

(様式1)

公益社団法人日本栄養・食糧学会 候補者研究業績

<学 会 賞>

1. 候補者

研究題目:(和)	代謝栄養異常による糖尿病合併症の基盤病態における Rho/Rho-kinase シグナルの意義		
(英)	A role of Rho/Rho-kinase signaling in the pathogenesis of diabetic complications caused by metabolic and nutritional disorder		
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所属機関:(和)	東京慈恵会医科大学内科学講座(糖尿病・代謝・内分泌内科)、主任教授		
(英)	Professor, Department of Internal Medicine, The Jikei University School of Medicine		
学 位:	医学博士	最終学歴:	東京慈恵会医科大学大学院医学研究科第三内科学博士課程 昭和 60 年 3 月修了
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 60 年 4 月東京慈恵会医科大学内科助手 平成 3 年 4 月大森赤十字病院内科部長 平成 5 年 4 月同上より復帰 平成 8 年 6 月東京慈恵会医科大学内科学講座第 3 講師 平成 8 年 6 月糖尿病・代謝・内分泌内科診療医長 平成 11 年 10 月同副部長 平成 13 年 1 月米国コロラド大学留学 平成 14 年 1 月東京慈恵会医科大学糖尿病・代謝・内分泌内科准教授 平成 22 年 4 月同上主任教授 平成 27 年 8 月東京慈恵会医科大学 内科学講座総括責任者 平成 28 年 4 月東京慈恵会医科大学医学科長、常任理事		
会員番号:		入会年度:	平成 27 年(2015 年)

2. 研究業績要旨(1,000字以内)

糖尿病治療の目的は、合併症の抑制にある。特に、糖尿病腎症(腎症)は透析導入原因疾患の第1位に至っており、その管理体制の確立が求められている。一方、腎症は心血管疾患の高いリスクなることから、全身の血管保護を視野に入れた包括的治療が不可欠であり、そのためには糖尿病の血管障害に共通する成因論的基盤の解明が必須である。申請者は早くから、かかる共通基盤を担う分子メカニズムに注目し、中でも低分子量 G 蛋白 Rho とそのエフェクター Rho-kinase(ROCK)の意義について検討を重ねてきた。2 型糖尿病のモデルである *db/db* マウスでは、腎皮質の Rho 活性が非糖尿病マウスに比較して亢進しており、あわせて ROCK の活性化が生じていることを見出した。ROCK の特異的阻害薬 fasudil を *db/db* マウスに投与すると、ROCK の抑制とともに、尿中アルブミン排泄が低減し、形態学的にも糸球体硬化やマクロファージ浸潤などの腎病変の改善を認め、腎症の発症に Rho/ROCK シグナルが関与することを明らかにした。そこで、培養メサンギウム細胞を用いて Rho/ROCK シグナルの下流を検討し、HIF-1 α 、NF- κ B などの転写因子を介して、細胞外基質増生、酸化ストレス産生ならびに炎症機転を惹起すること、足細胞では Notch シグナルによって、apoptosis を誘導することを見出した。さらに、糖尿病ラットの坐骨神経でも Rho/ROCK シグナルが亢進しており、このことがシュワン細胞間の接着を阻害し、伝導遅延をきたして神経障害に至ること、ROCK 阻害薬はこれを抑制して神経障害を改善することを明らかにし、細胞レベルでもこれを確認した。一方、糖尿病マウスの大動脈でも Rho/ROCK シグナルの過剰亢進が認められ、血管内皮障害から動脈硬化の進展に関与することを証明している。以上の成果は、Rho/ROCK シグナルが糖尿病における血管障害の共通基盤として重要な役割を演じ、包括的臓器保護のための治療標的となることを示したものであり、国際的評価をえている。また申請者は、12/15-LOX による酸化ストレスが心筋そのものの線維化をきたすこと、SGLT2 阻害薬が、基礎代謝の改善を介して糖尿病状態の是正に寄与することを明らかにするなど、糖尿病による臓器障害に関して広範な業績を残すとともに、腎症の臨床栄養学的研究も行ってきた。

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)

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(3) 過去 5 年間の本学会での活動状況

平成 27 年度から、代表理事・副会長、倫理審査委員長、学会活動強化委員長、将来構想検討委員、関東支部代議員、本学会選出日本医学会評議員

(4) 特記事項

なし