Serum Peptidome-Based Indicators Looking For Low Residual Monitoring.

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Abstract

The blood proteome's low-molecular-weight (LMW) region, which is made up of both intact small proteins and large protein fragments, is a gold mine of diagnostic data waiting to be mined by nanotechnology. The term "serum peptidome" refers to serum protein fragments and peptides, especially those of LMW, whose molecular weights are less than 20 kDa. Serum peptide profiling using mass spectrometry has become popular in recent years as a tool for studying markers in solid tumours. According to preliminary research, a group of serum peptides can be used to diagnose diseases and forecast their progression. ProteinChip has been phased out for sample preparation and enrichment in recent years in favour of magnetic beads with high separation capacities.

Keywords: Peptidome, Monitoring, Nanotechnology, Protein.

Introduction

Magnetic beads have been used extensively in studies of the serum peptidome in solid tumours because they are high-throughput, easy to use, and quick. Prior to now, our team developed a Quick classifier (QC) diagnostic model by ClinProt system that could distinguish adult AML patients from healthy controls with high sensitivity and specificity. The ubiquitin-like modifier activating enzyme fibrinogen alpha chain precursor and PF4 were recognised as the three peptides. The clinical outcome and relative intensities of the three peptides were associated with remission in adult AML patients. A Supervised Neural Network Algorithm (SNN) diagnostic model was developed using the ClinProt system to distinguish between newly diagnosed (ND) multiple myeloma and high-risk cancers (HCs) [1].

Weak cation exchange beads (MB-WCX) and matrix assisted laser desorption ionisation time of flight mass spectrometry (MALDI-TOF-MS) were used in our study to compare peptidomics methods in order to analyse the serum peptide profiles of adult ALL patients in the ND group, CR group, refractory & relapsed (RR) group, and HC group. We postulated that serum peptidomics using ClinProt could identify peptides that were differently expressed among several adult ALL subgroups. In serum and bone marrow cells from ALL various groups and the HC group, peptide expression varies. Additionally, variations in peptide expression are linked to both the treatment response to ALL and the timing of ALL relapse. These findings imply that the differentially produced peptides would be well-suited for relapse prediction, MRD monitoring, and adult patient therapy response evaluation ALL in clinical practice [2].

Our research demonstrated a correlation between the relative strengths of the five peptides and the reaction of ALL. Western blot and ELISA were used to validate the results. The platelet and WBC counts between sick and disease-free blood samples differ significantly. According to ELISA data, neither WBC nor PLT numbers in ANY of the groups, nor in the HC group, were correlated with the contents of the five peptides. The relative intensities of the five peptides in our investigation did not significantly change between B- and T-lineage ALL, indicating that the peptides were pan-leukemic biomarkers. However, B- and T-lineage ALL differ significantly in their immunophenotypic, genetic, and molecular markers. These findings imply that the peptides may serve as potential indicators for determining therapy efficacy and tracking MRD in adult patients [3].

A series of genetic and epigenetic events play a role in the pathogenesis, development, and response to treatments for ALL. These genetic/epigenetic changes that occur as the disease progresses may be reflected in the variable changes in peptide levels in patients' serums. And it is still unclear how these proteins and peptides might function in ALL evolutions. Fibrinogen is a dimer that circulates in plasma and is made up of three pairs of inequal polypeptide chains known as the alpha, beta, and gamma chains [4]. Numerous studies have shown that fibrinogen is overexpressed in a variety of malignant tumours and may serve as a standalone prognostic factor for patients with malignancies like pancreatic cancer, renal cell carcinoma, endometrial carcinoma, cervical cancer, oesophageal squamous cell carcinoma, and others. Fibrinogen was thought to be an acute phase reactant protein that rose in tumour growth and was linked to a continuing inflammatory

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response to the tumour. According to certain research, tumour cells may aid in the process of coagulation by interacting with endothelial cells and platelets, releasing biologically active chemicals that activate platelets, and then increasing the levels of fibrinogen in cancer blood [5].

Conclusion

As a result, the ClinProt system was used to build an ALL QC model that had a high sensitivity and specificity for differentiating between ALL patients and healthy controls. Relapse time point and ALL treatment response were linked with the relative concentrations of the peptides in the QC model. Western blot and ELISA were used to validate these results. We hypothesise that these peptides, including connective tissue active peptide III, platelet factor 4, glutathione S-transferase P1, fibrinogen alpha chain, isoform 1 of fibrinogen alpha chain precursor, and fibrinogen alpha chain precursor, could be used as potential markers for relapse prediction, treatment response evaluation, and minimal residual disease monitoring in adult ALL.

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