SCALABLE DETECTION OF VIRUS RNA IN TUMORS – EFFECTIVE TARGETS FOR NEW THERAPIES

Gitte Pedersen*. Genomic Expression, Beverly, MA, USA

Background Infectious agents are causing 20%–30% of all cancers. Non-human genes can act as effective tumor-specific targets. For an oncovirus, such as the Epstein-Barr virus (EBV), the viral genome is integrated into the cell genome and express viral proteins during the latency phase, which could be targets for immune therapies and other types of therapy. For example, therapies using autologous T lymphocytes targeting the EBV latent membrane proteins LMP1 and LMP2 have had impressive results in some lymphomas.

Methods Standard RNA-sequencing pipelines map the reads only to the human genome and do not, therefore, identify tumor-specific non-human antigens. Furthermore, the findings lack clinical validation.

We demonstrate that our clinically validated OneRNA® platform, which leverages RNA-sequencing in tissue and blood, can identify unique viruses and their expressed mRNAs, some of which could act as tumor-specific antigens. The OneRNA® platform is validated according to CLIA standards.

In this work, we identify and quantify viral RNA expressed in solid as well as in hematological tumors using an augmented version of the OneRNA® bioinformatics pipeline. We further show how we clinically validated these findings, enabling large-scale implementation in the clinic.

Results OneRNA® in FFPE demonstrated higher sensitivity to most viruses discovered than Truseq perform on FF samples from the same tumors. Truseq is not recommended in FFPE thus OneRNA® provides a clinically validated chemistry that can effectively detect viral and possibly other infectious agents in FFPE tumor tissue. Virus was detected in all of the samples, tumor and normal tissue.

Cytomegalovirus (CMV) reads were found in 70% of the breast cancer samples. However, only two viruses were found in significantly higher normalized read counts than normal tissue while CMV normalized read counts were similar to normal tissue.

Conclusions The identification and validation of the presence of additional vaccine targets for e.g. mRNA vaccines provides an exciting opportunity for biotech and pharma to improve the response rate of checkpoint inhibitors as recently seen with Moderna’s mRNA vaccine in melanoma. It also provides the opportunity to move immune therapy and the use of check-point inhibitors into low mutation frequency (low-mut) tumors such as breast cancer by providing the immune system with a non-human target as Neo-antigens are low in low-mut tumors. Finally, it can provide the opportunity to treat the tumor if the infectious agent is treatable with existing drugs.

REFERENCES
5. Anshuman Panda et al, Immune Activation and Benefit From Avelumab in EBV-Positive Gastric Cancer, JNCI: Journal of the National Cancer Institute, 2018;110(3):316–320, https://doi.org/10.1093/jnci/djp213

Ethics Approval Samples was obtained from a Biobank with all the required approvals

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0170