



# Targeting ART1 to overcome immune resistance in lung cancer treatment

**Immune checkpoint inhibitors have become the gold standard treatment for patients with advanced non-small cell lung cancer (NSCLC), but most people do not benefit from long-term clinical responses.**

**Scientists at The Institute of Cancer Research, London, have identified that the expression of ART1 by tumour cells mediates immune resistance in NSCLC patients – and that ART1-inhibition can improve tumour control in preclinical models.**

**The development team is now seeking commercial partners, to support the clinical transition of the project to achieve maximum patient benefit.**

## About the programme

Immune checkpoint inhibitors (ICI), alone or in combination with chemotherapy, have become the standard of care in patients with non-small cell lung cancer (NSCLC) without targetable molecular alterations. However, most patients with lung cancer either do not respond to or do not experience long-term benefits from ICI. There is an urgent need to identify other robust biomarkers predictive of response to ICI and to understand the mechanisms behind lung cancer resistance to immunotherapy.

The Institute of Cancer Research (ICR) researchers, in collaboration with scientists in New York, have discovered that the expression of mono-adenosine 5'-diphosphate (ADP)-ribotransferase 1 (ART1), an enzyme on the surface of tumour cells, mediates immune resistance in NSCLC (1). They demonstrated that high

levels of ART1 on cancer cells leads to a reduction in certain immune cells (CD8+ T cells) in the tumour microenvironment. Genetic and antibody-mediated ART1 inhibition slowed tumour growth in mouse NSCLC and melanoma models.

These findings suggest that ART1 expression may have prognostic and predictive value in patients with lung cancer undergoing immunotherapy. Pharmacologic targeting of ART1 could provide a way to boost immune responses in patients with NSCLC.

## Key publication

1. Wennerberg, E. et al. Expression of the mono-ADP-ribosyltransferase ART1 by tumor cells mediates immune resistance in non-small cell lung cancer. *Sci. Transl. Med.* 14, eabe8195 (2022).

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## Lead scientist/inventor



Dr Erik Wennerberg leads the Radiation-enhanced Immunotherapy Team at the ICR.

His team investigates how solid tumors shape their microenvironment to

evade the immune system by generating suppressive barriers and subverting immune homeostatic mechanisms.

They aim to identify pathways and biomarkers that predict response to radiotherapy/immunotherapy as well as find actionable markers that can be targeted in novel combination treatments for advanced cancers.

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## Key Points

- ♦ ART1 could be developed into a biomarker test to personalise treatment with ICI in patients with advanced NSCLC – ensuring each individual receives the best treatment option while minimising unnecessary side effects.
  - ♦ Therapeutic targeting of ART1 offers the potential to overcome resistance to immunotherapy – improving and widening the benefits of these drugs for lung cancer patients.
  - ♦ Further work is now needed to investigate the mechanisms by which ART1 disrupts anti-tumour immune responses and whether ART1 inhibition could provide a more general strategy for overcoming immune resistance in other cancers.
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## Industry collaboration at the ICR

The ICR has more than 100 current industrial partners and is consistently one of the top-ranked UK higher education institutions (HEIs) in industry collaboration.

We were the top-rated HEI in biological sciences, and second overall for research quality, in the influential REF 2021 assessment by the UK government. We have discovered 21 clinical drug candidates since 2005 and progressed 13 into clinical trials.



## Contact

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