

## Short Communication

# Adoptive Cell Therapy: The Syrian Community Knowledge

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## Abstract

Adoptive Cell Therapy (ACT) is a type of immunotherapy in which immune cells are implanted in patients to help them cure diseases, such as cancer. It is a new technique that has proven its effectiveness in treating different types of cancer, especially melanoma, breast cancer, and colon cancer. It has many factors that distinguish it from other cancer treatments, such as its selectivity towards cancer cells without harming normal body cells, therefore causing fewer side effects.

The aim of this study is to evaluate the knowledge of Syrian medical students on this new technique. The study is based on a questionnaire which was distributed to 822 participants, including students and graduates from medical schools, and people who show interest in the medical field or are informed about it. The questions address participants' knowledge of ACT, the possibility of applying it in Syria, and the obstacles, if any, facing its applicability. It was evident from the results that the participants were more familiar with chemotherapy and trusted it the most. As for ACT, few reported that they have heard of it, and many thought that it was not possible to be applied in Syria due to many obstacles.

**Keywords:** Questionnaire; Adoptive cell therapy; Syrian society

## Introduction

Adoptive Cell Therapy (ACT) is a type of immunotherapy in which immune cells are implanted in patients to help them cure diseases, such as cancer. Many types of immune cells can be used in Adoptive cell therapy; they can be either taken from the patient's own blood, tumor tissue, or from another donor. They are then grown in large numbers in vitro and activated using different techniques. After that they are infused back in the patient's body to help fight the cancer cells.

It has been noticed that in vitro modifying of the immune cells such as T-cells would make them more effective and selective to the antigens of the tumor cell. While the treatment is still under study, each year new discoveries are being made involving it and more obstacles are being overcome [1-3].

### ACT with genetically engineered T-cells

T-cells can recognize tumor cells with TCR (T-Cell Receptor), but this action is not effective enough to stop the tumor spreading or killing the cancer cells. Scientists found that the anti-tumor action can be improved when TCRs are genetically engineered.

Another way has been discovered to improve the effectiveness of T-cells, which is replacing the TCR with CAR (chimeric antigen receptor), then cultivating the engineered cells in large numbers and implanting them back in the patients. These new cells can immediately recognize cancer cells and attack them [4-6].

### ACT with Tumor-infiltrating lymphocytes (TILs)

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Tumor infiltrating lymphocytes are white blood cells that leach and invade the tumor. TILs express the body's natural response against a cancerous tumor, through their ability to identify cancer cells, which possess TAAs (tumor-associated antigens) and then destroy them as if they were foreign bodies.

TILs can be isolated from a fresh tumor sample and cultivated in large numbers in vivo. This technique has been very effective in the treatment of metastatic melanoma, and it can be used in many tumors and conditions such as colon cancer [7-9].

### Treating with ACT using peripheral blood mononuclear cells (PBMCs)

PBMCs have been used as a source for the cells used in ACT for 3 decades due to their ease of isolation and abundant availability. They develop from different cells, including lymphocytes (T cells, B cells, and the natural killer cells), monocytes, and the dendritic cells. They can be activated using more than one method, such as genetic modification. By activating these cells using high doses of IL-2, we get lymph Okine-Activated Killer cells (LAK), which are used to create the Cytokine-Induced Killer cells (CIKs) [10].

### ACT with Cytokine-induced killer cells (CIK's)

CIKs are considered the grandchild of LAKs, since they are easier to get and more effective, and do not show any toxicity for normal tissue cells. Studies have confirmed that these cells can be used to treat colorectal cancer safely, guaranteeing a good effect [11,12].

### ACT with natural killer cells

Natural killer cells belong to the innate immune system which form the most important defense line for humans against pathogens and mutant cells, and the significant feature for these cells, is expressing CD56 and/or CD16 but without the complex TCR-CD3.

These cells can recognize mutant or pathogen cells through specific antigens, whereas they can coordinate their job through the integration between the activating and deactivating signals of the receptors found on their surface, which lead to activating the natural killer cells.

These activating and deactivating receptors are considered responsible for these cells' ability to recognize abnormal cells and kill them; they are also responsible for the cells' inability to kill normal cells [13-15].

We aimed of this study to measure the knowledge of a sample of the Syrian society regarding the Adoptive cell therapy as a new strategy to cure cancer, and their opinion about the ability to apply this technique in Syria.

## Material and Methodology

An electronic questionnaire was designed for adoptive cell therapy and other cancer treatments in general. It was distributed to 822 participants, including students and graduates from medical schools (pharmacy, medicine, dentistry, medical engineering), and people who show interest in the medical field or are informed about it.

The questions addressed the following areas:

1. The academic specialization;
2. The different cancer treatments the participants were familiar with;
3. Their knowledge of ACT;
4. The most effective cancer treatment technique used nowadays based on the participants' point of view, or experience;
5. Their view on the possibility of applying ACT in Syria; and
6. The obstacles that might face the application of ACT in Syria.

## Results and Discussion

The study presents the following results:

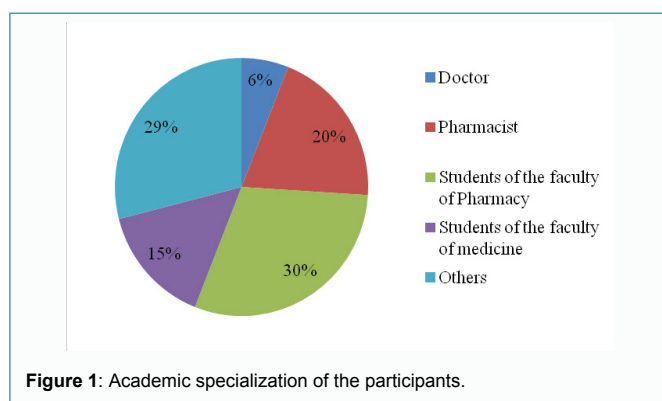
Percentage of participants according to their academic specialization (Figure 1).

The category "other" includes dentistry which amounts to 70%, medical engineering 15%, and college students who are interested in medical affairs and modern therapy techniques reached a percentage of 15%.

The participants were asked about the different cancer treatments they were familiar with and the results are represented in Figure 2.

As shown from the diagram, and as expected, the chemotherapy is the most commonly known therapy in Syria, followed directly by surgical treatment, followed by radiation therapy.

As for the question regarding the participants' knowledge of ACT, or if they heard of it before, and as shown, the majority has not heard of this treatment technique before Figure 3.



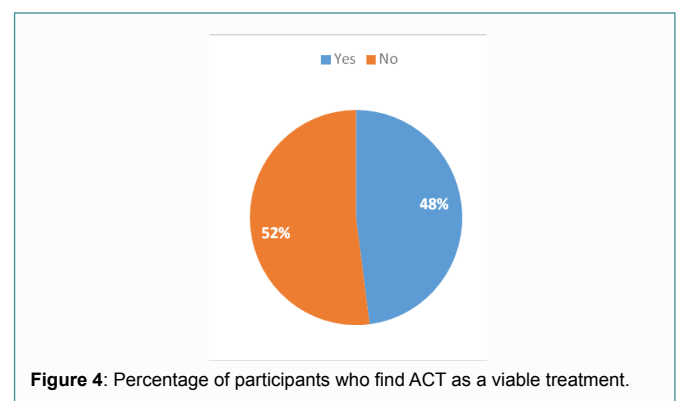
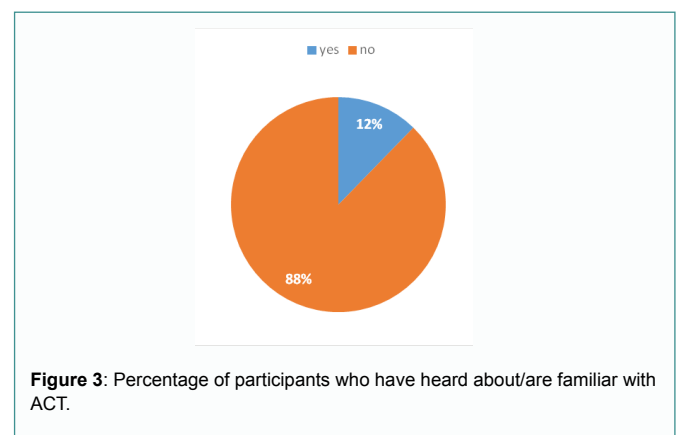
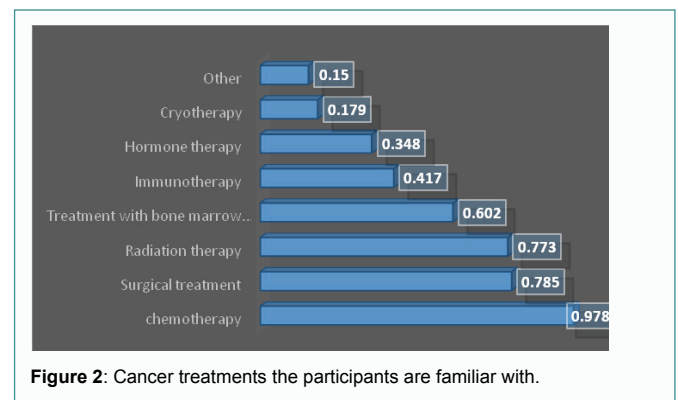
A percentage of (88%) of the answers to the previous question showed the participants' knowledge being shallow and limited to some general information about this technique. since they don't know the complete procedure; their knowledge was limited to the immunological techniques being used for cancer treatment.

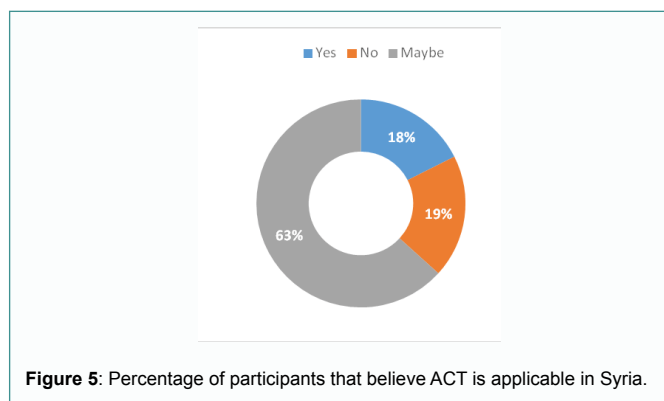
It was also noticed that chemotherapy took first place according to the participants based on trust and effectiveness, followed by surgical treatment, then radiation therapy, and finally immunotherapy.

As for the question regarding ACT being a significant technique and a new hope for cancer treatment, the results are shown in Figure 4.

The participants' views regarding the possibility of applying ACT in Syria are presented in Figure 5.

Regarding the obstacles that may face the possibility of applying ACT in Syria, the biggest and most important obstacle was the high material cost of this technique and the lack of experts and equipment in the country due to the circumstances of the current crisis. They





also confirmed that the lack of scientific research had a great effect on this issue.

## Conclusion

Adoptive cell therapy is a new promising strategy to reactivate the immune system to fight cancer cells. Third world countries lack the new techniques to make a research on humans, so we aimed of this questionnaire to measure the knowledge of Syrian society, especially health practitioners and medical students, about adoptive cell therapy to treat different types of cancer.

## References

- Cohen JE, Merims S, Frank S, Engelstein R, Peretz T, Lotem M. Adoptive cell therapy: past, present and future. *Immunotherapy*. 2017;9(2):183-96.
- Pages F, Galon J, Dieu-Nosjean MC, Tartour E, Sautes-Fridman C, Fridman WH. Immune infiltration in human tumors: a prognostic factor that should not be ignored. *Oncogene*. 2009;29(8):1093-102.
- Fefer A, Einstein AB, Cheever MA. Adoptive chemo-immunotherapy of cancer in animals: a review of results, principles, and problems. *Ann N Y Acad Sci*. 1976;277(1):492-504.
- Yang JC, Rosenberg SA. Adoptive T-cell therapy for cancer. *Advances in Immunology*. 2016;130:279-94.
- Wrzesinski C, Paulos CM, Kaiser A, Muranski P, Palmer DC, Gattinon L, et al. Increased intensity lymphodepletion enhances tumor treatment efficacy of adoptively transferred tumor-specific T cells. *J Immunother*. 2010;33(1):1-7.
- Rosenberg SA, Yang JC, Sherry RM, Hughes MS, Phan GQ, Citrin DE, et al. Durable complete responses in heavily pretreated patients with metastatic melanoma using T-cell transfer immunotherapy. *Clin Cancer Res*. 2011;17(13):4550-7.
- Cole DJ, Taubenberger JK, Pockaj BA, Yannelli JR, Carter C, Carrasquillo J, et al. Histopathological analysis of metastatic melanoma deposits in patients receiving adoptive immunotherapy with tumor infiltrating lymphocytes. *Cancer Immunol Immunother*. 1994;38(5):299-303.
- Shen X, Zhou J, Hathcock KS, Robbins P, Powell DJ Jr, Rosenberg SA, et al. Persistence of tumor infiltrating lymphocytes in adoptive immunotherapy correlates with telomere length. *J Immunother*. 2007;30(1):123-9.
- Radvanyi LG, Bernatchez C, Zhang M, Fox PS, Miller P, Chacon J, et al. Specific lymphocyte subsets predict response to adoptive cell therapy using expanded autologous tumor-infiltrating lymphocytes in metastatic melanoma patients. *Clin Cancer Res*. 2012;18(24):6758-70.
- Fan J, Shang D, Han B, Song J, Chen H, Yang JM. Adoptive cell transfer: Is it a promising immunotherapy for colorectal cancer? *Theranostics*. 2018;8(20):5784-800.
- Schlimper C, Hombach AA, Abken H, Schmidt-Wolf IG. Improved activation toward primary colorectal cancer cells by antigen-specific targeting autologous cytokine-induced killer cells. *Clin Dev Immunol*. 2012;2012:238924.
- Zoll B, Lefterova P, Csipai M, Finke S, Trojanek B, Ebert O, et al. Generation of cytokine-induced killer cells using exogenous interleukin-2,-7 or-12. *Cancer Immunol Immunother*. 1998;47:221-6.
- Veluchamy JP, Spanholtz J, Tordoir M, Thijssen VL, Heideman DA, Verheul HM, et al. Combination of NK cells and cetuximab to enhance anti-tumor responses in RAS mutant metastatic colorectal cancer. *PLoS One*. 2016;11(6):e0157830.
- Edsparr K, Basse PH, Goldfarb RH, Albertsson P. Matrix metalloproteinases in cytotoxic lymphocytes impact on tumour infiltration and immunomodulation. *Cancer Microenviron*. 2011;4:351-60.
- Song X, Hong SH, Kwon WT, Bailey LM, Basse P, Bartlett DL, et al. Secretory TRAIL-armed natural killer cell-based therapy: in vitro and in vivo colorectal peritoneal carcinomatosis xenograft. *Mol Cancer Ther*. 2016;15(7):1591-601.