

# **Evaluation of CD304 (Neuropilin-1) as a Novel Marker for Detection of Minimal Residual Disease in Childhood B-Acute Lymphoblastic Leukemia**

## **Thesis**

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# **تقييم CD304 (Neuropilin-1) كعلامة جديدة لاكتشاف المرض المتبقي الأصغر في سرطان الدم الحاد - ب في الأطفال**

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٢٠١٥

***To My parents, Mahmoud & Hoda.***

***To my beloved, caring, supporting and  
understanding husband, Osama.***

***To my son, Yousof.***

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## LIST OF ABBREVIATIONS

|                     |                                                                           |
|---------------------|---------------------------------------------------------------------------|
| <b>-ve</b> .....    | Negative                                                                  |
| <b>+ve</b> .....    | Positive                                                                  |
| <b>Ab</b> .....     | Antibody                                                                  |
| <b>ABL</b> .....    | Abelson murine leukemia viral<br>oncogene homolog 1                       |
| <b>AF4</b> .....    | Asymmetric flow field flow<br>fractionation                               |
| <b>AFF1</b> .....   | AF4/FMR2 Family member 1                                                  |
| <b>AL</b> .....     | Acute leukemia                                                            |
| <b>ALL</b> .....    | Acute lymphoblastic leukemia                                              |
| <b>ALT</b> .....    | Alanine aminotransferase                                                  |
| <b>AML1</b> .....   | Acute myeloid leukemia protein 1<br>(Runt related transcription factor 1) |
| <b>BACs</b> .....   | Bacterial artificial chromosome                                           |
| <b>BAL</b> .....    | Biphenotypic leukemias                                                    |
| <b>BCL-xl</b> ..... | B-cell lymphoma extra large (BCL2-<br>like isoform 1)                     |
| <b>BCR</b> .....    | Break point cluster region protein                                        |
| <b>BDCA4</b> .....  | Blood dendritic cell antigen 4                                            |
| <b>BIM</b> .....    | BCL2 interacting mediator of cell death                                   |
| <b>BM</b> .....     | Bone marrow                                                               |
| <b>BUN</b> .....    | Blood urea antigen                                                        |
| <b>CAE</b> .....    | Chloracetate esterase                                                     |
| <b>CALLA</b> .....  | Common acute lymphoblastic<br>leukemia-associated antigen                 |

|                   |       |                                                         |
|-------------------|-------|---------------------------------------------------------|
| <b>CBC</b>        | ..... | Complete blood count                                    |
| <b>CBFA2</b>      | ..... | core binding factor subunit alfa 2                      |
| <b>CD</b>         | ..... | Cluster of differentiation                              |
| <b>CDK</b>        | ..... | Cyclin dependant kinase                                 |
| <b>c-DNA</b>      | ..... | Complementary deoxy ribose nucleic acid                 |
| <b>CGH</b>        | ..... | Comprehensive genomic hybdization                       |
| <b>CLL</b>        | ..... | Chronic lymphoid leukemia                               |
| <b>CLL/SL</b>     | ..... | Chronic lymphocytic leukemia/small lymphocytic lymphoma |
| <b>CML</b>        | ..... | Chronic myelogenous leukemia                            |
| <b>c-myc</b>      | ..... | Cellular myelocytomatosis viral oncogene homolog        |
| <b>CNS</b>        | ..... | Central nervous system                                  |
| <b>CR</b>         | ..... | Complete response                                       |
| <b>CSF</b>        | ..... | Cerebrospinal fluid                                     |
| <b>Cy or c</b>    | ..... | cytoplasmic                                             |
| <b>DAPI</b>       | ..... | 4',6-diamidino-2-phenylindole                           |
| <b>DIC</b>        | ..... | Disseminated intravascular coagulation                  |
| <b>DLBCL</b>      | ..... | Diffuse large B cell lymphoma                           |
| <b>DNA</b>        | ..... | Deoxy ribose nucleic acid                               |
| <b>DW</b>         | ..... | Distilled water                                         |
| <b>E2A (TCF3)</b> | ..... | Transcription factor 3                                  |
| <b>EBV</b>        | ..... | Epstein-Barr virus                                      |
| <b>ECs</b>        | ..... | Endothelial cells                                       |
| <b>EDTA</b>       | ..... | Ethylene diamine tetra-acetic                           |



|                     |                                                                          |
|---------------------|--------------------------------------------------------------------------|
| <b>EGIL</b> .....   | European Group for the<br>Immunological Characterization of<br>Leukemias |
| <b>ENL</b> .....    | Eleven nineteen leukemia (MLL)                                           |
| <b>ETP</b> .....    | Early T-cell precursor                                                   |
| <b>F</b> .....      | Female                                                                   |
| <b>FAB</b> .....    | French-American-British                                                  |
| <b>Fc</b> .....     | Fragment crystalliable                                                   |
| <b>FCM</b> .....    | Flow cytometry                                                           |
| <b>FISH</b> .....   | Fluorescence in situ hybridization                                       |
| <b>FITC</b> .....   | Fluorescein isothiocyanate                                               |
| <b>FLT3</b> .....   | Fms-like tyrosine kinase 3                                               |
| <b>GAP</b> .....    | GTPase activating protein                                                |
| <b>G-CSF</b> .....  | Granulocyte colony-stimulating factor                                    |
| <b>GIT</b> .....    | Gastrointestinal tract                                                   |
| <b>GTPase</b> ..... | Guanosine triphosphatase                                                 |
| <b>GUT</b> .....    | Genitourinary tract                                                      |
| <b>Hb</b> .....     | Hemoglobin                                                               |
| <b>HCL</b> .....    | Hydrochloric acid                                                        |
| <b>HLA-DR</b> ..... | Human leukocyte antigen-DR                                               |
| <b>HLF</b> .....    | Hepatic leukemia factor                                                  |
| <b>HS</b> .....     | Highly significant                                                       |
| <b>HSCT</b> .....   | Hematopoietic stem cell transplantation                                  |
| <b>HTLV</b> .....   | Human T-cell leukemia/lymphoma<br>virus                                  |
| <b>HTRX</b> .....   | Human thioredoxin                                                        |
| <b>Ig</b> .....     | Immunoglobulin                                                           |

|                      |                                                      |
|----------------------|------------------------------------------------------|
| <b>IHC</b> .....     | Immunohistochemistry                                 |
| <b>IPT</b> .....     | Immunophenotype,<br>immunophenotyping                |
| <b>ISS</b> .....     | International Staging System                         |
| <b>ITP</b> .....     | Immune (idiopathic) thrombocytopenic                 |
| <b>IV</b> .....      | Intravenous                                          |
| <b>JAK2</b> .....    | Janus kinase 2                                       |
| <b>kb</b> .....      | Kilo base                                            |
| <b>KCL</b> .....     | Potassium chloride                                   |
| <b>kd, kDa</b> ..... | Kilo dalton                                          |
| <b>KDR</b> .....     | Kinase insert domain containing<br>receptor          |
| <b>LAP</b> .....     | Leukemia associated phenotype                        |
| <b>LDH</b> .....     | Lactate dehydrogenase                                |
| <b>Lin</b> .....     | Lineage specific antigen                             |
| <b>LN</b> .....      | Lymph nodes                                          |
| <b>LSI</b> .....     | Locus specific identifier                            |
| <b>M</b> .....       | Male                                                 |
| <b>MALT</b> .....    | Mucosa associated lymphoid tissue                    |
| <b>MAM</b> .....     | Meprin A5 and receptor tyrosine<br>phosphatase $\mu$ |
| <b>M-bcr</b> .....   | Major break cluster region                           |
| <b>m-bcr</b> .....   | Minor break cluster region                           |
| <b>MCA</b> .....     | Monoclonal antibody                                  |
| <b>MDM2</b> .....    | Mouse doubles minute 2 homolog                       |
| <b>MFI</b> .....     | Mean fluorescent intensity                           |

|                       |                                                                |
|-----------------------|----------------------------------------------------------------|
| <b>M-FISH</b> .....   | Multicolor fluorescence in situ<br>hybridization               |
| <b>MLL</b> .....      | Myeloid lymphoid leukemia, mixed<br>lineage leukemia           |
| <b>MN1</b> .....      | Meningioma 1                                                   |
| <b>MPO</b> .....      | Myeloperoxidase                                                |
| <b>MRD</b> .....      | Minimal residual disease                                       |
| <b>mRNA</b> .....     | Messenger ribonucleic acid                                     |
| <b>NaOH</b> .....     | Sodium bicarbonate                                             |
| <b>NIP</b> .....      | Neuropilin interacting protein-1                               |
| <b>NK</b> .....       | Natural killer                                                 |
| <b>No, n</b> .....    | Number                                                         |
| <b>NOS</b> .....      | Not otherwise specified                                        |
| <b>NP-40</b> .....    | Nonyl phenoxypolyethoxyethanol                                 |
| <b>NRP, Npn</b> ..... | Neuropilin                                                     |
| <b>NS</b> .....       | Non-significant                                                |
| <b>NSE</b> .....      | Non specific esterase                                          |
| <b>P53</b> .....      | Cellular tumor antigen, phosphor-<br>protein, tumor suppressor |
| <b>PAS</b> .....      | Periodic acid Schiff                                           |
| <b>Pax-5</b> .....    | Paired box protein-5                                           |
| <b>PB</b> .....       | Peripheral blood                                               |
| <b>PBS</b> .....      | Phosphate buffered saline                                      |
| <b>PBX1</b> .....     | Pre B cell leukemia homebox 1                                  |
| <b>PC</b> .....       | Plasma cell                                                    |
| <b>PC5</b> .....      | Phycoerythrin cyanine 5.1                                      |
| <b>PDCs</b> .....     | Plasmacytoid dendritic cells                                   |

|                       |                                                                           |
|-----------------------|---------------------------------------------------------------------------|
| <b>PDGF</b> .....     | Platelet derived growth factor                                            |
| <b>PDZ</b> .....      | PSD-94/D1g/ZO-1                                                           |
| <b>PE</b> .....       | Phycoerythrin                                                             |
| <b>PGF</b> .....      | Placental growth factor                                                   |
| <b>Ph</b> .....       | Philadilphia                                                              |
| <b>PLT</b> .....      | Platelet                                                                  |
| <b>PMTs</b> .....     | Photo multiplier tubes                                                    |
| <b>PO</b> .....       | Per-oss                                                                   |
| <b>PSI</b> .....      | Plexins, semaphorins and integrins                                        |
| <b>RAS</b> .....      | Rat sarcoma                                                               |
| <b>RBCs</b> .....     | Red blood cells                                                           |
| <b>RPMI</b> .....     | Roswell Park Memorial Institute<br>medium                                 |
| <b>RQ-PCR</b> .....   | Real time quantitative reverse<br>transcriptase polymerase chain reaction |
| <b>RT-PCR</b> .....   | Reverse transcriptase-polymerase chain<br>reaction                        |
| <b>RUNX</b> .....     | Runt related transcription factor 1                                       |
| <b>S</b> .....        | Significant                                                               |
| <b>SBB</b> .....      | Sudan black B                                                             |
| <b>SCLC</b> .....     | Small cell lung cancer                                                    |
| <b>SD</b> .....       | Standard deviation                                                        |
| <b>SEMA</b> .....     | Semaphorin                                                                |
| <b>SGOT</b> .....     | Serum glutamic pyruvic transaminase                                       |
| <b>Sig</b> .....      | Significance                                                              |
| <b>sIg/smIg</b> ..... | Surface immunoglobulin                                                    |

|                            |                                       |
|----------------------------|---------------------------------------|
| <b>SKY</b> .....           | Spectral karyotyping                  |
| <b>SSC</b> .....           | Saline sodium citrate                 |
| <b>t</b> .....             | Student's t test                      |
| <b>TBX1</b> .....          | T-box transcription factor 1          |
| <b>TCF3</b> .....          | Transcription factor 3                |
| <b>TCR</b> .....           | T-cell receptor                       |
| <b>TdT</b> .....           | Terminal deoxynucleotidyl transferase |
| <b>TEL (ETV6)</b> .....    | ETs variant 6                         |
| <b>TLC</b> .....           | Total leucocytic count                |
| <b>TM</b> .....            | Transmembrane                         |
| <b>USA</b> .....           | United States of America              |
| <b>VDJ</b> .....           | Variable Diversity Joining regions    |
| <b>VEGF</b> .....          | Vascular endothelial growth factor    |
| <b>VPF</b> .....           | Vascular permeability factor          |
| <b>WBCs</b> .....          | White blood cells                     |
| <b>WHO</b> .....           | World Health Organization             |
| <b>X<sup>2</sup></b> ..... | Chi-square                            |
| <b>YACs</b> .....          | Yeast artificial chromosome           |
| <b>Z</b> .....             | Mann-Whitney U test                   |

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