AB051. SOH22ABS035. Investigation of the role of CD161 in oesophageal adenocarcinoma

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Background: Oesophageal adenocarcinoma (OAC) is an aggressive cancer with five-year survival outcomes at just 30%. As incidence of OAC in Ireland is predicted to more than double by 2035, identifying prognostic immunological biomarkers to personalise treatment could dramatically improve treatment outcomes. CD161 is a surface marker expressed on NK cells and several other T cell subsets. Gentles *et al.* showed expression of KLRB1, the gene encoding CD161, was most frequently associated with favourable prognostic outcomes across 39 cancers; with KLRB1 expression on γδ T cells as one of the most highly correlated favorable prognostic T cell signatures. Twenty-five percent of peripheral T lymphocytes express CD161, however the effect of CD161 expression and ligation on T cells remains unclear. We aim to determine the profile of CD161 expression in Barrett's Oesophagus (BO) and OAC *vs.* healthy donor blood and assess if CD161 expression influences cell function.

Methods: Whole blood from healthy (n=3), BO (n=4) and OAC patients (n=15) was stained for FAC's analysis using FlowJo v_10. Stimulation of healthy donor PBMC's was performed using cell stimulators. Statistical analysis was performed by paired t tests and one-way ANOVA with the Tukey post-hoc test for multiple comparisons using GraphPad Prism software v_6.

Results: The composition of circulating lymphocytes expressing CD161 is altered in OAC vs healthy controls. CD161+CD3– cells were increased (P=0.05) and CD161+Vδ1+ γδ T cells were decreased (P=0.02) in OAC patient blood vs healthy controls. CD161+ lymphocytes share a similar functional trait of increased IFN-γ production in response to stimulation.

Conclusions: Our findings support studies indicating CD161+ lymphocytes share an enhanced innate immune response, producing increased levels of IFN-γ. By examining CD161 expression in relation to clinical outcomes in a large cohort of OAC patients over a longer period, CD161 may hold potential as an immunological prognostic tool to identify OAC prognostic subtypes and distinguish pathologic complete responders from non-responding patients to neoadjuvant chemotherapy.

Keywords: CD161; oesophageal adenocarcinoma (OAC); IFN-γ; prognostic tool; chemotherapy

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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