Late-Breaking Abstracts

Biomarkers, Immune Monitoring and Novel Technologies

MULTIOMIC FUNCTIONAL BIOMARKERS FOR CANCER PREDICTION AND EARLY DETECTION

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Background Adulthood cancer results from (epi)genomic cellular changes associated with chronic inflammatory processes and maladaptive immune responses. Identifying sensors of health to disease transition culminating in early carcinogenesis beyond cell autonomous cues is an unmet medical need. A holistic view might help defining a high-risk model based on functional biomarkers amenable to personalized screening interventions and interceptive measures.

Methods We conducted a prospective omics-based translational research study (PREVALUNG trial, NCT03976804) in 508 smokers with cardiovascular disease (CVD) aimed at predicting the 17 tobacco-associated cancers beyond the NLST, NELSON, PLCom2012 screening scores. After inclusion, patients were scheduled for a low-dose chest CT-scan, and blood and feces samples were collected concomitantly. PREVALUNG omics-based sensors of health to disease transition included analytes related to inflammation, immunity, metabolism, metagenome, gut barrier, plasma proteomics, and clonal hematopoiesis. To validate our hypotheses, we investigated a Li-Fraumeni cohort of TP53 germline mutation carriers (LIFSCREEN trial, NCT01464086), and performed the same omics assessment on biological sample taken before cancer detection.

Results We could estimate cancer risk of CVD patients based on 33 soluble markers and 2 clinical risk factors, with an AUC of 0.78 (0.67; 0.79). To challenge this model of inflammation-related cancer, we investigated a Li-Fraumeni cohort of TP53 germline mutation carriers who have a significantly increased lifetime cancer risk affecting multiple organ sites. Here, 13 soluble markers and 8 clinical risk factors predicted cancer with an AUC of 0.82 (0.66; 0.91). The functional pathways shared by both cohorts paving the way to carcinogenesis include the neutrophil/lymphocyte ratio, Th2 immunity (CCL24, CCL26, IL-4/IL-4R, IL-5, CCL11, CCL22, CD163, IL-33/ST2), inflammasome activation (IL-1b, IL-1R2, IL-1RN), gut barrier permeability (IL-33/ST2, CD14/LBP, MAdCAM-1, CCL25), cholesterol and biliary salt circuitries, tryptophan and vitamin B3 metabolism, polyamines and ketogenesis.

Conclusions These two studies suggest that health to cancer transition results from coordinated and cumulative pathological failures of the meta-organism, amenable to biologically-guided prophylactic measures beyond life style changes.

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Trial Registration Prevalence of Lung Cancer (PREVALUNG) study was approved according the French Jardé law; the study is referenced at the French ‘Agence Nationale de Sécurité du Médicament et des Produits de Santé’ (reference ID RCB: 2019-A00262-55) and registered on clinicaltrial.gov (NCT03976804).

LIFSCREEN (ClinicalTrials.gov Identifier: NCT01464086).

Ethics Approval Prevalence of Lung Cancer (PREVALUNG) study was approved according the French Jardé law; the study is referenced at the French ‘Agence Nationale de Sécurité du Médicament et des Produits de Santé’ (reference ID RCB: 2019-A00262-55) and registered on clinicaltrial.gov (NCT03976804).

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