powered by

dkfz.
GERMAN
CANCER RESEARCH CENTER
IN THE HELMHOLTZ ASSOCIATION

Contribution ID: **393** Type: **1 - Scientific Poster**

Risk reduction of cancers from a high physical activity level is associated with predicted tumour neoantigen count

Background: The magnitude of cancer risk reduction from physical activity is highly heterogeneous across different cancer types. Preclinical studies indicate that regular exercise enhances anti-tumour immunity, leading to the elimination of immune-susceptible tumour cell clones. Whether this mechanism explains variable risk reduction across clinical cancer types in physically active humans remains uncertain. **Purpose**: To determine whether variance in cancer risk reduction associated with physical activity relates to the immunogenomic landscape of tumour types, by integrating findings from large prospective cohort studies of lifestyle and cancer incidence with tumour multi-omics atlases. **Methods**: We performed a mixed effects meta-regression of published pooled clinical cancer incidence hazard ratios (HR) of 20 different cancers comparing high-vs-low (90th vs 10th percentile) leisure time physical activity levels from 12 prospective lifestyle cohort studies (Moore et al., 2016), against the immunogenomic profiles of >10,000 tumours across 20 corresponding cancer types in The Cancer Genome Atlas (TCGA). Immunogenomic variables included predicted tumour mutational burden, predicted neoantigen count, and tumour infiltration scores for immune cells. **Results**: A greater cancer incidence risk reduction from high-vs-low physical activity was associated with a higher median neoantigen count of corresponding cancers in TCGA (β=−0.0018, P<0.0001), accounting for 61.27% of the between-cancer variance in risk reduction, with each increase of 25 neoantigens associated with 4.5% greater cancer risk reduction. Similar, though weaker, associations were observed for TMB (R2=42.43%, β=−0.0417, P=0.0034). Conversely, key intra-tumoural immune measures including CD8+ T-cells and other immune effectors, showed weak or no relationships with physical activity HRs, perhaps reflecting immune dysfunction/failure within clinically manifested tumours in the TCGA cohort itself. **Conclusion**: Risk reduction of cancers from high-vs-low physical activity is linked to the predicted neoantigen burden of corresponding clinically detected cancers. These findings support the hypothesis that adaptive immunity contributes to the anti-cancer effects of physical activity in humans.

Keywords

Physical activity, Immunogenomics, Neoantigen burden, Tumour immunology

Conflict of Interest & Ethical Approval

yes

Abstract submitters declaration

yes

Author: CAMPBELL, John (University of Bath)

Co-authors: Ms GIANCOLA, Gabby (University of Bristol); Dr CORNISH, Naomi (University of Bristol); Dr GOUDSWAARD, Lucy (University of Bristol); Prof. GUNTER, Marc (Imperial College London)

Presenter: CAMPBELL, John (University of Bath)

Session Classification: Poster Session