CCLG: The Children & Young People's Cancer Association research:

# Harnessing the immune system to treat Ewing sarcoma in the lungs

**Project title:** Exploring γδT cells for the treatment of Ewing sarcoma in the lungs

**Project stage:** In progress (started March 2025, ending March 2027)

**Funded by:** Funded by Bone Cancer Research Trust, the Ewing's Sarcoma Research Trust, Great Ormond Street Hospital Charity, CCLG and CCLG Special Named Funds; #PearlPower, the Kieran Maxwell Legacy, Rosie Rocks the World, and the David Vernon Fund

**Led by:** Dr Jonathan Fisher, University College London Great Ormond Street Institute of Child Health

## About the project

When bone tumours such as Ewing sarcoma and osteosarcoma spread to the lungs (known as metastatic cancer), they are much harder to treat. This remains a major challenge despite intensive chemotherapy and radiotherapy, both of which cause major side effects. Furthermore, cancer cells can become resistant to these harsh treatments, leaving even fewer options.

Immunotherapy, using the power of the immune system to attack the cancer, is emerging as a strategy to address this challenge. Some types of immunotherapy involve collecting immune cells from patients and genetically engineering them so that they are able to recognise and kill cancer cells. The immune cells are then returned to the patient. Whilst effective, this process is both costly and time-consuming.

An exciting alternative is an 'off the shelf' version of immunotherapy, which uses immune cells of healthy donors. However, using standard donor cells risks 'graft versus host disease', where the donated immune cells recognise the patient's body as 'foreign' and mount an attack against it.

Researchers at the UCL Great Ormond Street Institute of Child Health, led by Dr Jonathan Fisher, have expertise in a type of immune cell called 'gamma-delta T cells' (γδT). These cells do not cause graft vs host disease and therefore represent a safe and exciting alternative. The team have already demonstrated that genetically engineered γδT cells can effectively kill cancer cells in laboratory models of Ewing sarcoma when combined with cancer-targeting proteins (antibodies). They have also developed γδT cells that are engineered to secrete antibodies capable of treating laboratory models of osteosarcoma.

To optimise treatment in primary bone cancers, the γδT cells can be combined with drugs which direct them towards bone (called 'bone sensitising agents'). However, in metastatic Ewing sarcoma, relapses occur outside the bone, most commonly in the lungs. This project will investigate the use of sensitising agents that will enable targeting of the γδT cells to the lungs rather than to bones. Dr Fisher and team will also set out to understand how the effectiveness of this potential new treatment approach may be influenced by other cells normally present in the lungs.

Metastatic Ewing sarcoma is a major challenge and affects both survival and quality of life for patients. This research aims to address this problem, taking steps towards a more targeted, more effective treatment.

## Progress

So far, the findings suggest that a new type of immune therapy could be an effective way to target tumour cells. The researchers have tested commonly used sensitising drugs that can make tumour cells easier for immune cells to attack. While these drugs worked well in simple lab conditions, they found that bone samples can trap the drugs. This means that less of the drug is available to act elsewhere in the body, such as in the lungs. To explore this further, the team have developed new models that mimic how tumours grow in bone and in the lung, including more realistic 3D mini tumours.

## What's next?

The next step is to test the γδT cell therapy and sensitising drugs in more realistic models that better mimic how Ewing sarcoma behaves in the body, particularly in the lungs where the disease often spreads. This will help the team understand whether alternative sensitising drugs that bind less strongly to bone could make the treatment more effective against tumours outside the bone.

#PearlPower

The Children & Young People's Cancer Association

Century House, 24 De Montfort Street, Leicester, LE1 7GB

**0333 050 7654** | **info@cclg.org.uk** | **www.cclg.org.uk**

**@cclgUK**

CCLG and The Children & Young People's Cancer Association are operating names of The Children's Cancer and Leukaemia Group, registered charity in England and Wales (1182637) and Scotland (SC049948).

CCLG: The Children & Young People's Cancer Association research:

# Harnessing the immune system to treat Ewing sarcoma in the lungs

**Project title:** Exploring γδT cells for the treatment of Ewing sarcoma in the lungs

**Project stage:** In progress (started March 2025, ending March 2027)

**Funded by:** Funded by Bone Cancer Research Trust, the Ewing's Sarcoma Research Trust, Great Ormond Street Hospital Charity, CCLG and CCLG Special Named Funds; #PearlPower, the Kieran Maxwell Legacy, Rosie Rocks the World, and the David Vernon Fund

**Led by:** Dr Jonathan Fisher, University College London Great Ormond Street Institute of Child Health

## About the project

When bone tumours such as Ewing sarcoma and osteosarcoma spread to the lungs (known as metastatic cancer), they are much harder to treat. This remains a major challenge despite intensive chemotherapy and radiotherapy, both of which cause major side effects. Furthermore, cancer cells can become resistant to these harsh treatments, leaving even fewer options.

Immunotherapy, using the power of the immune system to attack the cancer, is emerging as a strategy to address this challenge. Some types of immunotherapy involve collecting immune cells from patients and genetically engineering them so that they are able to recognise and kill cancer cells. The immune cells are then returned to the patient. Whilst effective, this process is both costly and time-consuming.

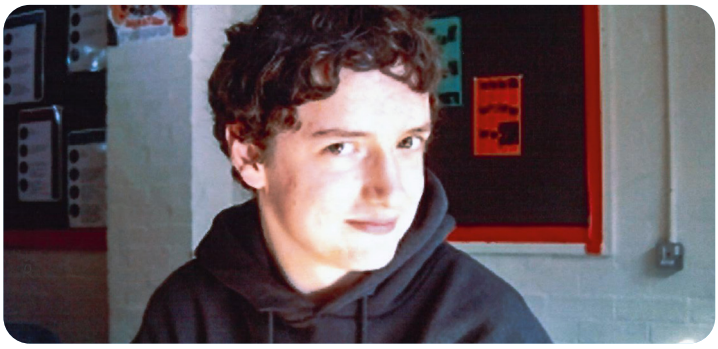
An exciting alternative is an 'off the shelf' version of immunotherapy, which uses immune cells of healthy donors. However, using standard donor cells risks 'graft versus host disease', where the donated immune cells recognise the patient's body as 'foreign' and mount an attack against it.

Researchers at the UCL Great Ormond Street Institute of Child Health, led by Dr Jonathan Fisher, have expertise in a type of immune cell called 'gamma-delta T cells' (γδT). These cells do not cause graft vs host disease and therefore represent a safe and exciting alternative. The team have already demonstrated that genetically engineered γδT cells can effectively kill cancer cells in laboratory models of Ewing sarcoma when combined with cancer-targeting proteins (antibodies). They have also developed γδT cells that are engineered to secrete antibodies capable of treating laboratory models of osteosarcoma.

To optimise treatment in primary bone cancers, the γδT cells can be combined with drugs which direct them towards bone (called 'bone sensitising agents'). However, in metastatic Ewing sarcoma, relapses occur outside the bone, most commonly in the lungs. This project will investigate the use of sensitising agents that will enable targeting of the γδT cells to the lungs rather than to bones. Dr Fisher and team will also set out to understand how the effectiveness of this potential new treatment approach may be influenced by other cells normally present in the lungs.

Metastatic Ewing sarcoma is a major challenge and affects both survival and quality of life for patients. This research aims to address this problem, taking steps towards a more targeted, more effective treatment.

# #PearlPower



The Children & Young People's Cancer Association

Century House, 24 De Montfort Street, Leicester, LE1 7GB

**0333 050 7654** | **info@cclg.org.uk** | **www.cclg.org.uk**

**@cclgUK**

CCLG and The Children & Young People's Cancer Association are operating names of The Children's Cancer and Leukaemia Group, registered charity in England and Wales (1182637) and Scotland (SC049948).