Screening for Interacting Proteins with Peptide Biomarker of Blood-Brain Barrier Alteration under Inflammatory Conditions

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Abstract
Neurodegenerative diseases are characterized by increased permeability of the blood-brain barrier (BBB) due to alterations in cellular and structural components of the neurovascular unit, particularly in association with neuroinflammation. A previous screening study of peptide ligands to identify molecular alterations of the BBB in neuroinflammation by phage-display, revealed that phage clone 88 presented specific binding affinity to endothelial cells under inflammatory conditions in vivo and in vitro. Here, we aimed to identify the possible target receptor of the peptide ligand 88 expressed under inflammatory conditions. A cross-link test between phage-peptide-88 with IL-1β-stimulated human hCMEC cells, followed by mass spectrometry analysis, was used to identify the target of peptide-88. We modeled the epitope-receptor molecular interaction between peptide-88 and its target by using docking simulations. Three proteins were selected as potential target candidates and tested in enzyme-linked immunosorbent assays with peptide-88: fibronectin, laminin subunit α5 and laminin subunit β-1. Among them, only laminin subunit β-1 presented measurable interaction with peptide-88. Peptide-88 showed specific interaction with laminin subunit β-1, highlighting its importance as a potential biomarker of the laminin changes that may occur at the BBB endothelial cells under pathological inflammation conditions.

Author keywords
blood–brain barrier
endothelium
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peptide biomarker