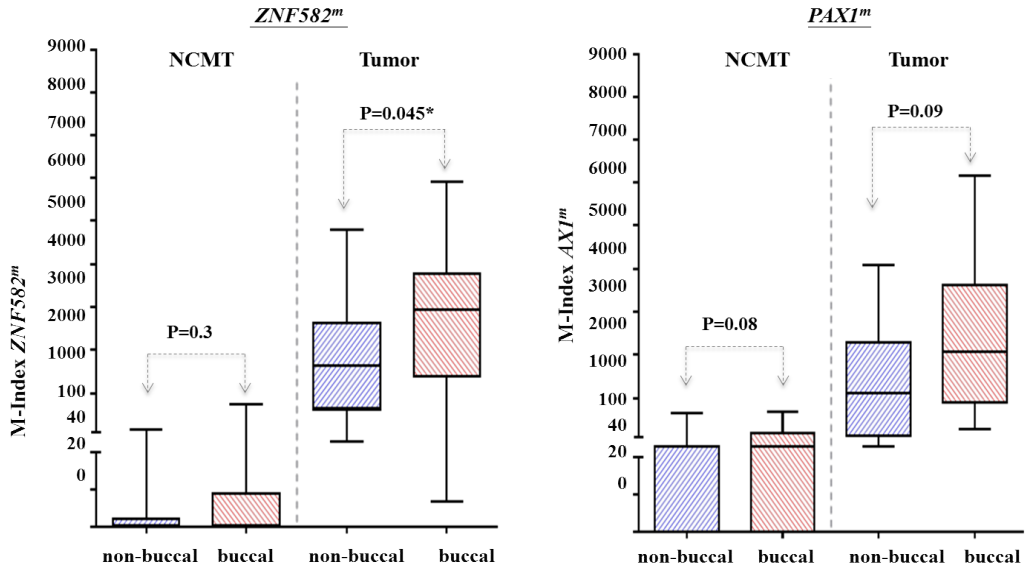
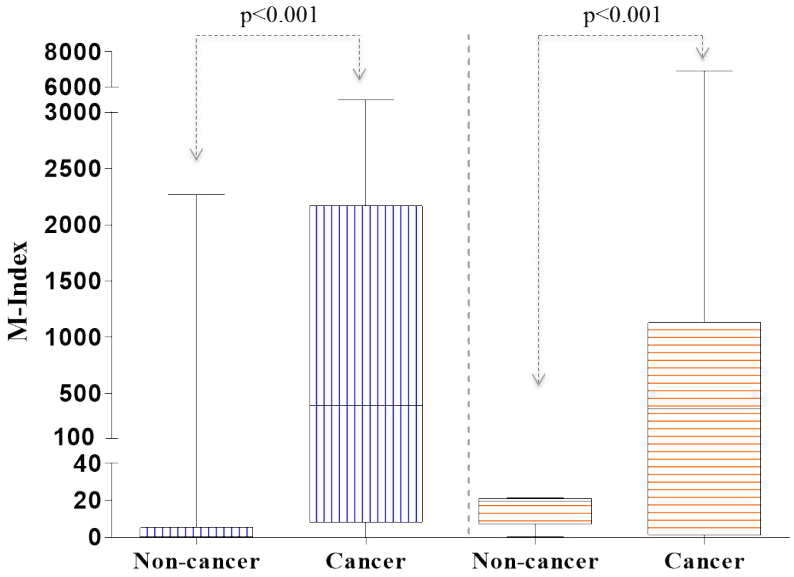


Supplement Figure S1. The methylation level of *PAX1*^{m} and *ZNF582*^{m} in different location in the training set. Buccal tumors had significantly higher *ZNF582*^{m} methylation levels than tumors in non-buccal areas (median M-index: 2932 and 1644, respectively, p=0.045). Similar methylation trends were observed in*PAX1*^{m}: buccal tumors had higher*PAX1*^{m} methylation levels than those tumors in non-buccal areas (median M-index: 2059 and 1199, respectively, p=0.09). No significant differences in the methylation of both *ZNF582*^{m} and *PAX1* ^{m} were observed in either buccal or non-buccal areas in NCMT.



Gene^{m}	Methylation-level		Cancer Detection			
	Non-cancer (n=19)	Cancer (n=44)	Sensitivity	Specificity	Odds ratio (95%CI)	*P*
ZNF582^{m}	0.36 ± 519.90	391.47 ± 1595.20	72.73%	89.47%	22.67 (4.54~113.21)	<0.001*
PAX1^{m}	19.78 ± 7.57	363.23 ± 1575.77	68.18%	78.95%	8.04 (2.25~28.68)	<0.001*

Supplement Figure S2. Difference M-index level between non-cancer & cancer group for ZNF582 & PAX1 in the validation set on tissue specimen. The methylation level of *ZNF582*^{m} and *PAX1*^{m} in cancer groups were significantly higher (391.47 ± 1595 vs. 20/363.23 ± 1575.77) than those in non-cancer groups (0.36 ± 519 vs. 90/19.78 ± 7.57). The sensitivity, specificity and odds ratio were calculated for the detection of cancer in the lower table. *ZNF582*^{m} showed a moderate sensitivity (72.73%) and high specificity (89.47%) and odds ratio (22.67), while *PAX1*^{m} had lower sensitivity (68.18%), specificity (78.95%) and odds ratio (8.04).