

Histologic and enzymatic background for biosynthesis of aberrant glycosylated prostate-specific antigen

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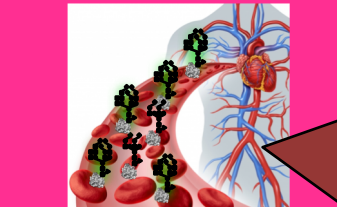
Background & Objective:

Although we previously reported that the prostate cancer (PC) diagnostic performance of serum aberrant Sia2,3Gal-glycosylated prostate-specific antigen (S2,3PSA) test or LacdiNAc-glycosylated PSA (LDN-PSA) test much superior to conventional PSA test (Ishikawa et al., *IJMS*, 2017; Yoneyama et al., *Cancer Sci.* 2019), histopathologic and enzymatic background for biosynthesis of aberrant-glycosylated PSA in prostate tissue has still unknown. In this study, we investigate the origin of aberrant-glycosylated PSA in prostate tissues.

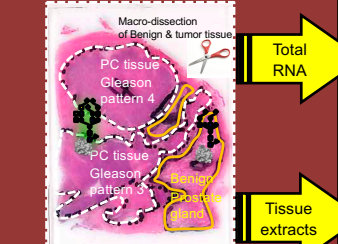
Material & Methods

Total RNA and protein were extracted from benign prostate gland and each Gleason pattern of PC tissue that was macro-dissected from FFPE prostate section in 71 patients who underwent radical prostatectomy in Hirosaki University. The expression level of sialylated- and LDN- synthesis-related glycosyltransferase genes were evaluated by droplet digital PCR, and also %S2,3PSA or LDN-PSA/total PSA levels were analyzed by automated immunoassay systems.

Aberrant glycosylated PSA in serum increased PC patients, especially greater than GS7. (Data shown in AUA2020 Podium presentation; PD52-10, PD53-07)



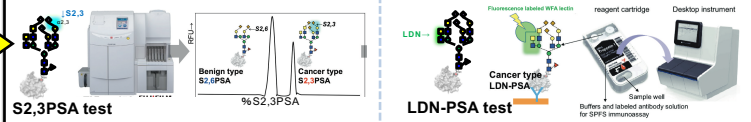
Biosynthesis of aberrant-glycosylated PSA in prostate tissue has still unknown



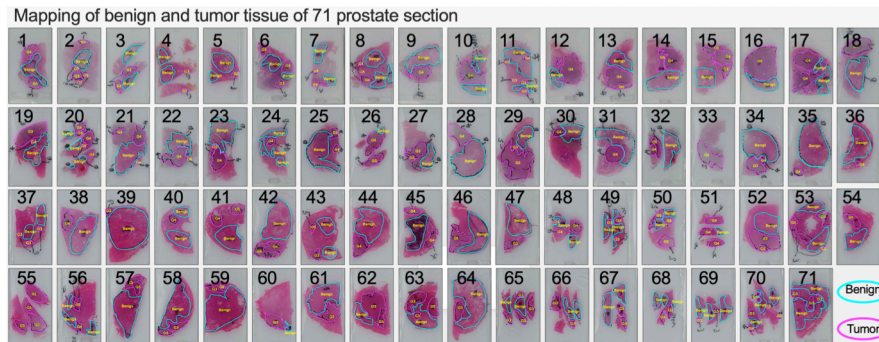
PC associated glycosyltransferase gene expression in tissue



Aberrant glycosylated PSA in tissue

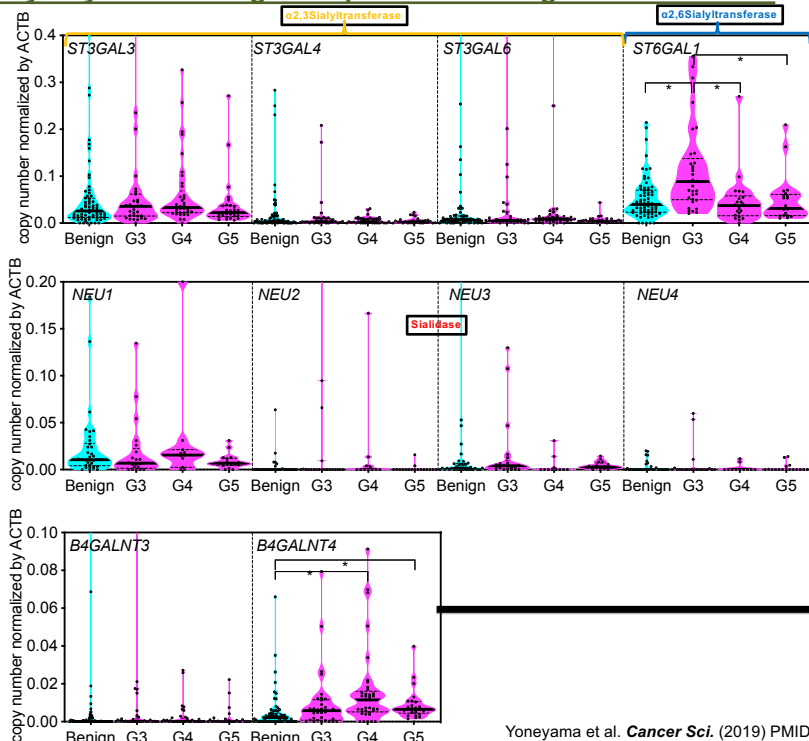


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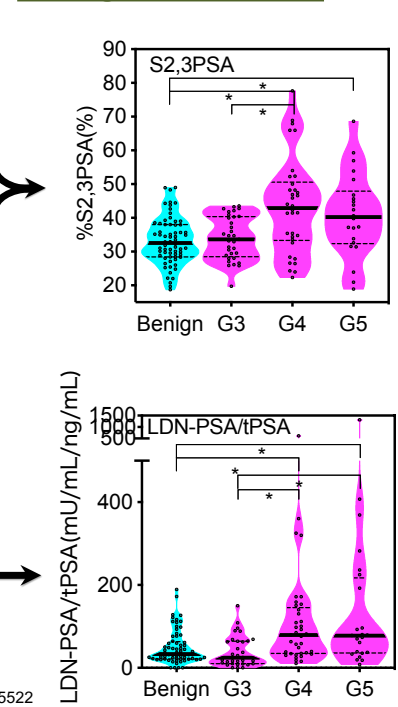


Sialylation related gene	Expression level in tissue	%S2,3PSA ratio in tissue
ST6GAL1	G 3 > Benign = G 4 & 5	
ST3GAL3,4,6	No change	Benign = G 3 < G 4 & 5
Sialidase	No change	
LacdiNAcAclyation related gene	Expression level in tissue	LDN-PSA/tPSA level in tissue
B4GALNT3	Very low & No change	
B4GALNT4	Benign = G 3 < G 4 & 5	Benign = G 3 < G 4 & 5

Glycosyltransferase gene expression in benign & tumor tissue



S2,3PSA ratio & LDN-PSA/tPSA in benign & tumor tissue



Conclusion:

- Variation of Sialyltransferase and GalNAc transferase gene expression well correlated with tissue aberrant glycosylated PSA ratio.
- Aberrant glycosylated PSA mainly secreted from PC cells, especially higher Gleason pattern.

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