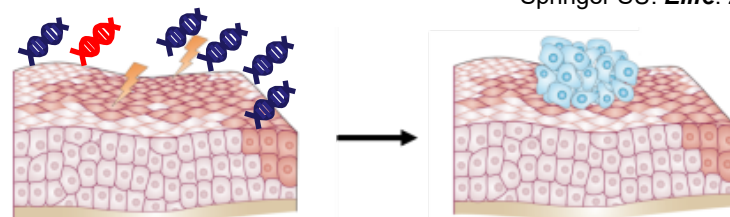
# Background

- ✓ *TERT* promoter mutations contribute to tumorigenesis by promoting immortalization and genomic instability.
- ✓ *TERT* promoter mutations are detected in urine from patients with no evidence of cancer, and is associated with developing urothelial carcinoma consequently.

Chiba K et al. *Science*. 2017

Hayashi Y et al. *Cancer Sci*. 2019  
Springer SU. *Elife*. 2018

- ✓ We hypothesized that mutated *TERT* promoter DNA might be released from non-malignant urothelium.

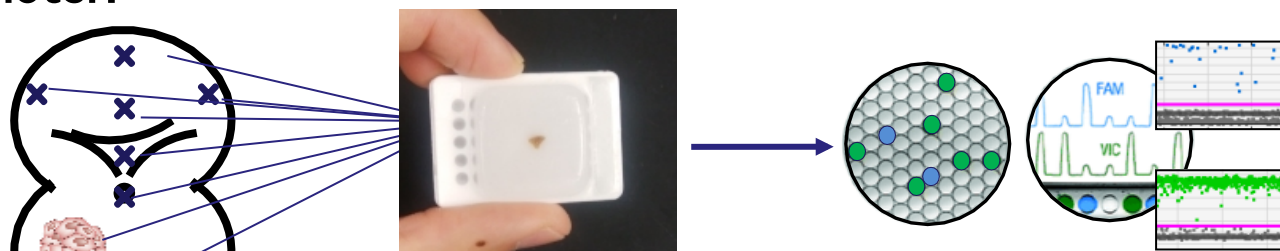


Non-malignant urothelium

Tumor formation

## Materials and Methods

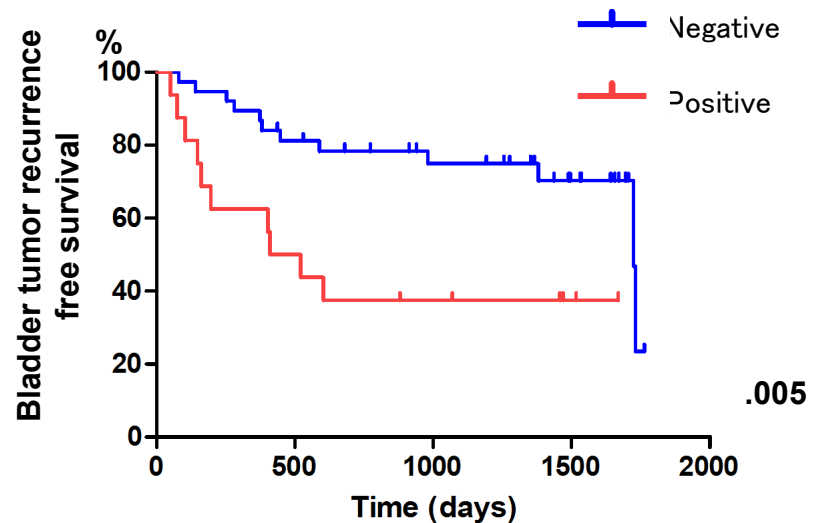
- ✓ We extracted DNA from biopsy samples and tumor from patients with non-muscle invasive bladder tumor, and performed droplet digital PCR analysis of *TERT* promoter.



Droplet digital PCR

# Summary of results

- ✓ *TERT* C228T mutation was detected in 9% of non-malignant urothelium.
- ✓ *TERT* C228T mutation was detected in 30% of patients with NMIBC
- ✓ *TERT* C228T mutation in non-malignant urothelium was significantly associated with bladder recurrence after TURBT ( $p=0.005$ ).



## Conclusions

The *TERT* C228T mutation analysis of systemic random biopsy specimens may lead to novel treatment strategy for patients with NMIBC.