Proteomic analysis of pathogenic alteration (Sho, 証) diagnosed by Kampo medicine and establishment of tailor-made treatment

Institute of Natural Medicine, University of Toyama, and The 21st Century COE Program

Ikuo SAIKI, Director & Professor
Pathogenic recognition in Kampo medicine (漢方医学), is based on the diagnosis of individual pathogenic alteration, so called “Sho (証)”, consisting of symptom and constitution (responder/non-responder) of patients with different disease states.
Kampo medical doctors have specialized knowledge and experiences for “Sho 証” diagnosis, and then determine appropriate Kampo formulations. However, it is difficult for western medical doctors to perform “Sho” diagnosis and to determine Kampo formulations.

If holistic patterns of “Sho 証”, which are associated with determination of Kampo formulations, are investigated by proteomic analysis using plasma of patients with different disease states, general medical doctors can easily understand and use Kampo medicines for patients.
Proteomic analysis of Sho of rheumatoid arthritis patients with or without oketsu (blood stagnant) according to diagnosis by Western medicine and Kampo medicine

**Diagnosis**
- **by Western medicine:** Rheumatoid arthritis (ACR core set)
- **by Kampo medicine:** Oketsu, i.e. blood stagnant syndrome (Oketsu score)

Kampo medicine: keishibukuryogan (pills)

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**Toyama Prefectural Central Hospital** 16 RA patients

- **0 weeks**
- **4 weeks**
- **12 weeks**

Keishibukuryogan 桂枝茯苓丸

- Oketsu score
- Proteomic analysis

- Respondesr/non-responder (ACR20)

- Data Mining
- “phenomic fingerprints”
Biomek 2000

SELDI-TOF/MS

陰イオン交換 陽イオン交換 金属イオン 順相 疏水性

Protein chip system
桂枝茯苓丸 Keishibukuryogan (KBG)

体力中等度もしくはそれ以上の人で、のぼせて赤ら顔のことが多く、下腹部に抵抗・圧痛を訴える場合に用いる。お血に伴う諸症状に用いる
Hierarchical cluster analysis of ProteinChip Array results for the expression profiles of plasma proteins in rheumatoid arthritis patients with or without Oketsu (瘀血)

Oketsu vs Non-Oketsu (瘀血vs 非瘀血) (266 peaks)

Clustering of plasma samples

Clustering of significant peak intensity

Oketsu (瘀血) score

20～30

30 <
Classification of rheumatoid arthritis patients with or without Oketsu (瘀血) treated with Keishi-bukuryo-gan (桂枝茯苓丸), by expression of peak A, B or C obtained from Protein Chip Array System.

<table>
<thead>
<tr>
<th>Classification of Rheumatoid Arthritis Patients</th>
<th>Oketsu/Non-oketsu Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Peak_A</td>
</tr>
<tr>
<td></td>
<td>Group = CLASS_1</td>
</tr>
<tr>
<td>Oketsu</td>
<td>Non-oketsu</td>
</tr>
</tbody>
</table>

Oketsu (瘀血) Non-oketsu (非瘀血)
Classification of rheumatoid arthritis patients with or without Oketsu (瘀血) by expression of peak A, B and C obtained from Protein Chip Array System

Oketsu-improving Kampo medicine: Keishi-bukuryo-gan

<table>
<thead>
<tr>
<th>Peak_A</th>
<th>Peak_B</th>
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Oketsu-improving Kampo medicine: Keishi-bukuryo-gan
Classification of rheumatoid arthritis patients with or without Oketsu (瘀血) treated with Keishi-bukuryo-gan (桂枝茯苓丸), by expression of peak A and B obtained from Protein Chip Array System.
I thank all the members in the projects for the promotion of collaborative works.

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Toyama New Industry Organization
富山新世紀産業機構 木我千鶴
Toyama Prefecture

Toyama Bay

Tateyama Mountain

Toyama Castle

University of Toyama (Sugitani campus)

WAKAN-YAKU Toyama-original Natural Medicine
Faculty of Medicine

University Hospital

Faculty of Pharmaceutical Science

Institute of Natural Medicine

Scientific research of traditional medicines from China and Japan, and other traditional medical treatments from all over the world in cooperation with domestic and international scientists.
In Toyama prefecture, public institutions are making efforts to improve their research and development system.

Toyama prefecture has the only prefectural pharmaceutical research institute and prefectural medicinal plants research center in Japan.

Invited Dr. Kiyoshi TAKATSU as a Director of this institute in April, 2007, who is very famous worldwide in immunology field as the first discoverer of interleukin-5.

Grow and disseminate the plants for pharmaceutical materials, establish growing techniques, educate, and expand knowledge of medical plants.
### Characteristics of the Pharmaceutical Industry in Toyama

<table>
<thead>
<tr>
<th>① Accumulation of manufacturers of various kinds of medicines</th>
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<td>- About 100 plants for developing new medicines, specialized agents, generics, self-medication products</td>
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<th>② Development of allied and support industry</th>
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<td>- Adequate industry of containers &amp; package printing</td>
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<th>③ Leading mfg. techniques &amp; GMP promotion</th>
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<td>- Latest mfg. facilities &amp; high technology</td>
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### Toward building a Major Production Center for Pharmaceutical Industry

- **Investment in plant & equipment** (recent 5 yrs.)
  - **600 million $**
Thank you for your attention!