LIfT BioSciences
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INNATELY CURING CANCER

# Transferring innate immunity to destroy cancers

**LIfT BioSciences' unique cell therapy against all solid tumors moves to clinical trials.**

A decisive factor in whether mutating cells develop into a tumor is the effectiveness of the immune system in detecting and destroying cancer cells. Currently, checkpoint inhibitors and adaptive immune therapies only work in a small percentage of cancer patients[1], but now studies are showing the key role of the innate immune system in both directing the rest of the immune system[2] and directly destroying all types of cancer[3]—including currently untreatable solid tumors.

In 1999, during a cancer study in mice, Zheng Cui at Wake Forest University discovered a mouse that despite injections with cancer cells did not develop tumors. These cancer-resistant mice produced a special type of neutrophil. Importantly, a single injection of the cancer-fighting neutrophils was sufficient to induce long-lasting immunity to cancer in normal mice[4].

After losing his mother to pancreatic cancer and having spent 15 years bringing novel biopharma assets to market, Alex Blyth, LIfT BioSciences' cofounder and CEO, approached Cui to develop LIfT into a reproducible Advanced Therapeutic Medicinal Product (ATMP) using stem cells. In October 2017, LIfT BioSciences successfully demonstrated the selective and exceptional cancer-killing ability of Neutrophil-only Leukocyte Infusion Therapy (N-LIfT) against pancreatic and cervical cancers, using neutrophils produced ex vivo from stem cells. The European Medicines Agency granted N-LIfT first-in-class ATMP classification. Now, following impressive preclinical results, LIfT BioSciences is preparing its first clinical trial in humans later this year.

"When we started to explore why some animals don't get cancer, we found that it often comes down to the effectiveness of their inherited innate immune system, particularly of their neutrophils, to quash mutating cells and prevent tumors developing," said Blyth.

Neutrophils are the most abundant type of white blood cell in mammals and mount a first-line of defense against infection. Often referred to as the eyes of the immune system, the cells recognize not only invading microorganisms, but also tumor cells. However, there are huge discrepancies in the ability of neutrophils to kill cancer cells, with some peoples being up to 20 times better at eliminating cancer cells than others. "N-LIfT transfers that superior innate immunity to patients who need it," said Blyth.

## Characterizing cancer-killing neutrophils

Neutrophils are typically classed as being of the N1 or N2 type, N1 being antitumour and T cell-recruiting, and N2 being protumour and non-T cell-recruiting. Typically, patients with cancer have a higher proportion of N2-type cells[5], whereas N-LIfT consists of N1a neutrophils, which are a subtype of N1-type neutrophils that have exceptionally high cancer-killing activity. N1a neutrophils are strongly attracted to cancer cells and show superior cancer cell binding and killing activity over normal N1 neutrophils. N1a cells also show better selectivity (**Fig. 1**).

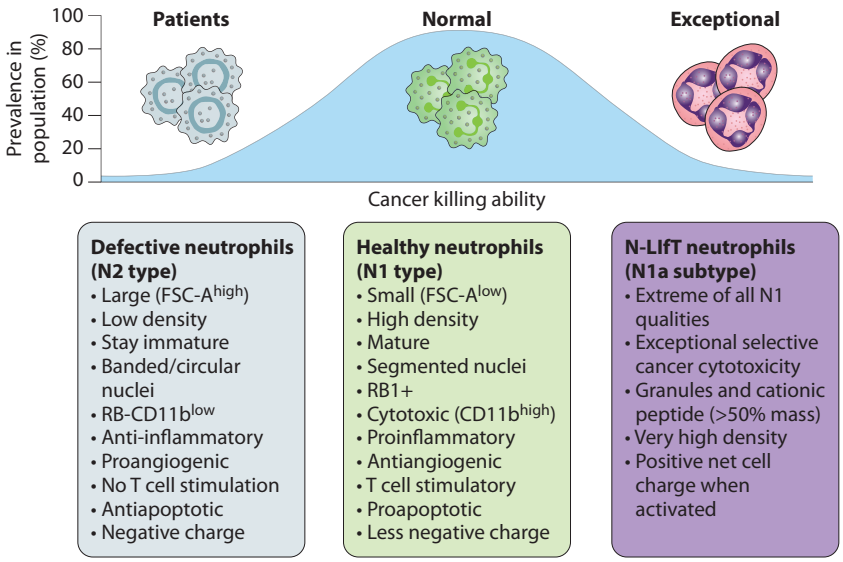


**Fig. 1 | Distribution of different types of neutrophils in the general population.** FSC-A, forward scatter A; RB1, retinoblastoma protein 1.

LIfT BioSciences has been collecting blood samples from select donors using a proprietary assay to determine the effects of their neutrophils on cancerous and healthy cell lines. Participants with N1a neutrophils, a new subtype of neutrophil discovered by LIfT BioSciences with protected and patented (pending) characteristics, are invited back to donate hematopoietic stem cells (HSCs). With the donor's consent, the cells are banked, expanded and differentiated to produce N-LIfT.

N-LIfT is now being mass produced in bioreactors in a closed good manufacturing practice (GMP) system to prepare for use in clinical trials. The cost of goods is expected to be substantially lower than recent personalized cell therapies owing to the economies of scale benefits of N-LIfT being an allogeneic 'off-the-shelf' product therapy.

## From bank to clinic

By the end of this year, LIfT BioSciences expects to have tested 300 donors for N1a cells. Thus far, of the 90 donors tested, six have been found to have N1a cells. HSCs from these donors have been expanded and differentiated to mass produce cells for N-LIfT. The next step is to conduct a proof-of-concept clinical trial that is planned to start in Q1 2020.

In a previous safety trial, in which low doses of granulocytes (not specifically N1a neutrophils) from young donors were given to terminally ill cancer patients, tumors shrank, with up to 80% tumor necrosis being observed[6]. "These findings are very encouraging. We expect N1a cells to be even more effective and even safer," said Blyth.

N-LIfT is being developed to demonstrate sustained remission in all solid tumors irrespective of strain or mutation. While N-LIfT is initially being tested as a monotherapy, there is an opportunity to use N-LIfT to improve the performance of existing therapies, such as checkpoint inhibitors, chimeric antigen receptor-T cells and monoclonal antibodies, owing to its ability to direct the adaptive immune system, even in solid tumors. LIfT BioSciences is now completing a second round of financing to fund the trials and manufacturing scale-up.

LIfT BioSciences is interested in institutional investors wanting to join its investment syndicate and in potential codevelopment and license partners.


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