

(様式1)

公益社団法人日本栄養・食糧学会 研究業績

<学 会 賞>

1. 候補者

研究題目:(和)	生活習慣病予防に資するポリフェノールの食品機能学的研究		
(英)	Food Functional Studies on Preventive Effects of Polyphenols on Life-style Related Diseases		
氏 名:(和)	芦田 均		
(英)	Hitoshi Ashida		
所属機関:(和)	神戸大学大学院農学研究科・教授		
(英)	Department of Agrobioscience, Graduate School of Agricultural Science, Kobe University, Professor		
学 位:	学術博士	最終学歴:	昭和 63 年 3 月、神戸大学大学院自然科学研究科資源生物科学専攻博士課程修了
専門分野	①栄養生理学、②栄養生化学、③分子栄養学、④公衆栄養学、⑤臨床・病態栄養学、⑥食生態学、⑦調理科学、⑧食品化学・食品分析学、⑨食品機能学、⑩食品工学、⑪食品加工・流通・貯蔵学、⑫食品衛生・安全学、⑬生理学、⑭生化学、⑮分子生物学、⑯臨床医学（内科系）、⑰臨床医学（外科系） ⑱その他		
履 歴	昭和 63 年 4 月 1 日	日本学術振興会特別研究員	
	平成 2 年 4 月 1 日	同上退職、神戸大学助手(農学部)	
	平成 6 年 4 月 1 日	University of California, Davis 博士研究員 (平成 7 年 9 月 30 日迄)	
	平成 11 年 2 月 1 日	神戸大学助教授(農学部)	
	平成 16 年 4 月 1 日	神戸大学教授(農学部)	
	平成 19 年 4 月 1 日	改組により神戸大学大学院教授(農学研究科)、現在に至る	
会員番号:		入会年度:	昭和 59 年

## 2. 研究業績要旨(1,000字以内)

ポリフェノールは多様な機能を有し、生活習慣病をはじめとする様々な疾病の予防・改善に関わる機能性を発揮することが期待されている。候補者は、フラボノイドに着目し、1) 化学発がん物質の作用軽減効果と、2) 高血糖・肥満の予防・改善効果に関わる研究を実施してきた。

### 1) 化学発がん物質の作用軽減効果

フラボノイドが、アリール炭化水素受容体 (AhR) を介した薬物代謝系の酵素発現を調節することで、化学発がん物質の作用を軽減することを明らかにした。具体的には、薬物代謝系第 I 相酵素の発現に関わる AhR の形質転換を抑制する食品因子を培養細胞で探索した結果、フラボノイドのうち、フラボンとフラボノールに属する化合物が AhR のアンタゴニストとなることを見出した。この作用には抗酸化性は無関係で、化合物の平面構造と疎水性が重要であること、フラボンとフラボノールは AhR を拮抗的に阻害すること、リン酸化を抑制することで AhR の核内移行を阻害し、結果的に AhR の転写因子としての作用を抑制することを明らかにした。さらに、動物実験で、フラボノイドを多く含む食品素材は、AhR のアゴニストであるベンゾ[a]ピレンやメチルコランスレンの毒性発現を軽減することを実証した。

### 2) 高血糖・肥満の予防・改善効果

フラボノイドが、グルコース輸送担体 4 型 (GLUT4) と AMP 活性化プロテインキナーゼ (AMPK) を鍵分子として、高血糖や肥満を予防・改善する可能性を示した。具体的には、血糖値の調節に関わる GLUT4 の細胞膜移行を調節する食品因子を培養細胞で探索した結果、エピガロカテキンガレート (EGCG) や、プロシアニジン、カルコンなどを見出した。EGCG はきわめて低濃度で、インスリンとは異なる機構でシグナル伝達に関わる PI3K (phosphoinositide 3-kinase) と aPKC (atypical protein kinase C) の活性化を介して GLUT4 の細胞膜移行を促進することを明らかにした。一方で、プロシアニジンは主に AMPK 経路を活性化するとともに、動物個体ではインクレチン効果を示すことで GLUT4 の細胞膜移行を促進することを示した。また、プロシアニジンやカルコンによる AMPK の活性化は、脂肪細胞の分化抑制や肝細胞におけるエネルギー代謝の亢進と脂肪蓄積抑制に関わることも明らかにした。さらに、ポリフェノールを多く含む黒大豆種皮抽出物や発酵茶が脱共役タンパク質 1 やミトコンドリアの生合成および酸化的リン酸化を促進する転写コアクチベーターの PGC1 $\alpha$  の発現を促進することで、ベージュ細胞の形成を促す可能性を示した。

### 3. 報文等リスト

#### (1) この研究に直接関連するもの(10編以内)

1. Zhang, T., Yamashita, Y., Yasuda, M., Yamamoto, N., Ashida, H. Ashitaba (*Angelica keiskei*) extract prevent adiposity in high-fat diet-fed C57BL/6 mice. *Food and Function*, 6, 135-145, 2015.
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4. Zhang, T., Kimura, Y., Jiang, S., Harada K., Yamashita, Y., **Ashida, H.** Luteolin modulates expression of drug-metabolizing enzymes through the AhR and Nrf2 pathways in hepatic cells. *Archives Biochemistry and Biophysics*. 557, 36-46, 2014.
5. Sawada, K., Yamashita, Y., Zhang, T., Nakagawa, K., **Ashida, H.** Glabridin induces glucose uptake via the AMP-activated protein kinase pathway in muscle cells. *Molecular and Cellular Endocrinology*, 393, 99-108, 2014.
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#### (2) その他の論文(編数制限なし)

##### <原著論文>

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12. Yamashita, Y., Ueda-Wakagi, M., Sakamoto, M., Tachibana, N., Wanezaki, S., Kohono, M., **Ashida, H.**  $\beta$ -Conglycinin peptides improve glucose uptake through the AMPK signalling pathway in L6 myotubes. *Food Science and Technology Research*, 21, 727-732, 2015.
13. Hayashi, D., Ueda, S., Yamanoue, M., Saito, N., **Ashida, H.**, Shirai, Y. Epigallocatechin-3-gallate activates diacylglycerol kinase alpha via a 67 kDa laminin receptor: A possibility of galloylated catechins as functional food to prevent and/or improve diabetic renal dysfunctions. *Journal of Functional Foods*, 15, 561-569, 2015.
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16. Nagano, T., Hayashibara, K., Ueda-Wakagi, M., Yamashita, Y., **Ashida, H.** Black tea

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  19. Yasuda, M., Kawabata, K., Miyashita, M., Okumura, M., Yamamoto, N., Takahashi, M., **Ashida, H.**, Ohigashi, H. Inhibitory effects of 4-hydroxyderricin and xanthoangelol on lipopolysaccharide-induced inflammatory responses in RAW264 macrophages. *Journal of Agricultural and Food Chemistry*, 62, 462-467, 2014.
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  27. Zhang, T., Jiang, S., He, C., Kimura, Y., Yamashita, Y., **Ashida, H.** Black soybean seed coat polyphenols prevent B(a)P-induced DNA damage through modulating drug-metabolizing enzymes in HepG2 cells and ICR mice. *Mutat Res*, 752, 34-41, 2013.
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< 総説・解説・総合論文 >

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(3) 過去 5 年間の本学会での活動状況

< 学会役員、委員、支部役員 >

平成 26 年 理事就任、現在に至る

平成 26 年 学会活動強化委員会委員、現在に至る

平成 23 年 評議員(平成 18 年就任)から代議員(支部参与)に変更となり、現在に至る

< 大会・支部大会での活動状況 >



平成 28 年 第 70 回日本栄養・食糧学会・行委員(総務委員)、シンポジウム・コーディネーター兼  
オーガナイザー  
平成 27 年 第 54 回日本栄養・食糧学会近畿支部大会・会頭、特別講演座長  
同上 ACN2015, Symposium Chairperson, Oral Session Chairperson  
平成 26 年 第 68 回日本栄養・食糧学会・シンポジウム・オーガナイザー兼座長、一般講演座長  
同上 第 53 回日本栄養・食糧学会近畿支部大会・一般講演座長  
平成 25 年 第 67 回日本栄養・食糧学会シンポジウム座長、一般講演座長  
平成 24 年 第 66 回日本栄養・食糧学会・一般講演座長  
同上 第 51 回日本栄養・食糧学会近畿支部大会・一般講演座長  
平成 23 年 第 65 回日本栄養・食糧学会・一般講演座長  
同上 第 50 回日本栄養・食糧学会近畿支部大会・一般講演座長

(4) 特記事項

平成 26 年 Royal Society of Chemistry (UK) Fellow.  
平成 26 年 ネーチャー・インダストリーアワード特別賞  
平成 22 年 日本生物工学会論文賞  
平成 21 年 日本農芸化学会英文誌 (Bioscience, Biotechnology, and Biochemistry) 論文賞