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Expression profile of innate immune genes in peripheral blood mononuclear cells as early detection of breast cancer

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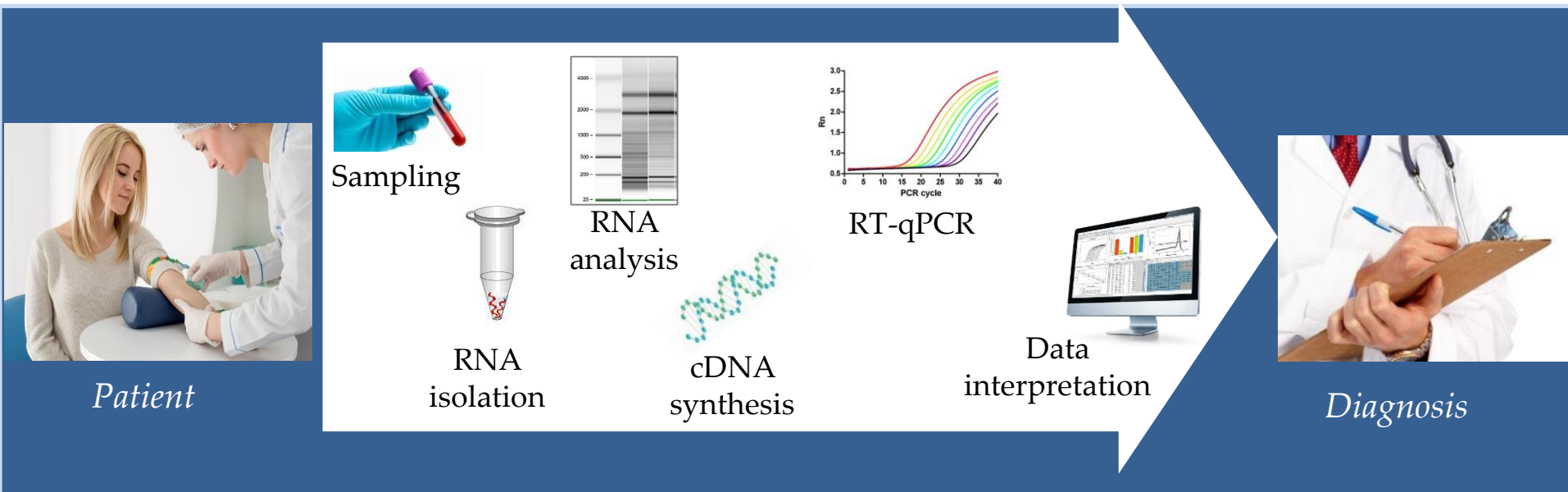
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Title of the Presentation

Our data demonstrate that the expression profile of innate immune genes in PBCs can be used for early detection of breast cancer and evaluation of efficiency treatment of this disease.



Schematic representation of the diagnostic procedure for early detection of breast cancer



Abstract:

Early detection of breast cancer plays a key role in successful treatment and patient survival. Using peripheral blood cells (PBCs) for gene expression analysis is valuable to evaluate disease-associated and drug-response related genes. In this study, we aimed to explore the innate immune gene expression profile of PBCs in patients with breast cancer.

Whole blood samples were collected from 30 breast cancer patients and 42 healthy volunteers. The gene expression of PBCs was determined by RT-qPCR. A healthy sample was created using the total RNA of healthy volunteers. We investigated the expression of receptors and its ligands, transcription factors, cytokines, chemokines, interferon-stimulated and pro-oxidation genes related to the innate immune system in breast cancer and healthy samples. Deregulated expression of a few genes was found out in the blood of breast cancer patients compared to the healthy sample.

We have identified the genes in whole blood that classifies breast cancer patients and healthy women with good accuracy. These results suggested that the expression of innate immune genes in PBCs can be used for early detection of breast cancer and evaluation of efficiency treatment of this disease.

Keywords: breast cancer; peripheral blood cells; innate immune gene expression profile



Introduction

Cancer of the breast is the most common cancer among women worldwide with an estimated 1,300,000 new cases and 465,000 deaths annually.

To reduce breast cancer mortality, early detection and appropriate treatment play a key role.

Mammographic screening is the main modalities for breast cancer detection today. However, rapid growing of tumors, dense breast tissue or menopausal hormone therapy can reduce efficiency breast cancer detection by mammography. So precise early-stage diagnosis of breast cancer is required.



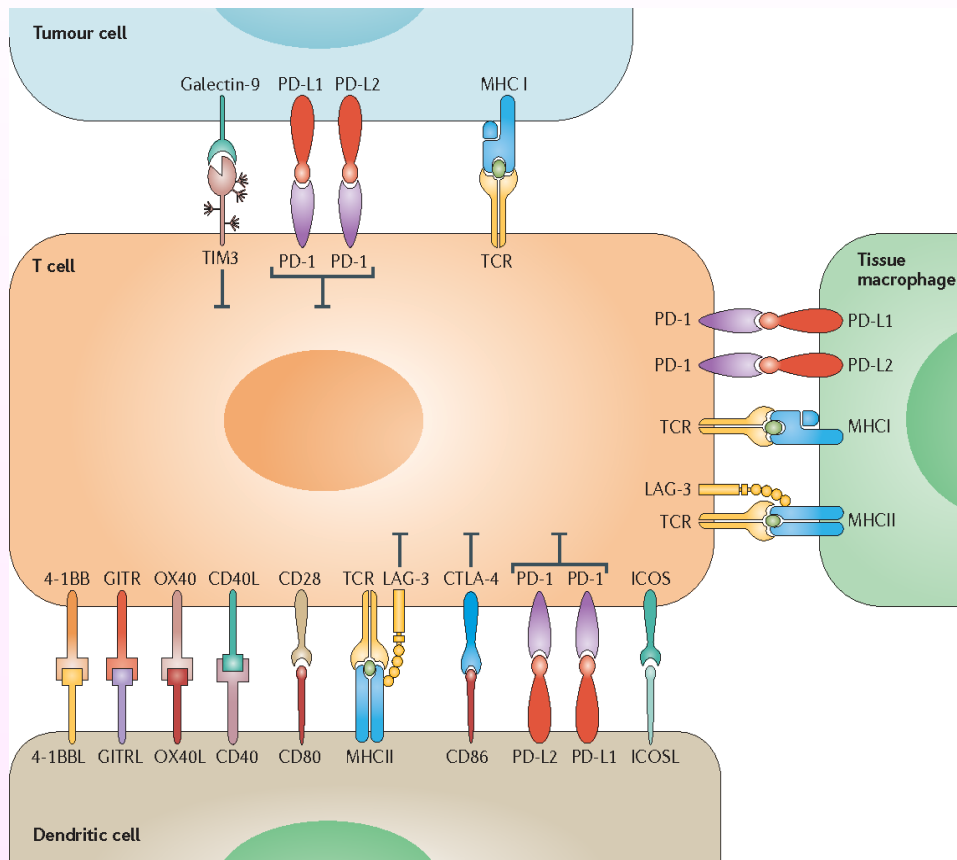
Breast cancer



Ligand–receptor interactions between tumour cells and immune cells in the tumour microenvironment

In the interaction between cancer cells and immune cells, the presence of cancer cells causes immune cells to undergo various phenotypic and functional changes and the affected immune cells kill cancer cells or promote proliferation and metastasis of cancer cells.

Thus the analysis of peripheral immune cells might be appropriate to evaluate host immune reaction against cancer cells in addition to analyzing tumor-infiltrated immune cells.



Mizuki Nishino et al. *Nature Reviews Clinical Oncology*. 2017



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Blood samples are easily available, minimally invasive and can be collected at low cost making them an attractive alternative modality for diagnostic purposes.

The rationale for using blood as a clinical sample is that breast cancer triggers a response in circulating blood cells, leading to a change genes expression in the whole blood.

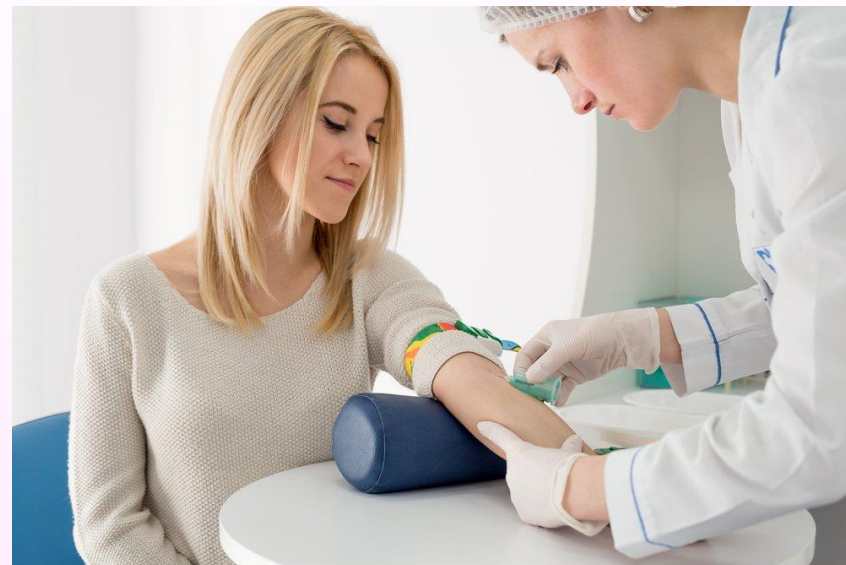
The current research was **aimed** at **studying** the innate immune gene expression profile of peripheral blood cells (PBCs) in patients with breast cancer.



Results and discussion

The innate immune gene expression profile was studied in whole blood of breast cancer patients and healthy volunteers.

Whole blood samples of breast cancer patients were collected by department of breast tumors and its reconstructive surgery, National Cancer Institute. Kyiv, Ukraine. Samples of whole blood of healthy volunteers were collected by clinical hospital "Theophany" of the State Administration Ukraine. Kyiv, Ukraine.



The gene expression of PBCs was determined by RT-qPCR. Samples were normalised to *TBP* as a control.



Results and discussion

The current research we investigated the expression of innate immune genes such as *OAS1*, *OAS2*, *OAS3*, *RNASEL*, *ABCE1*, *EIF2AK2*, *MX1*, *TNF*, *IFN α* , *IFN γ* , *IFN κ* , *IFNA2*, *IFNB1*, *IFNG*, *CXCL10*, *CXCL9*, *IL12A*, *CXCL8*, *IL1B*, *IL10*, *IL18*, *IL22*, *IL22R1*, *IL10R2*, *IL21*, *IL6*, *CCL5*, *CCL3*, *CCL*, *CCR5*, *CD80*, *CD86*, *CD40*, *CD14*, *NOS2*, *ARG2*, *XDH*, *CALB1*, *PLA2G4A*, *PTGS2* (*COX2*), *S100A1*, *LBP*, *HLA-C*, *MICB*, *HLA-B*, *HLA-DQB1*, *HLA-DQA1*, *HLA-A80*, *HLA-F*, *HLA-E*, *PD1*, *PDI1*, *CTLA4*, *CD4*, *CD8*, *CD3*, *CD137*, *CD137L*, *CD44*, *CD223*, *NF-KB1*, *NF-KBREL*, *NF-KBIA*, *STAT1*, *STAT2*, *STAT3*, *STAT4*, *STAT5*, *STAT6*, *TLR3*, *TLR7*, *MMP7* and *FN1*.

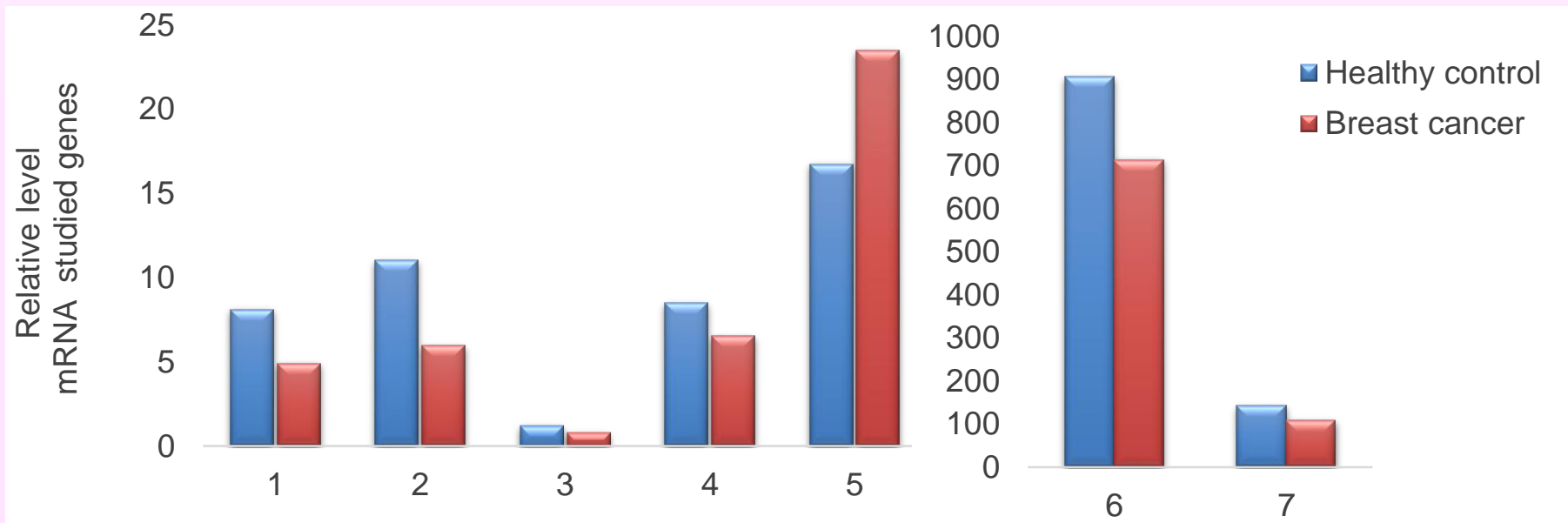
In this presentation, we demonstrate a few genes, whose expression changed in the blood of patients with breast cancer.



Results and discussion

Expression genes of receptor-ligand pairs of the immune system in PBCs of breast cancer patients

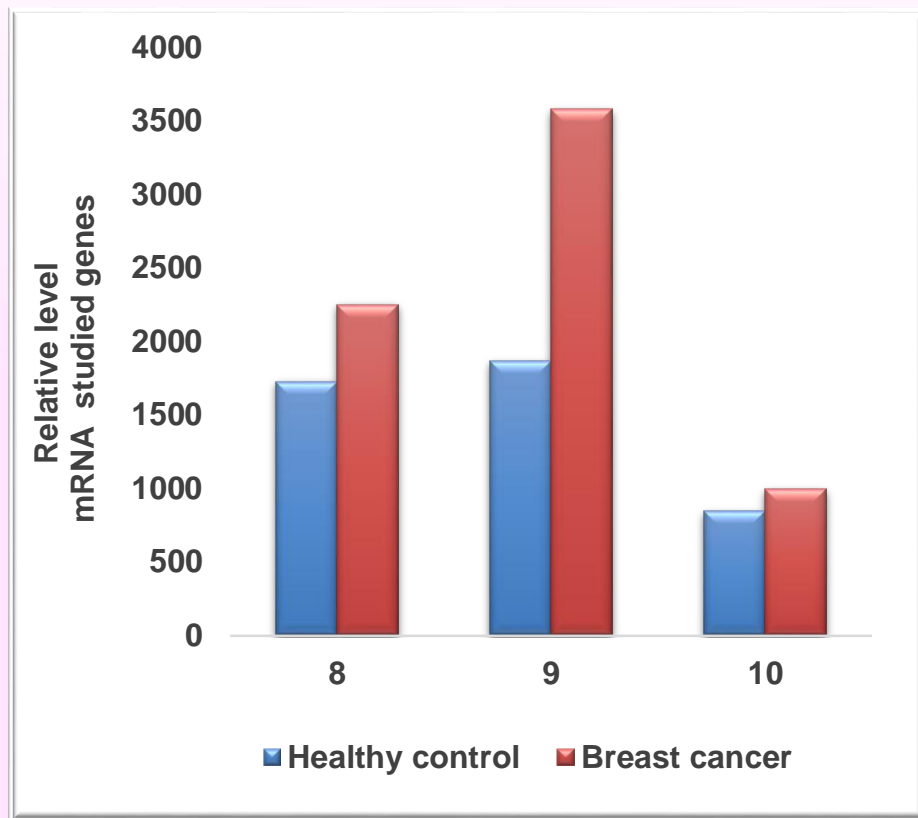
Investigating of expression immune system receptor-ligand genes, we found out that in PBCs of breast cancer patients the mRNA level of some gene decreased and others – increased compared to the healthy control.



The mRNA level some genes of receptor-ligand pairs of the immune system in PBCs



Expression genes of transcription factors in PBCs of breast cancer patients



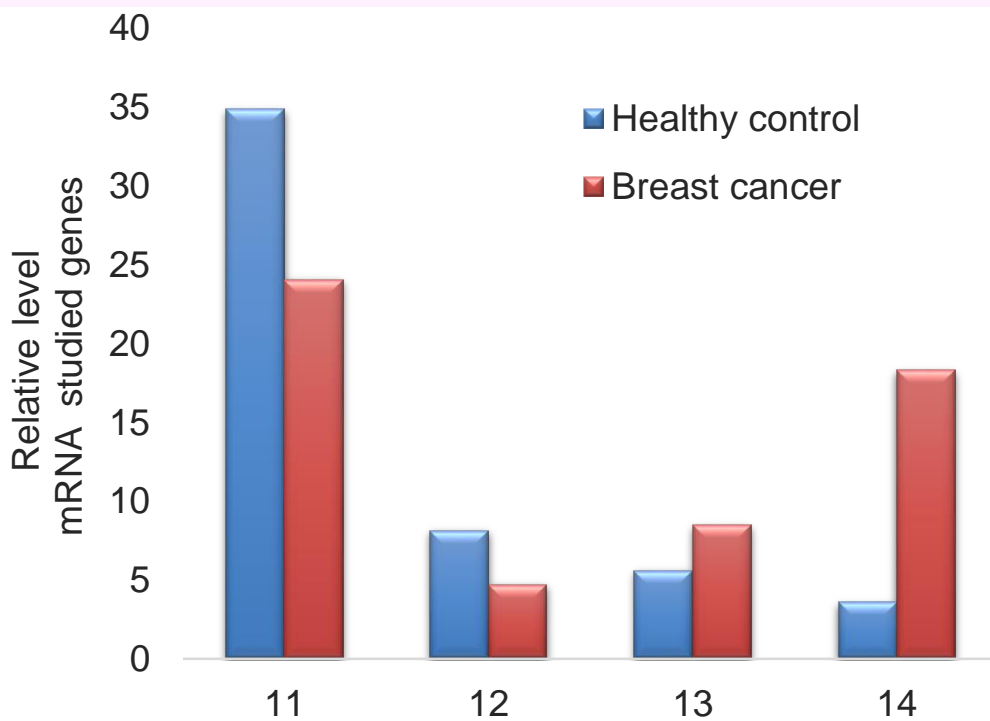
The mRNA level some genes of transcription factors in PBCs

Using RT-qPCR, it was detected the mRNA levels of the transcription factors genes increased in PBCs of breast cancer patients in comparing the healthy sample.

These data indicate increasing expression of transcription factors in PBCs of breast cancer patients.



Expression cytokines, chemokines, interferon-stimulated genes in PBCs of breast cancer patients



The mRNA level some cytokines, chemokines, interferon-stimulated genes in PBCs

The mRNA levels of cytokines, chemokines, interferon-stimulated genes were shown to up-regulated and down-regulated in the blood of breast cancer patients vs healthy control.

These data indicate that the expression of cytokines, chemokines, interferon-stimulated genes is deregulated in PBCs of breast cancer patients.



Conclusions

- Expression of the innate immune genes is deregulated in the peripheral blood cells of breast cancer patients;
- The some innate immune genes in whole blood classify breast cancer patients and healthy women with good accuracy;
- Expression profile of innate immune genes in PBCs can be used for early detection of breast cancer and evaluation of efficiency treatment of this disease.



Acknowledgments

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