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ELEVENTH ANNUAL MEETING

CXCL12 Chemokine and Relationship with Multiple Myeloma

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INTRODUCTION

Approximately 50 chemokines have been identified in humans (1). Chemokines are protein molecules with a molecular weight of 8-12 kD and multiple domains. Chemokine proteins have important roles in inflammation and immunity (2). Chemokines are small, structurally related proteins which play a significant role in leukocyte trafficking by producing chemotactic activity in cells expressing corresponding chemokine receptors (3).

AIM

Studies have shown that cytokines are effective in the pathogenesis and treatment processes of Multiple Myeloma (MM).
CXCR4 is a pleiotropic chemokine receptor that acts through its ligand CXCL12 to regulate various physiological processes.
CXCR4-CXCL12 interaction contributes to different vital biological processes by activating various extracellular and intracellular signaling pathways.
The aim of this study was to assess the potential role of CXCL12 on the pathogenesis of MM by bioinformatics tool.
CXCL12 is a heparin-binding chemokine that regulates lymphopoiesis, enhances the survival of myeloid progenitor cells, regulates the patterning and cell number of neural progenitors, and promotes angiogenesis.

METHOD

GeneCard

(https://www.genecards.org/)

STRING

(https://string-db.org/)

miRDB

(https://mirdb.org/)

GeneMANIA

(https://genemania.org/)

GWAS

(https://www.ebi.ac.uk/gwas/)

KEGG PATHWAY

(https://www.genome.jp/kegg/pathway.html)

RESULTS

STRING identified 32 genes interaction with CXCL12, including 8 additional CXCL genes in the vicinity of CXCL12 (Figure 1).

GeneMANIA showed 77.64% of CXCL12-related physical interactions (Figure 2).

Predicted to be targeted by 223 miRNAs in miRDB.

As a result of examining the disease associations of SNPs from each miRNA gene region in GWAS databases,

- It was determined that P<7E-40 for B lymphoblastic leukemia/lymphoma,
- CXCL12 roles at Leukocyte chemotaxis (FDR=3.33e-08),
- Leukocyte migration (FDR=3.91e-08),
- Lymphocyte chemotaxis (FDR=0.00050),
- It is involved in MM disease using the chemokine signaling pathway (FDR=5.93e-08).

It has been shown in multiple tissues and cells. CXCL12 is expressed in multiple sites, including the thymus, kidney, heart, spleen, liver, lung, brain, and bone marrow (Figure 3, Table 1).
GeneCard showed chromosomal and cellular localisation (Figure 4) .GeneCard, Stromal cell-derived factor 1 is a chemokine coded by the CXCL12 gene and this gene on chromosome 10 in human (Figure 5).

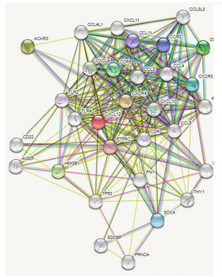


Figure 1: STRING Database gene interactions

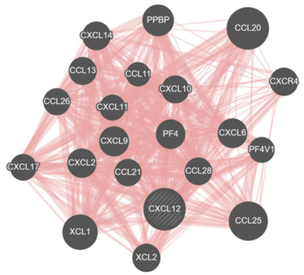


Figure 2: GENEMANIA Database gene interactions

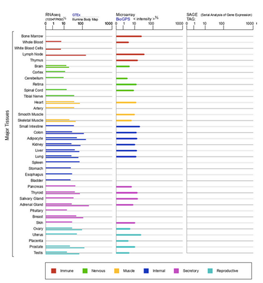
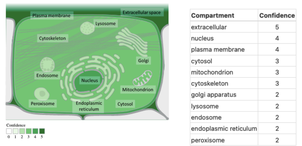


Figure 3: Expression range of CXCL12

TZM-bl cell, FDR=0.0055
Cytotoxic T-lymphocyte, FDR=0.0170
Helper T-lymphocyte, FDR=0.0184
Mononuclear cell, FDR=0.0170
Leukocyte, FDR=0.0184
Lymphoid tissue, FDR=0.0184
Blood, FDR=0.0239
Hematopoietic system, FDR=0.0060

Table 1: Locations CXCL12 is most highly expressed



Compartment	Confidence
extracellular	5
nucleus	4
plasma membrane	4
cytosol	3
mitochondrion	3
cytoskeleton	3
golgi apparatus	2
lysosome	2
endosome	2
endoplasmic reticulum	2
peroxisome	2

Figure 4: Cellular localisation of CXCL12

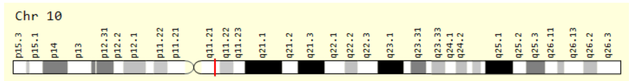


Figure 5: Chromosomal localisation of CXCL12

CONCLUSIONS

We found strong evidence for miRNA-mediated CXCL12 expression, the variants near miRNA's showed stronger genetic associations with lymphoblastic leukemia/ lymphoma and MM.

We conclude that the role of CXCL12 is stronger in autoimmunity, inflammation and MM.

This study demonstrates the feasibility of preliminary dry laboratory projects before starting wet laboratory experiments.
It is thought that CXCL12 may play a strong role in MM.

In this sense, it can also be a referral for treatment.

To understand the mechanism of CXCL12 in MM disease, experimental studies with large cohorts should be carried out with the help of bioinformatics databases.

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