Simple blood tests could predict immunotherapy effectiveness

Research Objectives

Dr George Laliotis and his team predict the response of head and neck squamous cell carcinoma (HNSCC) patients to immunotherapy using precision-medicine techniques.

References


Personal Response

Could you tell us more about your future research plans based on these findings?

Based on the findings of this study, future research could focus on further investigating the clinical markers identified in the study to better understand how they predict response to immunotherapy. Additionally, researchers may also try to develop new immunotherapies that are specifically targeted to patients with the identified clinical markers. Additionally, researchers could also look into combination therapies that could be used to enhance the effectiveness of immunotherapies for patients with these markers.
Immune checkpoint inhibitors (ICIs) have been a major game changer in the treatment of cancer, including head and neck squamous cell carcinoma (HNSCC). ICIs are drugs used in immunotherapy, a type of cancer treatment that stimulates the immune system to target cancer cells. Although ICIs are a standard first- and second-line treatment, the drugs have many limitations – including adverse side effects – and only a small percentage of patients respond to the therapies. Genetic and molecular predictive factors are already used to help select suitable candidates for treatment. However, researcher Dr George Laliotis points out that, “Their assessment is currently expensive and time-consuming,” and notes the limitations. Not everyone responds to treatment and current therapies can have serious adverse side effects. When working at the Johns Hopkins School of Medicine, Sidney Kimmel Comprehensive Cancer Center, USA, Dr George Laliotis and his team discovered that biochemical factors, measured from a simple blood draw, could predict patient response to immunotherapy. This breakthrough represents an advancement for personalised treatment approaches to cancer.

Despite the extensive use of immunotherapy in patients suffering from head and neck squamous cell carcinoma, this therapy has significant limitations. Not everyone responds to treatment and current therapies can have serious adverse side effects. When working at the Johns Hopkins School of Medicine, Sidney Kimmel Comprehensive Cancer Center, USA, Dr George Laliotis and his team discovered that biochemical factors, measured from a simple blood draw, could predict patient response to immunotherapy. This breakthrough represents an advancement for personalised treatment approaches to cancer.

Identifying simple, precise, reproducible, and inexpensive predictive factors would improve clinical care in medical oncology. Excitingly, Laliotis and his team have identified new predictive factors that can quickly and affordably measure – plus accurately predict – the response of HNSCC patients to immunotherapy.

**IMMUNOTHERAPY FOR HEAD AND NECK CANCER**

ICIs represent a new class of immunotherapy drugs that consist of monoclonal antibodies, such as nivolumab (programmed cell death protein 1 inhibitor) and pembrolizumab. These antibodies have the ability to target inhibitory receptors and ligands expressed in tumour cells and cause an anti-tumour response by stimulating the immune system. In short, these molecules pause the progression of cancer. Due to their mechanism, they are already widely used to treat cancer, such as head and neck squamous cell carcinoma. Pembrolizumab, for example, was approved in 2019 as a first-line treatment for patients with metastatic or unresectable recurrent HNSCC.

Despite the wide use of ICIs, clinicians face serious drawbacks when considering clinical implementation:

- only a small percentage of patients respond to ICI treatment (up to 20%) and typically respond for a prolonged period of time.
- immune checkpoint inhibitors are characterised by adverse side effects and severe toxicities, including nausea, vomiting, skin rash, and arthritis.
- ICIs are expensive, costing an average of US$100,000 per patient.

**SIMPLE PREDICTIVE FACTORS DISCOVERED**

To overcome these limitations, there is a need to identify new predictive factors that could accurately evaluate whether a patient would benefit from an ICI treatment to help plan better treatment. The idea behind these factors is that immune cells secrete various signalling molecules, like tumour growth factor EGFR and other effectors that sustain tumour angiogenesis (new blood vessel formation) and stimulate cancer cell proliferation, tumour invasion, and metastasis. The currently available predictive markers, like PD-L1 expression, are suboptimal for identifying patients likely to respond to ICI, and patient response varies between different solid tumours. In a recent breakthrough, Laliotis and his colleagues have found new simple, precise, reproducible, and inexpensive predictive factors to evaluate whether a HNSCC patient could benefit from an ICI treatment – and even identify the correct sequence of treatment for patients with metastatic or recurrent HNSCC.

Laliotis’ team propose straightforward predictive tools that could be obtained from a standard blood draw. These tools provide the full blood count, measuring red blood cells, platelets, an enzyme called lactate dehydrogenase (LDH), haemoglobin, and albumin levels. In combination with some basic epidemiological variables (eg, BMI, sex, and age), plus additional clinical criteria, the tools could predict the response of HNSCC patients to ICI treatment.

**A PROMISING START**

Laliotis and his colleagues collected data from a small sample of 100 patients who were treated with a single-agent PD-1 inhibitor and monitored for a short follow-up period of two years. As a result, the researchers created the first nomograms to predict the overall survival (OS) in patients treated with ICI in HNSCC patients, monitoring readily available inflammatory biomarkers obtained from a simple blood draw. To expand the scope of the research, Laliotis and his team repeated the study – this time including more patients who were monitored over a longer period of time. Specifically, they monitored over 200 patients undergoing ICI treatment for almost four years between 2016 and 2020. The researchers conclusively found that lymphocyte counts, LDH, and albumin and haemoglobin levels are strong predictors of the clinical outcomes of these patients. Their proposed prediction model can clearly separate patients into three groups. Each is categorised according to the progression of cancer and likely response to ICI by the potential HNSCC patient candidates, using inexpensive and clinical parameters that are widely available and easily applicable in every hospital. The groups were ranked according to how likely they were to benefit from immunotherapy: poor, medium, or good responders.

From a public health perspective, the researchers’ findings have important implications for global healthcare. The ability to stratify patients into categories of responders or non-responders – even in developing countries with limited resources, smaller hospitals, and no access to specialised testing – means that many low or middle-income countries could now have reliable, affordable cancer treatment tools for their populations.

**NEW ERA FOR PRECISION MEDICINE**

Laliotis and his team are among the first to show how commonly used clinical techniques, like taking blood samples and looking at a patient’s clinical history, can help predict clinical outcomes, thereby facilitating the transition of immunotherapy treatments towards personalised medicine.

**The researchers demonstrated that lymphocyte counts, LDH, and albumin and haemoglobin levels are strong predictors of clinical outcomes.**

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**FACTORS DISCOVERED**

**SIMPLE PREDICTIVE**

**Blood tests**

Blood tests: Patient Demographics

**Liver tests**

**Full blood counts**

**Clinical outcome prediction**

**Survival**

**Variables High**

**Variables Low**

**Time**

**Clinical evaluation**

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**Clincal outcome prediction**

**Blood tests**

**Liver tests**

**Full blood counts**

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