

Proteomics-based Analysis of Blood-Brain Barrier Transport System

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【Outline of survey】

The purpose of this project is elucidating the physiological function of the blood-brain barrier by developing new analytical methodologies using high-sensitive quantitative and qualitative mass spectrometer. In general, membrane proteins have difficulties to be analyzed because they contain many hydrophobic amino acids. To overcome the difficulties, we are going to develop new method measuring expression amount of transporters using LC-MS/MS. Using this method, we will complete quantitative transporter map of the blood-brain barrier by determining expression amount of transporter proteins at each brain side membrane or blood side membrane. We are also developing ultra-sensitive nano-mass spectrometry using nano-LC-MS/MS to make possible to analyze small brain sample for the pathophysiological blood-brain barrier research.

【Expected results】

The present bottleneck of the blood-brain barrier research is clarifying the membrane localization and identifying substrates of transporters. Developing new analytical methodology using mass spectrometry will enable to overcome this bottleneck fundamentally within short-period. Using this method, it is possible to clarify the membrane localization quantitatively and identify substrate from non-radio-labeled compounds. Therefore, we are going to lead blood-brain barrier proteomics using newly developed methodology using high-sensitive mass spectrometry.

【References by the principal researcher】

- T. Terasaki, S. Ohtsuki: Brain-to-blood transporters for endogenous substrates and xenobiotics at the blood-brain barrier: Overview of biology and methodology, *NeuroRx*, **2** : 63-72 (2005)
- T. Terasaki, S. Ohtsuki, S. Hori, H. Takanaga, E. Nakashima, K. Hosoya. New approaches to in vitro models of blood-brain barrier drug transport. *Drug Discov Today* **8**:9 44-954 (2003)

【Term of project】 FY2006 - 2010

【Budget allocation】 9,200,000 yen

【Homepage address】

<http://www.pharm.tohoku.ac.jp/~soutatsu/dds/index.htm>