漢方診断学分野　　Division of Kampo Diagnostics

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◇研究目的

漢方薬は様々な疾患の治療において幅広く使用されており，慢性あるいは難治性疾患における漢方薬による治療及び進展予防効果への期待も大きい。その一方で，漢方医学は経験的であるとの批判もあり，臨床研究や基礎研究を通した科学的エビデンスの蓄積が求められている。エビデンスの蓄積には，漢方医学的概念や証（適応病態）の客観化し，漢方薬の薬理効果や作用機序の解明することにより，漢方医薬学を普遍的なものとする必要である。そこで，本分野は，漢方医学的病態や漢方薬に関する臨床研究と実際の臨床を考慮した基礎研究により，新たな漢方医学を確立することを目指している。

◇研究概要

Ⅰ）漢方方剤・生薬の薬理効果の基礎的研究

1) 浮腫・慢性腎臓病・糖尿病に対する効果
2) 粘膜免疫活性効果
3) 粘膜ワクチンアジュバント効果
5) 生体内動態解析
6) 漢方方剤の去加方に起因する効果の変化
7) 生薬の品質による効果発現の変化

Ⅱ）証の科学的翻訳に関する臨床的研究

1) 漢方医学的病態の数値化
2) 自律神経系と漢方医学的病態との関連性
3) ストレス対応漢方方剤の薬理効果
4) 各種疾患に対する臨床効果

Ⅲ）漢方医薬学研修に関する研究

1) 教育効果に関する検討
2) 漢方医薬学研修プログラムの開発

◇著　書

1) 櫻井宏明，小泉桂一，済木育夫：「TNF-αは転移になぜ必要か，がん転移−臨床と研究の羅針盤−」監修：丸義朗，細胞工学　別冊 pp139-143，学研メディカル 秀潤社，2010.
2) 李英娥，趙恩珠，山邉典子，趙琦，松本欣三，横澤隆子：柿果実由来プロアントシアニジンオリゴマーによる抗老化作用．「腎とフリーラジカル－第10集」，福永 惠，槇野博史監修，腎とフリーラジカル研究会企画，116-120，東京医学社，東京，2010.

◇原著論文

1) **Park CH., Noh JS., Yamabe N., Okamoto T., Kang KS., Zhao Q., Matsumoto K., Shibahara N., and Yokozawa T.: Renoprotective effect of Kangen-karyu on the development of diabetic nephropathy in type 2 diabetic *db/db* mice. J. Trad. Med., 27: 192-203, 2010.**

Abstract: The present study was conducted to examine whether Kangen-karyu, a Chinese prescription, has an ameliorative effect on diabetes-induced alterations such as oxidative stress, apoptosis, inflammation, and/or morphological changes in the kidney of type 2 diabetic *db/db* mice. Kangen-karyu (100 or 200 mg/kg body weight/day, p.o.) was administered every day for 18 weeks to *db/db* mice, and its effect was compared with vehicle-treated *db/db* and *m/m* mice. The administration of Kangen-karyu decreased the elevated serum glucose concentration in *db/db* mice, and reduced the increased oxidative biomarkers including the generation of reactive oxygen species and lipid peroxidation in the serum and kidney. The increased serum creatinine and urea nitrogen levels, which reflect renal dysfunction, and renal structural changes, representing glomerular enlargement, in *db/db* mice were significantly lowered by Kangen-karyu administration. The *db/db* mice exhibited the up-regulation of nicotinamide adenine dinucleotide phosphate oxidase subunits, nuclear factor-kappaB, cyclooxygenase-2, and inducible nitric oxide synthase levels in the kidney; however, Kangen-karyu treatment significantly reduced those expressions. Moreover, the augmented expressions of apoptosis-related proteins, cytochrome *c* and Bax, were down-regulated by Kangen-karyu administration. Taken together, these results provide important evidence that Kangen-karyu exhibited a pleiotropic effect on several oxidative stress-related parameters and exerted a renoprotective effect on the development of diabetic nephropathy in type 2 diabetic *db/db* mice.

2) **Prangsaengtong O., Koizumi K., Senda K., Urano T., Nagata A., Sakurai H., Tohda C., and Saiki I.: Methanol extract of Polygonati Rhizoma enhances the tube formation of rat lymphatic endothelial cell. J. Trad. Med., 27: 59-65, 2010.**

Abstract: Lymphangiogenesis plays important roles in physiological and pathological conditions. The induction of new lymphatic vessel formation is important for promoting wound repair and treatment in lymphatic diseases such as lymphedema. Polygonati Rhizoma (root of *Polygonatum kingianum* Coll. et Hemsl.), a traditional Chinese herbal medicine, has been shown to exhibit a variety of pharmacological activities *in vivo* and *in vitro*, such as anti-aging, hypoglycemic, neuroprotective and neuroremodeling effects. The network formation process of neurons is similar to the vascular system. The propose of this study was to investigate the effect of Polygonati Rhizoma methanol extract on lymphangiogenesis by using conditionally immortalized lymphatic endothelial (TR-LE) cells, a newly developed cell line originating from the thoracic duct of a transgenic rat expressing the temperature-sensitive SV40 large T-antigen. The results show that non-toxic doses of Polygonati Rhizoma at concentrations of 20 μg/ml and 50 μg/ml produced a slight and significant increase in capillary-like tube formation length of TR-LE cells (increased 15.8% and 40.7% from control, respectively) ($p<0.01$) after 4 h incubation on Matrigel. In addition, 50 μg/ml Polygonati Rhizoma significantly increased adhesion ability of TR-LE cells at 30 min (increased 44% from control) ($p<0.05$) and migration at 4 h of incubation (increased 37.5% from control) ($p<0.01$). However, the expansion of TR-LE cells treated with this extract (50 μg/ml) for 24 and 48 h did not show any statistically significant effect on cell proliferation. Here, we report, for the first time, that Polygonati Rhizoma induces lymphangiogenesis *in vitro*. This finding may provide an attractive reagent for pro-lymphangiogenic therapy.

3) **Shimada K., Kawase M., Shibahara N., Nakamura Y., Saito T., and Takahashi K.: The relation between clinical effects of Tokishakuyakusan and the identity of Paeonia lactiflora materials. J. Ethnopharmacol., 132: 438-442, 2010.**

Abstract: AIM OF THE STUDY: To investigate the relation between the clinical effects and the quality of crude drugs, we focused on Tokishakuyakusan (TS), consisted of 6 crude drugs.
MATERIALS AND METHODS: We prepared two kinds of TS containing either medicinal cultivar of Paeonia lactiflora (MTS) or ornamental one (OTS). Other components were the same. First, we assessed the clinical effects of two TS formulations by cross-over study among the anemia patients. Second, we

investigated the chemical differences between them by using Inductively Coupled Plasma Mass Spectrometry (ICP-MS) and Mössbauer analysis.
RESULTS: The clinical effects of these formulations (3 g/day for 8 weeks) were tested in the cross-over study consisted of 12 women patients who were diagnosed as having anemia (Hb ≤ 11 g/dl) and consented to participate to this study. Both TS formulations were effective for anemia symptoms as shown by the improvement of several hematological parameters, whereas their comprehensive effects were distinguishable by Genetic Algorithm Partial Least Squares (GA-PLS) analysis. There were no significant differences in organic ingredients and Fe content measured by ultra performance liquid chromatography (UPLC) and ICP-MS, respectively. Interestingly, Mössbauer spectra of Fe ion were remarkably different between two formulations. Fe ion in MTS was only one form, but that in OTS was at least two forms.
CONCLUSIONS: This study suggested that clinical effects of TS formulation reflect the quality of Paeoniae Radix.

4) Suzuki S., Zhou Y., Refaat A., Takasaki I., Koizumi K., Yamaoka S., Tabuchi Y., Saiki I., and Sakurai H.: Human T cell lymphotropic virus 1 manipulates interferon regulatory signals by controlling the TAK1-IRF3 and IRF4 pathways. Biol. Chem., 285: 4441-4446, 2010.

Abstract: We previously reported that human T cell lymphotropic virus 1 (HTLV-1) Tax oncoprotein constitutively activates transforming growth factor-β-activated kinase 1 (TAK1). Here, we established Tax-positive HuT-102 cells stably transfected with a short hairpin RNA vector (HuT-shTAK1 cells) and investigated the physiological function of TAK1. Microarray analysis demonstrated that several interferon (IFN)-inducible genes, including chemokines such as CXCL10 and CCL5, were significantly down-regulated in HuT-shTAK1 cells. In contrast, Tax-mediated constitutive activation of nuclear factor-κB (NF-κB) was intact in HuT-shTAK1 cells. IFN-regulatory factor 3 (IRF3), a critical transcription factor in innate immunity to viral infection, was constitutively activated in a Tax-dependent manner. Activation of IRF3 and IRF3-dependent gene expressions was dependent on TAK1 and TANK-binding kinase 1 (TBK1). On the other hand, IRF4, another member in the IRF family of transcription factors overexpressed in a Tax-independent manner, negatively regulated TAK1-dependent IRF3 transcriptional activity. Together, HTLV-1 manipulates IFN signaling by regulating both positive and negative IRFs.

5) Suzuki S., Zhou Y., Refaat A., Takasaki I., Koizumi K., Yamaoka S., Tabuchi Y., Saiki I., and Sakurai H.: HTLV-1 manipulates interferon regulatory signals by controlling TAK1-IRF3 and IRF4. J. Biol. Chem., 285: 4441-4446, 2010.

Abstract: We previously reported that human T cell lymphotropic virus 1 (HTLV-1) Tax oncoprotein constitutively activates transforming growth factor-β-activated kinase 1 (TAK1). Here, we established Tax-positive HuT-102 cells stably transfected with a short hairpin RNA vector (HuT-shTAK1 cells) and investigated the physiological function of TAK1. Microarray analysis demonstrated that several interferon (IFN)-inducible genes, including chemokines such as CXCL10 and CCL5, were significantly down-regulated in HuT-shTAK1 cells. In contrast, Tax-mediated constitutive activation of nuclear factor-κB (NF-κB) was intact in HuT-shTAK1 cells. IFN-regulatory factor 3 (IRF3), a critical transcription factor in innate immunity to viral infection, was constitutively activated in a Tax-dependent manner. Activation of IRF3 and IRF3-dependent gene expressions was dependent on TAK1 and TANK-binding kinase 1 (TBK1). On the other hand, IRF4, another member in the IRF family of transcription factors overexpressed in a Tax-independent manner, negatively regulated TAK1-dependent IRF3 transcriptional activity. Together, HTLV-1 manipulates IFN signaling by regulating both positive and negative IRFs.

6) Lirdprapamongkol K., Sakurai H., Suzuki S., Koizumi K., Prangsaengtong O., Viriyaroj A., Ruchirawat S., Svasti J., and Saiki I.: Vanillin enhances TRAIL-induced apoptosis in cancer cells through inhibition of NF-κB activatin. In Vivo, 24: 501-506, 2010.

Abstract: BACKGROUND: Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) is a promising anticancer agent which selectively kills cancer cells with little effect on normal cells. However, TRAIL resistance is widely found in cancer cells. We have previously reported antimetatstatic and antiangiogenic effects of vanillin, a flavoring agent from vanilla. Here we have evaluated the sensitizing effect of vanillin on a TRAIL-resistant human cervical cancer cell line, HeLa.

MATERIALS AND METHODS: Cell viability after treatments was determined by the WST-1 cell counting kit. Apoptosis was demonstrated by detection of caspase-3 activation and cleavage of poly (ADP-ribose) polymerase using immunoblot analysis. Effect of treatments on TRAIL signaling pathway and nuclear factor kappaB (FN-κB) activation was studied using immunoblot analysis and luciferase reporter assay.
RESULTS: Pretreatment of HeLa cells with vanillin enhanced TRAIL-induced cell death through the apoptosis pathway. Vanillin pretreatment inhibited TRAIL-induced phosphorylation of p65 and transcriptional activity of NF-κB.
CONCLUSION: Vanillin sensitizes HeLa cells to TRAIL-induced apoptosis by inhibiting NF-κB activation.

7) **Kato S., Koizumi K., Yamada M., Inujima A., Takeno N., Nakanishi T., Sakurai H., Nakagawa S., and Saiki, I.: A phagocytotic inducer from herbal constituent, pentagalloylglucose (PGG) enhances lipoplex-mediated gene transfection in dendritic cells. Biol. Pharm. Bull., 33: 1878-1885, 2010.**

Abstract: Antigen-presenting cells are key vehicles for delivering antigens in tumor immunotherapy, and the most potent of them are dendritic cells (DCs). Recent studies have demonstrated the usefulness of DCs genetically modified by lipofection in tumor immune therapy, although sufficient gene transduction into DCs is quite difficult. Here, we show that Paeoniae radix, herbal medicine, and the constituent, 1,2,3,4,6-penta-O-galloyl-β-D-glucose (PGG), have an attractive function to enhance phagocytosis in murine dendritic cell lines, DC2.4 cells. In particular, PGG in combination with lipofectin (LPF) enhanced phagocytic activity. Furthermore, PGG enhanced lipofection efficacy in DC2.4 cells, but not in colorectal carcinoma cell lines, Colon26. In other words, PGG synergistically enhanced the effect of lipofectin-dependent phagocytosis on phagocytic cells. Hence, according to our data, PGG could be an effective aid in lipofection using dendritic cells. Furthermore, these findings provide an expectation that constituents from herbal plant enhance lipofection efficacy.

8) **Yamabe N., Kim HY., Kang KS., Zhao Q., Matsumoto K., Yokozawa T.: Effect of Chinese prescription Kangen-karyu on lipid metabolism in type 2 diabetic *db/db* mice. J. Ethnopharmacol., 129: 299-305, 2010.**

Abstract: AIM OF THE STUDY: Chinese prescription Kangen-karyu is clinically used as a treatment for cardiovascular diseases, and we have reported the beneficial effects on chemically induced hyperlipidemic animal models. The present study was investigated to evaluate the hypolipidemic effect of Kangen-karyu in type 2 diabetic db/db mice which has not been explored yet.
MATERIALS AND METHODS: Male db/db mice were divided into three groups, vehicle (control), Kangen-karyu 100, or 200 mg/kg body weight/day, and orally administered for 5 weeks every day. Age-matched non-diabetic m/m mice were used as a normal group.
RESULTS: Serum triglyceride (TG) and total cholesterol levels in db/db mice were increased compared with those of m/m mice. However, the administration of Kangen-karyu reduced hyperlipidemia in db/db mice through a decline in the serum levels of TG and total cholesterol. The hepatic TG and total cholesterol levels of db/db mice were markedly higher than those of m/m mice, but these elevated lipid levels were significantly reduced by 200 mg/kg Kangen-karyu administration. Also, oil red O staining showed that the increased lipid deposition level in the liver of db/db control mice was improved by Kangen-karyu administration. The expression of sterol regulatory element-binding protein-1 in the liver of db/db mice was significantly down-regulated by the administration of Kangen-karyu at a dose of 200 mg/kg body weight. Kangen-karyu caused a slight elevation in the expression of peroxisome proliferator-activated receptor alpha in the liver of db/db mice.
CONCLUSIONS: This study provides scientific evidence that Kangen-karyu improves hyperlipidemia and lipid deposition via the regulation of hepatic SREBP-1 expression in type 2 diabetic db/db mice.

9) **Park CH., Noh JS., Yamabe N., Kang KS., Tanaka T., Yokozawa T.: Beneficial effect of 7-*O*-galloyl-D-sedoheptulose on oxidative stress and hepatic and renal changes in type 2 diabetic *db/db* mice. Eur. J. Pharmacol., 640: 233-242, 2010.**

Abstract: The aim of the present study was to evaluate the beneficial effects of 7-O-galloyl-D-sedoheptulose (GS), isolated from Corni Fructus, on hepatic and renal lipid metabolisms

and advanced glycation endproduct formation followed by oxidative stress and inflammation using type 2 diabetic mice. GS was orally administered to db/db mice at doses of 20 and 100 mg/kg body weight per day for 8 weeks, and its effects were compared with those of the vehicle in db/db and m/m mice. The serum, hepatic, and renal biochemical factors, and protein expressions related to lipid metabolism, inflammation, advanced glycation endproducts, and their receptors, were measured. After 8 weeks of GS treatment, elevation of serum adiponectin as well as an improvement of hepatic and renal functional parameters was shown in db/db mice, and significant reductions of lipids in serum, liver, and kidney were observed according to the down-regulation of sterol regulatory element-binding protein-1. Moreover, GS inhibited oxidative stress and advanced glycation endproduct formation and their receptor expressions in the liver and kidney of db/db mice. These results suggest that GS could effectively inhibit advanced glycation endproduct formation caused by oxidative stress and/or dyslipidemia in the liver and kidney of db/db mice. Furthermore, the augmented expression of nuclear factor-kappa B p65 and its related inflammatory protein expressions were down-regulated in GS-treated groups. In conclusion, GS could have hepato- and reno-protective effects against abnormal lipid metabolism and the reactive oxygen species-related formation of advanced glycation endproducts with inflammation in type 2 diabetes.

10) **Kang KS., Yamabe N., Kim HY., Park JH., Yokozawa T.: Effects of heat-processed ginseng and its active component ginsenoside 20(S)-Rg_3 on the progression of renal damage and dysfunction in type 2 diabetic Otsuka Long-Evans Tokushima Fatty rats. Biol. Pharm. Bull., 33: 1077-1081.**

Abstract: The effects of heat-processed ginseng (HPG) and ginsenoside 20(S)-Rg(3) on the progression of renal damage in type 2 diabetic rats were investigated. Twenty-two-week-old male Otsuka Long-Evans Tokushima Fatty (OLETF) rats were divided into 4 orally administered groups: vehicle (diabetic control), HPG water extract (100 mg/kg) and 20(S)-Rg(3) (5, 10 mg/kg). Non-diabetic Long-Evans Tokushima Otsuka (LETO) rats were used as a normal group. OLETF rats showed markedly higher blood glucose, triglyceride, and total cholesterol levels than those of LETO rats. The elevated blood glucose level of OLETF rats was significantly lowered by 20(S)-Rg(3) administration. The elevated serum triglyceride and total cholesterol levels were significantly reduced by the administrations of HPG and 20(S)-Rg(3). The serum levels of thiobarbituric acid-reactive substance, an index of lipid peroxidation, were markedly increased in OLETF compared to LETO rats, but it was significantly reduced by HPG and 20(S)-Rg(3) administrations. The urinary protein level, an indicator of advanced diabetic nephropathy, of OLETF rats was 4.4 times higher than in LETO rats, but it was reduced significantly by the administrations of HPG and 20(S)-Rg(3). Creatinine clearance of OLETF rats was significantly increased after HPG and 20(S)-Rg(3) administrations. The elevation of inducible nitric oxide synthase and N(epsilon)-(carboxymethyl)lysine protein expressions in renal tissues of OLETF rats was prevented by 20(S)-Rg(3) administration. This study provides scientific evidence that 20(S)-Rg(3) prevents the progression of renal damage and dysfunction in type 2 diabetic rats via inhibiting oxidative stress and advanced glycation endproduct formation.

11) **Zhao Q., Yokozawa T., Yamabe N., Tsuneyama K., Li X., Matsumoto K.: Kangen-karyu improves memory deficit caused by aging through normalization of neuro-plasticity-related signaling system and VEGF system in the brain. J. Ethnopharmacol., 131: 377-385, 2010.**

Abstract: AIM OF THE STUDY: Kangen-karyu (KK) is a traditional Chinese prescription consisting of six different herbs. This study was conducted to investigate the anti-dementia effect of KK on aging-induced cognitive deficits and the underlying mechanism using senescence-accelerated mice prone (SAMP8).

MATERIALS AND METHODS: Twenty-week old SAMP8 (older SAMP8) were used as an animal model of aging and age-matched senescence-resistant inbred strain (SAMR1) and 8-week-old SAMP8 (young SAMP8) were as controls. Older SAMP8 received daily administration of KK (100 mg/kg, p.o.) or water vehicle for 22 days.

RESULTS: Compared to the controls, older SAMP8 exhibited cognitive deficits in the object recognition and object location tests; however, KK improved the deficits caused by aging. Moreover, the older SAMP8 treated with vehicle exhibited reduced anxiety-like behavior in the elevated plus-maze test compared to SAMR1, but KK had no effect on emotional disorder of older SAMP8. The levels of biochemical factors related to neuro-plasticity and learning and memory; i.e., phosphorylated forms of

N-methyl-D-aspartate receptor 1, Ca^{2+}/calmodulin-dependent protein kinase II, and cyclic AMP-responsive element-binding protein, and brain-derived neurotrophic factor, were significantly decreased in older SAMP8 compared to those in the control animals. KK normalized the levels of these factors. Moreover, the mRNA and protein levels of vascular endothelial growth factor (VEGF) and its receptor type 2 in the cerebral cortices of older SAMP8 were down-regulated by aging, but these levels were reversed by KK.
CONCLUSIONS: These findings suggest that normalization of neuro-plasticity-related neuronal signaling and VEGF systems in the brain may be of the mechanisms underlying the ameliorative effects of KK on the cognitive deficits in older SAMP8.

12) **Yamabe N., Noh JS., Park CH., Kang KS., Shibahara N., Tanaka T., Yokozawa T.: Evaluation of loganin, iridoid glycoside from Corni Fructus, on hepatic and renal glucolipotoxicity and inflammation in type 2 diabetic *db/db* mice. Eur. J. Pharmacol., 648: 179-187, 2010.**

Abstract: Previously, we have reported that Corni Fructus possessed hypoglycemic and hypocholesterolemic effects in streptozotocin-induced type 1 diabetic rats and diet-induced hypercholesterolemic rats. Herein, we have focused on the effect and mechanism of loganin, a major iridoid glycoside of Corni Fructus, on the type 2 diabetic db/db mice. Loganin was orally administered to db/db mice at a dose of 20 or 100 mg/kg body weight daily for 8 weeks. The biochemical factors and expressions of protein and mRNA related to lipid metabolism, inflammation, advanced glycation endproducts, and its receptor were measured. In loganin-treated db/db mice, hyperglycemia and dyslipidemia were ameliorated in both the serum and hepatic tissue; however, in the kidney, only triglyceride was reduced. The enhanced oxidative stress was alleviated by loganin through a decrease in thiobarbituric acid-reactive substances (liver and kidney) and reactive oxygen species (serum, liver, and kidney), as well as augmentation of the oxidized to reduced glutathione ratio (liver and kidney). The marked lipid-regulatory effect of loganin was exerted in the liver of type 2 diabetic mice via suppressing mRNA expressions related to lipid synthesis and adjusting the abnormal expression of peroxisome proliferator-activated receptor α and sterol regulatory-element binding protein in the nucleus. Furthermore, loganin inhibited advanced glycation endproduct formation and the expression of its receptor, and nuclear factor-κB-induced inflammation in the hepatic tissue of db/db mice. Loganin exhibits protective effects against hepatic injury and other diabetic complications associated with abnormal metabolic states and inflammation caused by oxidative stress and advanced glycation endproduct formation.

◇総　説

1) Yokozawa T., Kang KS., Park CH., Noh JS, Yamabe N., Shibahara N., Tanaka T.: Bioactive constituents of Corni Fructus: The therapeutic use of morroniside, loganin, and 7-*O*-galloyl-D-sedoheptulose as renoprotective agents in type 2 diabetes. Drug Discov Ther., 4: 223-234, 2010.
2) Kang KS., Yamabe N., Kim HY., Yokozawa T.: The changes in the constituents of American ginseng caused by heat-processing and its antioxidant activity. J Trad Med., 27: 97-108, 2010.
3) 柴原直利，条美智子：【温故知新　伝統医薬学からの挑戦】Mahalanobis-Taguchi法を用いた漢方医学的病態の数量化．生物工学会誌，88: 389-391, 2010.

◇症例報告　Case reports

1) 関矢信康，平崎能郎，植田圭吾，岡本英輝，柴原直利，寺澤捷年：七物降下湯治験．漢方の臨床，56: 2077-2084, 2009.
2) 関矢信康，岡本英輝，平崎能郎，植田圭吾，柴原直利，寺澤捷年：甘連石膏湯が奏効した体感異常の一例．漢方の臨床，57: 111-14, 2010.
3) 後藤博三，藤本誠，渡辺哲郎，引網宏彰，小尾龍右，野上達也，永田豊，柴原直利，嶋田豊：視床痛に対する漢方治療の試み．日東医誌，61: 189-197, 2010.

4) 引網宏彰，柴原直利，村井政史，永田豊，井上博喜，八木清隆，藤本誠，後藤博三，嶋田豊：リウマチ性多発筋痛症に対する漢方治療経験．日東医誌，61: 699-707, 2010.

◇学会報告　（*：特別講演，シンポジウム，ワークショップ等）

1) 柴原直利：漢方問診データの MT システムによる定量化. 品質工学会 第 21 回企業交流会，2010, 3, 12，大阪.
2) Shibahara N.: The clinical effects of Kampo medicine relate to the quality of crude drugs. 第 28 回日本薬理学会年会，2010, 3, 16-18，大阪.
3) 柴原直利，藤本孝子：糖尿病性腎症における桂枝茯苓丸の有効性．伝統医薬学シンポジウム富山．2010, 3, 19，富山.
4) 山邉典子：八味地黄丸の糖尿病性腎症への創薬研究. 伝統医薬学シンポジウム富山. 2010, 3, 19，富山.
5) 朴鑽欽，盧貞淑，山邉典子，姜奇成，田中隆，横澤 隆子：山茱萸由来成分の 2 型糖尿病に対する影響と作用機序．日本薬学会第 130 年会．2010, 3, 28-30，岡山.
6) 鄭ダミ，渡公佑，白水隆喜，小野真弓，小泉桂一，済木育夫，金ユンチュル，樋口隆一，宮本智文：天然由来新規リンパ管新生阻害剤の探索　第 1 報，日本薬学会第 130 回年会，2010, 3, 28-30，岡山.
7) 渡邊貴信，長野一也，山下琢矢，岡村賢孝，金崎聡一郎，阿部康弘，吉川友晃，吉岡靖雄，鎌田春彦，伊藤徳夫，小泉桂一，角田慎一，堤康央：プロテオームミクスによる非アルコール性脂肪性肝疾患（NAFLD/NASH）のバイオマーカー探索，日本薬学会第 130 回年会，2010, 3, 28-30，岡山.
8) 河西美保，申明淑，西村美紀，小泉桂一，済木育夫，櫻井宏明：肺がん細胞における EGFR の Ser/Thr リン酸化の制御機構の解析．第 28 回日本生化学会北陸支部大会，2010, 5, 29，福井.
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◇研究費取得状況

1) 文部科学省科学研究費，基盤研究（B）（分担：柴原直利，継続）「サステイナブル伝統薬を志向した薬用資源植物の多様性の解析」20万
2) 文部科学省科学研究費，基盤研究（C）（分担：柴原直利，新規）「漢方薬による褥瘡治療の作用機序の解明」30万
3) 文部科学省科学研究費，基盤研究（C）（代表：小泉桂一，新規）「ケモカイン機能を利用したがん細胞呼び込み型DDS製剤の開発と腹膜播種治療への応用」170万
4) 厚生労働省科学研究費，地域医療基盤開発推進研究事業（代表：柴原直利，新規）「日本・中国・韓国における生薬と治療処方の異同性に関する国際比較調査研究」156万
5) 厚生労働省科学研究費，創薬基盤推進研究推進事業（代表：小泉桂一，新規）「粘膜免疫機能を増強する漢方薬の探索とその有効成分の同定」1700万
6) 和漢薬・バイオテクノロジー研究（分担：柴原直利，継続）「中高年者疾患に有効な富山県ブランド生薬及び和漢薬方剤の開発研究」45万
7) 知的クラスター創成事業（ほくりく先導型研究開発の国際連携拠点形成）（分担：柴原直利，継続）「天然薬物の標準化に向けた評価系の確立，基源－成分－薬効リレーショナルデータベース（伝統薬統合データベースの開発）」300万

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