Predictive potential of protein glycovariants for head and neck cancer therapy

Sadie Salminen, M.Sc Erica Routila, Ph.D., adj. prof. Janne Leivo
and M.Sc Khirul Islam
University of Turku
MOLECULAR BIOTECHNOLOGY AND DIAGNOSTICS

UNIVERSITY OF TURKU

BACKGROUND

Head and neck cancer commonly originates in the squamous epithelial lining of upper aerodigestive tract, and each case is very heterogeneous. Nearly 900 000 new incidences and 400 000 mortality cases are reported annually. Presently, head and neck cancers lack specific diagnostic or prognostic biomarkers and predictive biomarkers for targeted treatments.

Glycovariants are researched as potential biomarkers for various cancer types. Glycosylation is a crucial post-translational step as it modifies and determines stability, composition and function of lipids and proteins. Integrins are transmembrane receptor proteins, and their aberrant glycosylation has been linked to metastasis and chemo-/radioresistance.
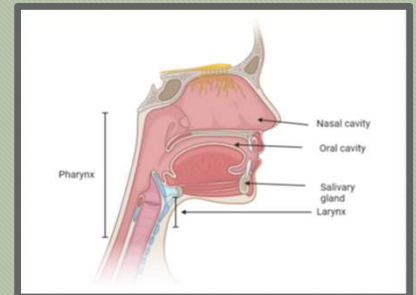

Fig 1. Common sites of head and neck cancer.

STUDY AIM

Investigate integrin glycovariants that could be used to evaluate the nature of the cancer and potentially help determine the appropriate course of care for the patient.

METHOD AND MATERIAL

Tissue samples provided by TYKS hospital were homogenized to access the cell membrane bound proteins.
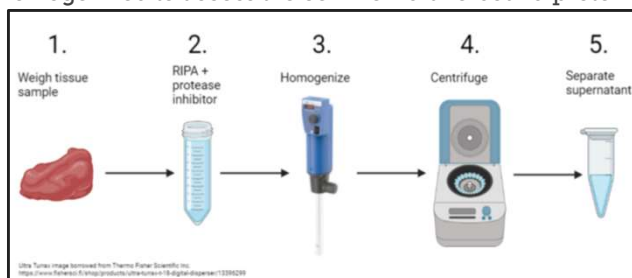

Fig.2. Tissue sample homogenization .

Lectin nanoparticle immunoassay was used to analyse the aberrant glycosylation of integrins from tumour tissue samples (n=21) and adjacent healthy tissue samples (n=15).
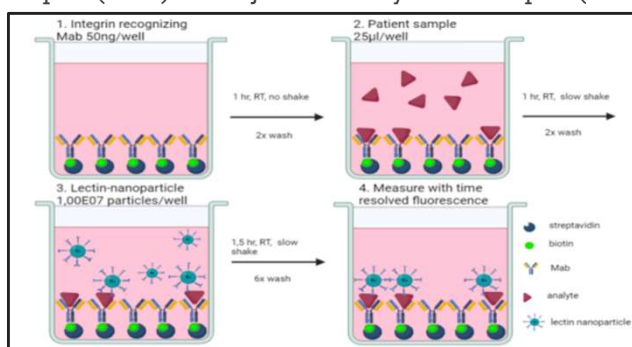

Fig.3. Lectin immunoassay protocol.

Integrin-recognizing Mabs (ITGA2, ITGA3, ITGA5, ITGA6, ITGB4, ITGB1) and lectin nanoparticles (ConA, AAL, UEA, MAA, SBA, WFL) were used as captures and tracers, respectively.

The prognostic potential in diagnosing locoregional tumour recurrence and neck metastasis was evaluated by Student's t-test and ROC -analysis.

RESULTS & CONCLUSIONS

With the 36 different lectin – integrin –combinations studied, the signal received from tumour samples were higher compared to the healthy adjacent samples signals, indicating that the observed glycosylation of integrins could be a cancer-linked abnormality.
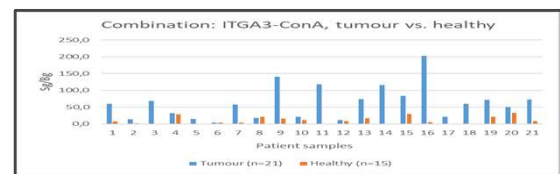

Fig 4. Integrin – lectin combination: ITGA3 - ConA healthy vs tumor.

Regarding neck metastasis, significantly lower expression of the combination ITGA5 + WFL was observed in metastatic tumours and for local tumour recurrence, significantly lower ITGA5 + UEA expression was observed.

Analysis	Combination	p-value	Sg/Bg-ratio
Neck metastasis	ITGA5-WFL	0,04	9.51 vs 4.11
Locoregional recurrence	ITGA5-UEA	0,05	9.35 vs 3.94

Table 1. Significant values from Student's t-test for neck nodal recurrence and locoregional recurrence.

Neck nodal metastasis significant ROC – analysis values: AUROC=0.16; 95 % CI: 0.00 to 0.35, p=0.014. Significant ROC- analysis values for locoregional recurrence: AUROC=0.14; 95 % CI: 0.00 to 0.30, p=0.017.
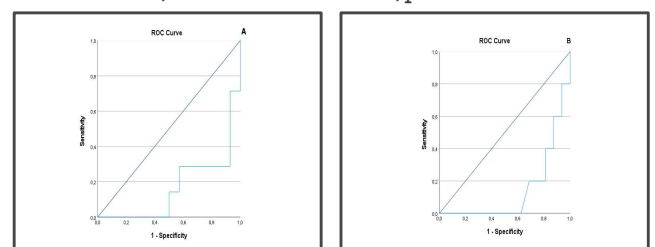

Fig 5. ROC – analysis for ITGA5 – WFL for nodal metastasis at presentation (A) and ITGA5-UEA for recurrence (B).

The positive findings of this study could potentially be used to predict locoregional and neck nodal metastasis, but the results should be validated in larger patient cohorts.

References:
Gidwani et al. 2016. A Nanoparticle-Lectin Immunoassay Improves Discrimination of Serum CA125 from Malignant and Benign Sources. Clinical Chemistry 62:10 1390–1400. DOI: 10.1373/clinchem.2016.257691
International Agency for Research on Cancer. WHO. Global Cancer Observatory. Site accessed 28.2.2022. https://gco.iarc.fr/
Image: Thermo Ficher Scintific Inc. 2022. IKA™ ULTRA-TURRAX™ T 18 Digital Disperser. Site accessed 22.3.2022.
https://www.fishersci.fi/shop/products/ultra-turrax-t-18-digital-disperser/13396299