10. スタチンのアミロイドβ蛋白低下作用とそのメカニズム：培養神経細胞を用いた検討 12:58

玉岡晃[1)]、○保坂愛(ほさかあい)[1,2)]、織田彰子[1)]、冨所康志[1)]、荒木亘[2)]
筑波大学医学医療系神経内科学[1)]、国立精神・神経医療研究センター神経研究所[2)]

11. 造血幹細胞を利用した脳アミロイドーシス治療戦略の開発 13:11

芦原英司、○高田和幸(たかたかずゆき)、北村佳久
京都薬科大学病態生理学分野

12. フェノール化合物は特異的結合によってAβオリゴマー形成及びシナプス毒性を抑制する 13:24

山田正仁[1)]、○小野賢二郎(おのけんじろう)[1)]、Lei Li[2)]、高村雄策[3)]、吉池裕二[4)]、池田篤平[1)]、
西条寿夫[3)]、高島明彦[4)]、David B. Teplow[5)]、Michael G. Zagorski[2)]
金沢大学大学院脳老化・神経病態学（神経内科学）[1)]、
Department of Chemistry、Case Western Reserve University[2)]、
富山大学大学院医学薬学研究部システム情動科学[3)]、国立長寿医療研究センター研究所[4)]、
Department of Neurology、David Geffen School of Medicine at UCLA[5)]

国際シンポジウム（14：00〜16：40）

International Symposium on Intra and Extracellular Amyloid Formation Mechanism in Amyloidosis

IV.　透析アミロイドーシス　(16:50～17:42)　　座長　内木宏延

13.　透析患者の手根管症候群手術既往歴の疫学調査　16:50

西槇一[1)]、山縣邦弘[2)]、中井滋[3)]、星野純一[4)]、椿原美治[5)]
神戸大学大学院腎臓内科 腎血液浄化センター[1)]、筑波大学医学医療系腎臓内科学[2)]、
藤田保健衛生大学臨床工学科[3)]、虎ノ門病院分院内科[4)]、
大阪大学大学院医学系研究科腎疾患統合医療学寄付講座[5)]

14.　アミロイドの沈着部位・程度が透析患者の QOL に与える影響について　17:03

○星野純一、澤直樹、三瀬広記、住田圭一、平松里佳子、長谷川詠子、山内真之、
早見典子、諏訪部達也、乳原善文、高市憲明
虎の門病院腎センター

15.　C-末端 unfolded β_2-microglobulin のモデル蛋白としての$\Delta N_6\beta_2$-mの検証　17:16

安東由喜雄[1)]、○本宮善恢[2)]、城野博史[1)]、宇治義則[3)]
熊本大学大学院生命科学研究部神経内科学分野[1)]、医療法人翠悠会[2)]
富山大学付属病院検査部[3)]

16.　β2 - ミクログロブリンアミロイド線維の細胞毒性に関する検討　17:29

内木宏延、○大越忠和、長谷川一浩、小澤大作
福井大学医学部病因病態医学講座分子病理学領域

18:00～意見交換会
(11 階　朱鷺の間)

1月25日（金）

V.　FAP　(9:00～9:39)　　座長　安東由喜雄

17.　肝移植後のFAP患者における組織沈着アミロイドの病理組織学的特徴と生化学的検討　　9:00

安東由喜雄[1)]、○大嶋俊範（おおしまとしのり）[1)]、植田光晴[1)]、山下太郎[1)]、三隅洋平[1)]、田崎雅義[1)]、神力悟[2)]、大林光念[2)]、大矢雄希[3)]、阿曽沼克弘[3)]、猪股裕紀洋[3)]
熊本大学大学院生命科学研究部神経内科学分野[1)]、
熊本大学医学部附属病院アミロイドーシス診療体制構築事業[2)]、
熊本大学大学院生命科学研究部小児移植外科学分野[3)]

18.　FAP患者肝を用いたドミノ移植患者剖検例におけるアミロイド沈着様式の検討　　9:13

○山下太郎（やましたたろう）[1)]、小池春樹[2)]、大嶋俊範[1)]、田崎雅義[1)]、三隅洋平[1)]、神力 悟[3)]、植田光晴[1)]、城野博史[4)]、大林光念[2)]、祖父江元[2)]、安東由喜雄[1)]
熊本大学大学院生命科学研究部神経内科学分野[1)]、名古屋大学大学院神経内科[2)]、熊本大学医学部附属病院アミロイドーシス診療体制構築事業[3)]、熊本大学大学院生命科学研究部臨床薬物動態学分野[4)]

19.　霊長類トランスサイレチンの立体構造解析　　9:26

○水口峰之（みずぐちみねゆき）[1)]、植田光晴[2)]、安東由喜雄[3)]
富山大学大学院医学薬学研究部[1)]、熊本大学医学部附属病院中央検査部[2)]、
熊本大学大学院生命科学研究部神経内科学分野[3)]

VI.　FAP　(9:39～10:05)　　座長　池田修一

20.　FAPにおける肝移植後の末梢神経障害の進行に対する加齢の影響　　9:39

○小池春樹（こいけはるき）[1)]、大山健[1)]、橋本里奈[1)]、川頭祐一[1)]、飯島正博[1)]、亀井秀弥[2)]、木内哲也[2)]、祖父江元[1)]
名古屋大学神経内科[1)]、名古屋大学移植外科[2)]

21.　高齢発症ATTR Val30Met FAP患者の末梢神経機能に対するジフルニサルの有効性の検討　　9:52

池田修一[1)]、○関島良樹（せきじまよしき）[1)]、東城加奈[1)]、森田洋[1)]、小池春樹[2)]、祖父江元[2)]
信州大学脳神経内科 リウマチ・膠原病内科[1)]、名古屋大学医学部附属病院神経内科[2)]

VII. その他のアミロイドーシス（10:05～10:31）　座長　樋口京一

22. アミロイドーシス特有の病理像を認識するプローブの探索(7)　10:05

○工藤幸司[1)]、小熊幸恵[1)]、岡村信行[1,2)]、古川勝敏[3)]、荒井啓行[3)]、星井嘉信[4)]、宇田裕史[5)]、佐伯修[5)]、奥田恭章[6)]、中村正[7)]、坂井勇仁[8)]、和田庸子[8)]、中野正明[8)]、佐藤弘恵[9)]、小関由美[10)]、田村裕昭[11)]、神谷百合香[12)]、寺井千尋[12)]、亀田智宏[13)]、谷口義典[14)]、公文義雄[14)]、松下正人[15)]、江原重幸[16)]、楢崎雅司[17)]、岩崎由恵[18)]、川上純[19)]、吉崎和幸[20)]

東北大学病院臨床研究推進センター[1)]、東北大学医学系研究科機能薬理学分野[2)]、東北大学加齢医学研究所[3)]、山口大学医学系研究科情報解析医学系学域病理形態分野（病理学第一講座）[4)]、堺温心会病院内科[5)]、道後温泉病院リウマチセンター内科[6)]、熊本リウマチセンターリウマチ膠原病内科[7)]、新潟大学大学院医歯学総合研究科内部環境医学講座（第2内科）[8)]、新潟県立リウマチセンター[9)]、東京女子医大付属膠原病リウマチ痛風センター[10)]、勤医協中央病院内科（リウマチ・膠原病）[11)]、自治医科大学付属さいたま医療センターアレルギーリウマチ科[12)]、香川大学医学部内分泌代謝・血液・免疫・呼吸器内科[13)]、高知大学医学部内分泌代謝・腎臓内科[14)]、大阪南医療センター[15)]、神戸徳洲会病院[16)]、大阪大学大学院医学系研究科免疫アレルギー内科[17)]、八尾徳洲会総合病院[18)]、長崎大学病院第一内科[19)]、大阪大学先端科学イノベーションセンター[20)]

23. マウスAApoAIIアミロイド線維の形成・伸長はapoA-IIタンパク質の62番アミノ酸組成に影響される　10:18

○澤下仁子[1)]、田耕[1)]、羅宏敏[1)]、李琳[1)]、森政之[1)]、亀谷富由樹[2]、樋口京一[1)]

信州大学医学系研究科疾患予防医科学系加齢生物学講座[1)]、

(財)東京都医学総合研究所 認知症・高次脳機能研究分野[2)]

Coffee Break (10:31～10:46)

VIII. ALアミロイドーシス Part 1 (10:46～11:38) 座長 今井裕一

24. LC-MS/MSでのみ確定診断できたALアミロイドーシスの4症例 10:46
○畑裕之[1,5]、大林光念[2]、田崎雅義[3]、内場光[4]、安東由喜雄[3]、満屋裕明[1]
熊本大学医学部附属病院血液内科[1]、熊本大学医学部附属病院中央検査部[2]、熊本大学大学院生命科学研究部神経内科学分[3]、熊本大学医学部附属病院輸血細胞治療部[4]、熊本大学大学院生命科学研究部生体情報解析学[5]

25. ALとTTRアミロイド心のLC-MS/MS解析 10:59
○畑裕之[1,5]、大林光念[2]、田崎雅義[3]、高潮征爾[6]、内場光浩[4]、安東由喜雄[3]、
満屋裕明[1]
熊本大学医学部附属病院血液内科[1]、熊本大学医学部附属病院中央検査部[2]、熊本大学大学院生命科学研究部神経内科学分[3]、熊本大学医学部附属病院輸血細胞治療部[4]、熊本大学大学院生命科学研究部生体情報解析学[5]、熊本大学医学部附属病院循環器内科[6]

26. シェーグレン症候群に合併した多源性結節性ALアミロイド症3例の検討 11:12
○池田修一、日根野晃代
信州大学医学部脳神経内科 リウマチ・膠原病内科

27. 多彩なニューロパチを呈したIgMλ型 ALアミロイドーシスの1例 11:25
○野畑宏信、山田祐一郎、鈴木啓介、菅憲広、北川渡、三浦直人、今井裕一
愛知医科大学腎臓・リウマチ膠原病内科

IX. ALアミロイドーシス Part 2 (11:38～12:30) 座長 島崎千尋

28. 原発性全身性ALアミロイドーシスにおける大量メルファラン療法後非寛解例および再発例に対する治療の検討 11:38
○加藤修明[1]、松田正之[2]、池田修一[1]
信州大学医学部脳神経内科、リウマチ・膠原病内科[1]、
信州大学医学部附属病院難病診療センター[2]

29. AL amyloidosis患者に対するBortezomibを使用した維持療法 11:51
麻奥英毅[1]、○片山雄太[2]、板垣充弘[2]、大地哲朗[2]、岡谷健史[2]、今中亮太[2]、許鴻平[2]、岩戸康治[3]、辰元為仁[4]、岡田武規[5]、許泰一[2]
広島赤十字・原爆病院検査部[1]、広島赤十字・原爆病院血液内科部[2]、広島赤十字・原爆病院輸血部[3]、広島赤十字・原爆病院腎臓内科部[4]、広島赤十字・原爆病院循環器内科部[5]

30. 原発性 AL アミロイドーシスに対するボルテゾミブ・メルファラン・デキサメタゾン療法の安全性と有用性に関する研究：臨床第 I/II 相試験の進捗状況（II） 12:04

○島崎千尋[1]、淵田真一[1]、石田禎夫[2]、澤村守夫[3]、鈴木憲史[4]、小谷岳春[5]、今井裕一[6]、麻奥英毅[7]、安倍正博[8]、宮本敏浩[9]、畑　裕之[10]、飯田真介[11]、村上博和[12]、安東由喜雄[13]
社会保険京都病院血液内科[1]、札幌医科大学第一内科[2]、国立病院機構西群馬病院血液内科[3]、日本赤十字医療センター血液内科[4]、金沢大学血液内科[5]、愛知医科大学腎臓・膠原病内科[6]、広島赤十字原爆病院血液内科[7]、徳島大学血液内科[8]、九州大学血液腫瘍内科[9]、熊本大学血液内科[10]、名古屋市立大学血液・化学療法内科[11]、群馬大学保健学科[12]、熊本大学大学院生命科学研究部神経内科学分野[13]

31. 当院で行った全身性 AL アミロイドーシスに対する自家末梢血幹細胞移植 35 例の検討 12:17

○塚田信弘、宮崎寛至、阿部有、関根理恵子、中川靖章、鈴木憲史
日本赤十字社医療センター　血液内科

12:30～13:30　昼食

X.　AA アミロイドーシス　Part 1　(13:30～14:09)　座長　山田俊幸

32. チーターは複数回の遺伝子重複により形成された 4 個の serum amyloid A 遺伝子をもつ 13:30

陳磊[1]、宇根有美[2]、○樋口京一[1]、劉穎業[1]、丁欣[1]、澤下仁子[1]、森政之[1]
信州大学医学系研究科疾患予防医科学系加齢生物学講座[1]、麻布大学獣医学部病理学研究室[2]

33. アミロイド特異成分 AA76 の検出 13:43

○山田俊幸[1]、佐藤純司[1]、奥田恭章[2]
自治医科大学臨床検査医学[1]、道後温泉病院リウマチセンター[2]

34. SAA のアミロイド線維形成におけるアイソフォームの影響 13:56

山田俊幸[1]、○田中将史[2]、高瀬ひろか[2]、向高弘[2]
自治医科大学臨床検査医学[1]、神戸薬科大学薬品物理化学研究室[2]

XI.　AAアミロイドーシス　Part 2　(14:09～14:48)　　座長　奥田恭章

35.　Caplan症候群に合併したAAアミロイドーシス　14:09

中村正[1)]、○太良史郎(たらしろう)[2)]、高岡宏和[1)]、貞松智貴[2)]、大林光念[3)]、安東　由喜雄[3)]
くまもと森都総合病院リウマチ膠原病内科[1)]、くまもと森都総合病院血液内科[2)]、
熊本大学アミロイドーシス診療体制構築事業[3)]

36.　尿検査による腎アミロイドーシスの診断法および腎臓内のアミロイドの動態について　14:22

西慎一[1)]、○黒田毅(くろだたけし)[2)]、伊藤由美[3)]、今井直史[3)]、中枝武司[3)]、和田庸子[3)]、
中野正明[4)]、山田俊幸[5)]
神戸大学大学院腎臓内科・腎血液浄化センター[1)]、新潟大学保健管理センター[2)]
新潟大学大学院医歯学総合研究科腎・膠原病内科学分野[3)]、新潟大学医学部保健学科[4)]
自治医科大学臨床検査医学講座[5)]

37.　リウマチ性疾患に合併する反応性AAアミロイドーシスに対する抗IL-6　14:35
レセプター抗体療法と抗TNF療法の臨床的有用性の比較・検討 - 第二報

○奥田恭章(おくだやすあき)
道後温泉病院リウマチセンター

Coffee Break (14:48～15:03)

XII.　AAアミロイドーシス　Part 3　(15:03～15:55)　　座長　吉崎和幸

38.　ＡＡアミロイドーシスにおけるエタネルセプトのアミロイド沈着に与える影響　15:03
－腎と消化管との相違について－

○佐伯修(さいきおさむ)、宇田裕史、三上有子、水本綾、原田環、髙間俊郎
東大阪市立総合病院内科

39.　低分子化合物による血清アミロイドA（SAA）発現の制御（RA滑膜細胞での検討）　15:16

○右田清志(みぎたきよし)[1)]、中村正[2)]
独立行政法人国立病院機構長崎医療センター臨床研究センター[1)]、
くまもと森都総合病院リウマチ膠原病内科[2)]

40. T 細胞活性化調整剤による関節リウマチ合併 AA アミロイドーシス治療： 15:29
抗 fPRL1 抗体を用いた検討

○中村正(なかむらただし) [1]、公文義雄 [2]、平田真哉 [3]、高岡宏和 [1]、下村泰三 [4]、
鈴島仁 [4]、飯干明 [5]、伊勢紘平 [5]
くまもと森都総合病院リウマチ膠原病内科 [1]、高知大学医学部病態情報診断学 [2]、熊本大学附属病院血液・膠原病・感染免疫診療部 [3] 、くまもと森都総合病院血液内科 [4]、くまもと森都総合病院整形外科 [5]

41. AA アミロイドーシスのトシリズマブによる治療研究 15:42
7．AA アミロイドーシス臨床研究会による治療経過終了

○吉崎和幸(よしざきかずゆき) [1]、山田正仁 [2]、池田修一 [3]、安東由喜雄 [4]、今井裕一 [5]、奥田恭章 [6]、河野裕夫 [7]、工藤幸司 [8]、黒田毅 [9]、高市憲明 [10]、中里雅光 [11]、山田俊幸 [12]、江口勝美 [13]、寺井千尋 [14]、中村正 [15]、葦田清次 [16]、田中敏郎 [17]、稲田進一 [18]、公文義雄 [19]、小関由美 [20]、佐伯修 [21]、田村裕昭 [22]、土橋浩章 [23]、中野正明 [24]、松原司 [25]、山名征三 [26]、佐伯行彦 [27]
大阪大学大学院工学研究科応用化学専攻免疫医科学 [1]、金沢大学 [2]、信州大学 [3] 、熊本大学 [4]、愛知医科大学 [5]、道後温泉病院 [6]、山口大学 [7]、東北大学 [8]、新潟大学 [9]、虎ノ門病院 [10]、宮崎大学 [11]、自治医科大学 [12]、長崎大学 [13]、自治医科大学 [14]、熊本整形外科病院 [15]、自治医科大学 [16]、大阪大学 [17]、都立多摩総合医療センター[18]、高知大学 [19]、東京女子医科大学 [20]、堺温心会病院 [21]、勤医協中央病院 [22]、香川大学 [23]、新潟大学 [24]、松原メイフラワー病院 [25]、東広島記念病院 [26]、国立病院機構大阪南医療センター[27]

16:00 終了挨拶 研究代表者 安東由喜雄

International Symposium on Intra and Extracellular Amyloid Formation Mechanism in Amyloidosis

PROGRAM & ABSTRACTS

Date: January 24 (Thu) 2013
14 : 00～16 : 40

Place: KKR Hotel Tokyo, 1-4-1 Otemachi Chiyoda-ku Tokyo, Japan

Speakers:

Satoshi Yamashita (Kumamoto University, Japan)
Seung-Jae Lee (Konkuk University, Korea)
Yoshitaka Nagai (National Center of Neurology and Psychiatry, Japan)
Maria João Saraiva (University of Port, Portugal)

Organized by the Amyloidosis Research Committee, Research on Intractable Diseases, Health and Labour Sciences Research Grants, The Ministry of Health, Labour and Welfare, Japan

Chairperson: Yukio Ando, MD, PhD

Kumamoto University Graduate School of Medical Science, Department of Neurology

International Symposium on Intra and Extracellular Amyloid Formation Mechanism in Amyloidosis

General information

Date: January 24, 2013

14:00～16:40 (Registration Fee: Free)

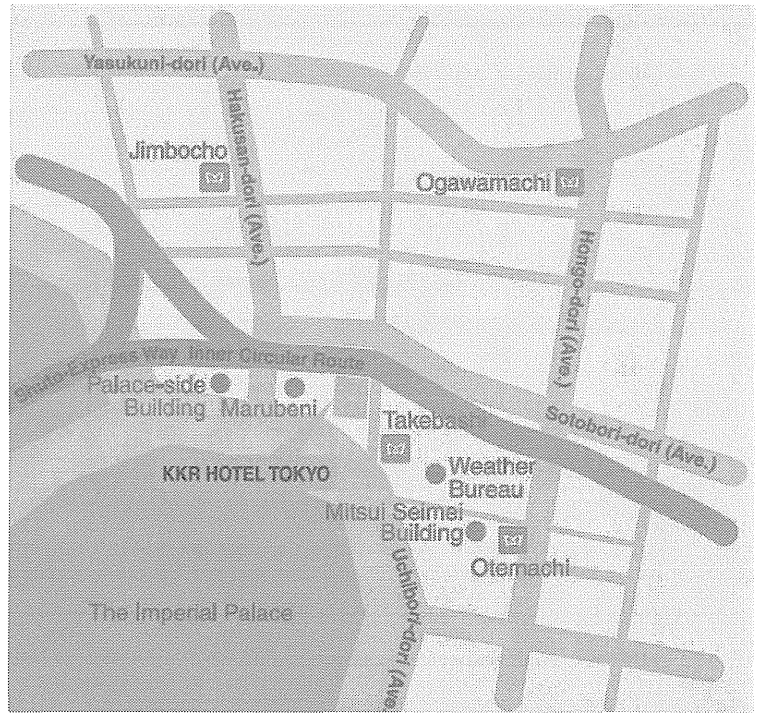
Place: KKR Hotel Tokyo, 11th Floor Banquet Room KUJAKU
1-4-1 Otemachi Chiyoda-ku Tokyo, Japan Phone: 03-3287-2921 FAX: 03-3287-2913

Reception Party: January 24, 2013

18:00～ (Registration Fee: 6,000Yen)

KKR Hotel Tokyo, 11th Floor Banquet Room TOKI

Neighboring the Imperial Palace, KKR Hotel Tokyo is conveniently located 5 minutes by car from Tokyo Station, 40 minutes from Haneda Airport and 80 minutes from Narita Airport by car. The Hotel is also directly connected to a subway station. Nearby attractions include Ginza, Akihabara, Tsukiji, Asakusa, Ueno, Roppongi and Odaiba.



Accessing from nearby train stations

20 minutes on foot, 5 minutes by car from the Marunouchi north exit of Tokyo Station

Directly connected from Exit 3b of Takebashi Station on Tozai Line

5 minutes on foot from Exit C2 of Otemachi Station on Chiyoda Line

5 minutes on foot from Exit A9 of Jinbocho Station on Metro Subway

Contact: Secretariat
Department of Neurology, Graduate School of Medical Sciences, Kumamoto University
1-1-1 Honjo Chuo-ku Kumamoto 860-8556, Japan
Phone: 096-373-5893 FAX: 096-373-5895
Email: amyloid@kumamoto-u.ac.jp

Program

January 24, 2013,
KKR Hotel Tokyo, 11th Floor Banquet Room KUJAKU

Opening Remarks
14:00-14:10 Yukio Ando (Kumamoto University, Japan)

Lecture 1
Chairpersons: Shu-ichi Ikeda (Shinshu University, Japan)
14:10-14:40 Satoshi Yamashita (Kumamoto University, Japan)

Lecture 2
Chairpersons: Keiichi Higuchi (Shinshu University, Japan)
14:40-15:10 Seung-Jae Lee (Konkuk University, Korea)
Mechanism of disease progression through cell-to-cell amyloid propagation in neurodegenerative diseases

Coffee Break
15:10-15:30

Lecture 3
Chairpersons: Hironobu Naiki (University of Fukui, Japan)
15:30-16:00 Yoshitaka Nagai (National Center of Neurology and Psychiatry)
Toxic protein conformational transition and amyloid fibril formation in the polyglutamine diseases.

Lecture 4
Chairpersons: Yukio Ando (Kumamoto University, Japan)
16:00-16:30 Maria João Saraiva (IBMC, University of Port, Portugal)
Clearance of extracellular misfolded proteins in systemic amyloidosis: experience with transthyretin

Closing Remarks
16:30-16:40 Yukio Ando (Kumamoto University, Japan)

Role of TDP-43 aggregation in neurodegenerative disease

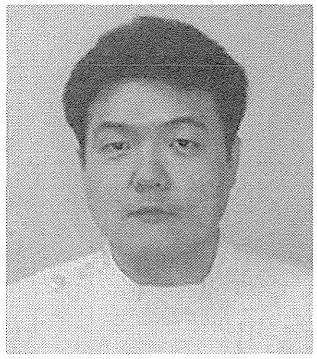
Satoshi Yamashita, M.D., Ph.D.
Department of Neurology, Graduate School of Medical Sciences, Kumamoto University

TAR-DNA-binding protein of 43kDa (TDP-43) was found to be one of the major disease proteins in the pathological inclusions of amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD). Recently, several studies have shown the abnormal accumulation of TDP-43 in skeletal muscles of patients with sporadic inclusion body myositis (sIBM).

sIBM is a progressive myopathy characterized by muscle weakness and atrophy and onset of symptoms after 50 years of age. Although the disease is one of the most common myopathies in Caucasian people, a successful treatment for this disease is unavailable. sIBM belongs to the category of inflammatory myopathies and can be considered a conformational disorder, because it is associated with abnormal intracellular accumulation of multiple unfolded/misfolded proteins, including amyloid-beta (Aβ), phosphorylated tau (p-tau) in the form of paired helical filaments, and others, with ubiquitin immunoreactivity.

Increasing evidences suggest a similarity in the pathophysiological mechanisms of neuronal cell death in ALS and myofiber degeneration in sIBM. We here demonstrate that TDP-43, optineurin (OPTN), and to a lesser extent fused in sarcoma/translocated in liposarcoma (FUS/TLS) were more frequently accumulated in the cytoplasm in patients with sIBM and oculopharyngeal muscular dystrophy (OPMD) than in patients with polymyositis (PM), dermatomyositis (DM), or neurogenic muscular atrophy. Cu/Zn superoxide dismutase (SOD1) was accumulated in a small percentage of myofibers in patients with sIBM and OPMD, and to a very small extent in patients with PM and DM. Interestingly, confocal microscopy imaging showed that TDP-43 proteins more often colocalized with OPTN than with FUS/TLS, p62, and phosphorylated Tau. These findings suggest that OPTN in cooperation with TDP-43 might be involved in the pathophysiological mechanisms of skeletal muscular degeneration in myopathy with rimmed vacuoles.

To confirm the primary toxicity of TDP-43 to myofibers, we are generating transgenic mice having wild-type TDP-43 gene that is driven by muscle creatine kinase promoter. In the preliminary data at 8 week-old, the transgenic mice showed TDP-43-immunoreactive cytoplasmic aggregation in the quadriceps muscles. Interestingly, the mean diameter of myofibers with TDP-43 aggregates was significantly smaller than that of myofibers without aggregates or myofibers on non-transgenic littermates. For the better understanding of role of TDP-43 aggregation in neuromuscular degenerative diseases, the analyses of TDP-43 aggregation both in the sIBM patients and muscle-specific TDP-43 transgenic mice would be a useful tool.



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EDUCATION:

Kumamoto University, Japan	M.D.	1995	Medicine
Kumamoto University, Japan	Ph.D.	2003	Medical Science

POSITIONS:

2009-present: Assistant Professor, Dept. of Neurology, Kumamoto University Hospital

2007-2009: Neurologist and Research scientist, Dept. of Neurology, Kumamoto University Hospital

2004-2007: Postdoctoral research scientist, Dept. of Neurology, Columbia University, NY, USA

2003-2004: Neurologist (Dept. of Neurology, Kumamoto University Hospital, and Dept. of Neurology, National Kumamoto Hospital)

1999-2003: Ph.D. program, Graduate School of Medical Sciences, Kumamoto University

1995-1999: Medical Residency (Dept. of Internal Medicine, Kumamoto University Hospital, Dept. of Internal Medicine, Kumamoto City Hospital, and Dept. of Neurology, Kumamoto Saishunso Hospital)

OTHER EXPERIENCE AND PROFESSIONAL MEMBERSHIPS

1995: Japanese National License to practice medicine
2003: Diplomat, Japanese Board of Neurology
Member: Society for Neuroscience, Japanese Society of Neurology, The Japanese Society of Internal Medicine, The Japan Neuroscience Society

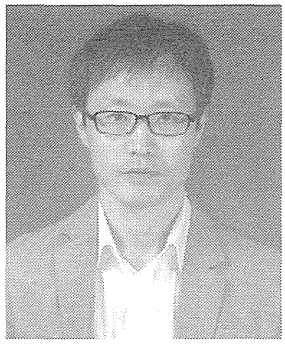
Mechanism of disease progression through cell-to-cell amyloid propagation in neurodegenerative diseases

Seung-Jae Lee, Ph.D.

Department of Biomedical Science and Technology,

Konkuk University, Seoul, Korea

Progressive accumulation of specific protein aggregates is a defining feature of many major neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, fronto-temporal dementia, Huntington's disease, and Creutzfeldt-Jakob disease (CJD). Findings from several recent studies have suggested that aggregation-prone proteins, such as tau, α-synuclein, polyglutamine-containing proteins, and amyloid-β, can spread to other cells and brain regions, a phenomenon considered unique to prion disorders, such as CJD and bovine spongiform encephalopathy. Cell-to-cell propagation of protein aggregates may be the general underlying principle for progressive deterioration of neurodegenerative diseases. This may also have significant implications in cell replacement therapies, as evidenced by the propagation of α-synuclein aggregates from host to grafted cells in long-term transplants in Parkinson's patients. In this talk, I will review recent progress in protein aggregate propagation in experimental model systems and discuss outstanding questions and future perspectives. Understanding the mechanisms of this pathological spreading may open the way to unique opportunities for development of diagnostic techniques and novel therapies for protein misfolding-associated neurodegenerative diseases.



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POSITIONS:

2011-present	Professor, Department of Biomedical Science and Technology, Konkuk University, Seoul, Korea
2006-2011	Associate Professor, Department of Biomedical Science and Technology, Konkuk University, Seoul, Korea
2000-2006	Assistant Professor, The Parkinson's Institute, Sunnyvale, CA
1998-2000	Instructor in Neurology, Center for Neurologic Diseases, Harvard Medical School and Brigham and Women's Hospital, Boston, MA
1996-1998	Postdoctoral Fellow, Center for Neurologic Diseases, Harvard Medical School and Brigham and Women's Hospital, Boston, MA
1995-1996	Postdoctoral Fellow, Laboratory of Molecular Cardiology, NHLBI, NIH, Bethesda, MD

EDUCATION:

1992-1995	PhD Department of Life Science, Pohang University of Science and Technology, Pohang, Korea
1990-1992	M.S. Department of Life Science, Pohang University of Science and Technology, Pohang, Korea
1985-1989	B.S. Department of Biology Education, Seoul National University, Seoul, Korea

AWARDS:

1995-1997	NIH Postdoctoral Fellowship from Fogarty International Center
2000	International Parkinson's Research Award (Parkinson's disease foundation)
2010	Excellence in Basic Research (Ministry of Education, Science, and Technology)

PROFESSIONAL SOCIETIES:

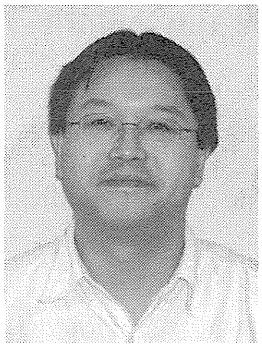
1999-	member, Society for Neuroscience
2002-	member, American Society for Biochemistry and Molecular Biology
2009-	member, Korean Society for Molecular and Cellular Biology
2007-	member, Korean Society for Brain and Neural Science
2007-	member, Korean Society for Neurodegenerative disease

Toxic protein conformational transition and amyloid fibril formation in the polyglutamine diseases.

Yoshitaka Nagai, M.D., Ph.D.

Department of Degenerative Neurological Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry

Abnormal aggregation and deposition of misfolded proteins in the brain have been recognized as a common molecular pathogenesis of various neurodegenerative diseases including Alzheimer's disease, Parkinson's disease, and the polyglutamine (polyQ) diseases, which are classified as the conformational diseases. The polyQ diseases are a group of at least nine inherited neurodegenerative diseases including Huntington's disease and various spinocerebellar ataxias, which are caused by an abnormal expansion of the polyQ stretch (>35-40) within each unrelated disease-causative protein. The expansion of the polyQ stretch is thought to trigger misfolding and aggregation of the disease-causative proteins, leading to their deposition as inclusion bodies inside affected neurons, and eventually resulting in neurodegeneration. To elucidate the structural alterations of the expanded polyQ protein during the aggregation process, we performed structural analyses of the polyQ protein. We found that the expanded polyQ protein undergoes a conformational transition to a β-sheet dominant structure in the monomeric state, which precedes its assembly into insoluble amyloid-like fibrillar aggregates. Most importantly, we further revealed that the soluble β-sheet monomer of the expanded polyQ protein triggers cytotoxicity by microinjection experiments. From a therapeutic point of view, we identified QBP1 (SNWKWWPGIFD), a peptide sequence that preferentially binds to the expanded polyQ stretch by phage display screening. We showed that QBP1 prevents the toxic β-sheet transition and amyloid-like aggregation of the expanded polyQ protein *in vitro*, and further that QBP1 suppresses polyQ-induced neurodegeneration in *Drosophila*. From high-throughput screening of a chemical compound library (46,000), we have identified approximately 100 polyQ aggregate inhibitors as therapeutic candidates so far. We also utilized molecular chaperones, which belong to the quality control system against protein misfolding, and demonstrated that genetic expression and pharmacological induction of molecular chaperones suppress polyQ-induced neurodegeneration in *Drosophila* and mouse models. Finally, we demonstrated therapeutic effects of selective degradation of the expanded polyQ protein on a polyQ disease mouse model. We therefore conclude that protein misfolding and aggregation are promising therapeutic targets not only for the polyQ diseases, but also for other conformational neurodegenerative diseases.



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BIOGRAPHY:

2008-present	Section Chief, Department of Degenerative Neurological Diseases, National Institute of Neuroscience, National Center of Neurology and Psychiatry
2007-2008	Associate Professor, Div of Clinical Genetics, Dept of Medical Genetics, Osaka University Graduate School of Medicine, Japan
2001-2007	Assistant Professor, same as the above
2000-2001	JSPS Postdoctoral fellow, Dept of Molecular Medical Science, Osaka Bioscience Institute, Japan
1997-2000	Research Associate, Div of Neurology, Dept of Medicine, Duke University Medical Center, NC, USA
1995	Ph.D. (Dr. of Medical Science), Osaka University Graduate School of Medicine, Japan
	M.D., Osaka University Medical School, Japan

AWARDS:

The Award for Young Investigator of Japanese Society for Neurochemistry

SELECTED PUBLICATIONS:

Nagai Y, Popiel HA. *Curr Pharm Des* 14: 3267-3279 (2008)
Fujikake N, *et al. J Biol Chem* 283: 26188-26197 (2008)
Takahashi Y, *et al. J Biol Chem* 282: 24039-24048 (2007)
Nagai Y, *et al. Nat Struct Mol Biol* 14: 332-340 (2007)
Popiel HA, *et al. Mol Ther* 15: 303-309 (2007)
Nagai Y, *et al. Hum Mol Genet* 12: 1253-1260 (2003)
Nagai Y, *et al. J Biol Chem* 275: 10437-10442 (2000)

Clearance of extracellular misfolded proteins in systemic amyloidosis: experience with transthyretin

Maria João Saraiva, Ph.D.
Institute for Molecular and Cellular Biology (IBMC) and Institute for Biomedical Sciences (ICBAS), University of Porto, Portugal

Extracellular protein misfolding and aggregation occurring in systemic amyloidosis triggers inflammation, oxidative stress, matrix remodeling, the unfolded-protein-response and ER pathways that resemble in many aspects, including common molecular players and scenarios, to those described in local amyloidoses affecting for example the central nervous system (CNS), such as Alzheimer Disease. Thus, similarities and dissimilarities in toxicity found between the CNS and the periphery are very useful to pinpoint and guide us to the treatment of aging-associated neurodegenerative disorders. Understanding the two-way crosstalk between the extracellular milieu and the cell is a major trend in diseases related to protein aggregation. In particular, mechanisms involved in the clearance of protein aggregates, both extra and intracellular are pivotal and need detailed analyses for the development of therapeutic strategies. Studies with small compounds or molecules, such as antibodies, known to recognize and disrupt amyloidogenic structures, have proven efficient in removing and promoting clearance of protein aggregates in studies with experimental models of misfolding disorders. However, the mechanisms and key players in these processes are largely unknown. Extracellular molecular chaperones are capable to repair or target damaged proteins to degradation by binding to extracellular misfolded proteins and promoting their disposal either by endocytosis for intracellular degradation or degradation by the extracellular matrix. It is clear that more than a single approach to treat FAP effectively is mandatory; in this regard, the experience achieved so far with clearance based approaches is very promising and will be discussed.

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EDUCATION:

1971-1976	B.Sc. (Biology), University of Porto (grade:16/20)
1976-1978	M.Sc. (Biochemistry), University of London
1980-1984	Ph.D. with Honors (Biochemistry), University of Porto
1991-	Qualified as Professor in Biochemistry ("agregação"), University of Porto

RESEARCH AND PROFESSIONAL EXPERIENCE

1977-1984	Research Assistant, (leading to a PhD), Instituto de Ciências Biomédicas
1981-1983	Staff Associate, Medicine, Columbia, Univ. College of P&S, P&S, New York
1984-1986	Visiting Scientist, Medicine, Columbia University, College of P&S, New York (6 mo./year)
1984-1989	Assistant Professor (Biochemistry), Instituto de Ciências Biomédicas
1989	Visiting Scientist, Neurogenetics Unit, Massachusetts Gen Hospital, Boston, (Feb-July)
1989-1993	Associate Professor (Biochemistry), Instituto de Ciências Biomédicas
1990-1994	Member of the Board of Directors, Centro de Estudos de Paramiloidose
1992-1994	Visiting Scientist in the Institute of Cancer Research, Columbia University (3 months/ year)
1984-1996	Research Associate, Centro de Estudos de Paramiloidose, Porto
1994-1995	Chairman of the Department of Molecular Biology, Instituto de Ciências Biomédicas
1997-2001	Director of the Amyloid Unit of Institute for Molecular and Celular Biology, Universidade do Porto
2007-2009	Coordinator of the Basic and Clinical Neurobiology Division at Institute for Molecular and Celular Biology - IBMC, Universidade do Porto
1999-present	Member of the Board of Directors of the Center for Predictive and Preventive Medicine at the Institute for Mol and Celular Biology, Universidade do Porto
1994-present	Full Professor (Biochemistry), Instituto de Ciências Biomédicas, Universidade do Porto, Portugal
2002-present	Director of the Molecular Neurobiology Group at Institute for Molecular and Celular Biology - IBMC, Universidade do Porto
2010-present	Vice-Director of Institute for Molecular and Celular Biology - IBMC, Universidade do Porto