

anti-PD-1 [2]. Simulated tumour growth curves were compared to experimental data and sensitivity study of key parameters was performed.

Results

Simulated tumour growth curves are in good agreement with experimental data. Maximum deviation of simulated control tumour volume (solid line – blue) to experimental data (blue squares) is –25% (day 13). On the other hand, the model slightly underestimates the effect of treatment with anti-PD-1. Maximum deviation of simulated anti-PD-1-treated tumour volume (solid line – red) to experimental data (red squares) is +40% (day 17). Sensitivity study reveals that dosing and scheduling regimen does not importantly affect treatment outcome (data not shown). The most sensitive parameter of the model is MHC class I appearance. By modulating MHC class I appearance from 1% to 100%, while keeping other parameters fixed, we are able to simulate responders as well as non-responders to anti-PD-1.

Conclusions

Model predictions of antitumour response to anti-PD-1 are within expectations. The predictions might be even more reliable if model parameters were, due to their inter-patient variability and presumably dynamic nature, actually measured for every specific experiment/patient. The emphasis should be on MHC class I appearance as it might be one of the predictive biomarkers of response to anti-PD-1.

References

1. Kleffel, Sonja, et al. Melanoma cell-intrinsic PD-1 receptor functions promote tumor growth. *Cell*. 2015; 162.6:1242-1256.
2. Sánchez-Paulete, Alfonso R., et al. Cancer immunotherapy with immunomodulatory anti-CD137 and anti-PD-1 monoclonal antibodies requires BATF3-dependent dendritic cells. *Cancer discovery*. 2016; 6.1:71-79.

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Unravelling the immune contexture of pre-invasive lesions of the lung by multispectral imaging

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Background

Lung cancer is the leading cause of cancer deaths world- wide and despite advances in therapy, the overall survival rate for lung cancer patients remains only 15%.

As most of sporadic cancers, lung cancer emerges from pre-neoplastic lesions characterized by morphological and molecular changes. If morphological changes of pre-invasive bronchial lesions are well characterized, the cause and effect relationship between those changes and the immune response is still un- known. Though, we identified gene expression alterations that suggest a role of the innate and adaptive immunity in the transformation towards carcinoma.

Methods

In order to characterize the evolution of the immune response in pre-invasive bronchial lesions, we have optimized different multispectral 7 colors immunofluorescence panels, by using the Tyramide Signal Amplification (TSA) technology.

Results

We have performed multiplex staining on FFPE human bronchial biopsies (N=114) at 8 successive morphological stages of lung squamous carcinogenesis, from normal, to low grades dysplasia, high grades, to carcinoma. Images of each biopsy have been acquired multispectrally and digitally analyzed to identify and quantify the density and the tissue distribution of different immune cell types. We

aimed to characterize the immune infiltrates at different stages of carcinogenesis and elucidate the role of different cell subtypes in tumor development and progression and the possible causal relationship between the immune phenotypes in pre-neoplastic lesions and tumor progression and patient prognosis.

Conclusions

Evaluation of the immune contexture and prognostic assessment of precancerous lesions of the lung may identify promising new biomarkers for early detection and targets of novel therapeutic strategies for lung cancer.

Immune Modulation, Cytokines, and Antibodies

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A protein extract from fermented wheat germ promotes NK cell-mediated lymphoma eradication in mouse xenografts

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Background

Proteomic and genomic data has allowed for the development of promising targeted agents for NHL [1]. Most have acute and chronic toxicities that limit efficacy. The use of complementary and alternative medicines has increased during the last decade. However, scientific evidence of their efficacy is scarce. Fermented wheat germ extract (FWGE) has been claimed to have anti-cancer properties in many tumor types. FWGE therapeutic activity has been attributed to its content of benzoquinones [2].

Methods

A protein fraction (FWGP) was isolated by FPLC and proteins identified by mass spectrometry. Direct cytotoxic was studied *in vitro* using NHL cell lines. Immunomodulatory properties were evaluated *ex vivo* by measure immune cell activation in human PBMCs and isolated NK cells. *In vivo* experiments used nu/nu NHL xenografts with or without NK cell depletion; endpoints were tumor volume and toxicity. *In vivo* immunomodulatory effects were evaluated by treating tumor-free BALB/c mice with FWGP and measuring NK cell killing activity and degranulation.

Results

FWGP was cytotoxic in 17 cancer cell lines (IC50 = 20-171 µg/ml in NHL, 12-27 µg/ml in colon and 70-144 µg/ml in lung) and induced apoptosis by increasing levels of caspase-3, PARP, BAK, BAD and p53, while reducing levels of AKT. FWGP increased % NK cells, production of IFγ and GrB, and NK-mediated killing. *In vivo* efficacy was confirmed, with no toxicity, in pre-emptive and established models. *In vivo* treatment with FWGP+rituximab was as effective as R-CHOP, with 90% complete remission. NK depletion resulted in no response to FWGP. These results support the hypotheses that FWGP augments NK-mediated tumor killing. Proteomic profiling identified 844 proteins. An active fraction consisted of 169 proteins.

Conclusions

FWGP represents a promising immunomodulatory agent with anti-tumor activity, minimal toxicity and low cost. Our results suggest FWGP has direct lymphomacidal activity by inducing apoptosis and indirect anti-tumor efficacy by enhancing NK-mediated tumor eradication. Further experimental validation will allow translation of an "alternative" product into mainstream medicine.

References

1. Abuhay, M., et al. The HB22.7-vcMMAE antibody-drug conjugate has efficacy against non-Hodgkin lymphoma mouse xenografts with minimal systemic toxicity. *Cancer Immunol Immunother*. 2016; 65(10):1169-75.
2. Hidvegi, M., et al. MSC, a new benzoquinone-containing natural product with antimetastatic effect. *Cancer Biother Radiopharm*. 1999. 14(4):277-89.