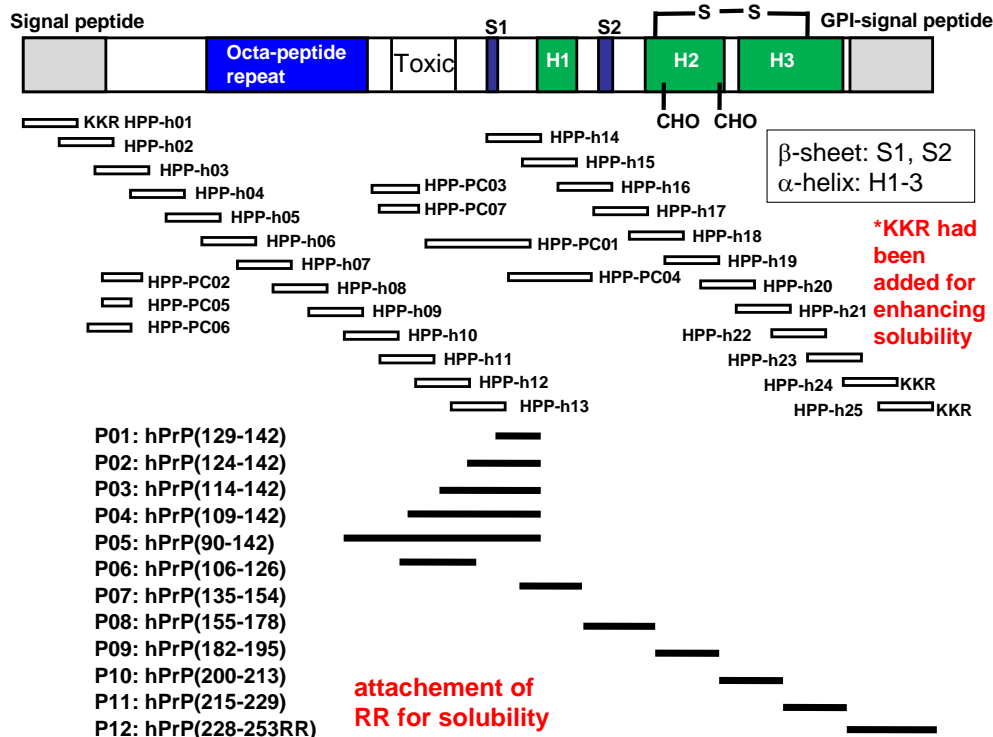


Prion protein related peptide library

HiPep laboratories offer various prion-protein related peptides which had been designed and prepared. These peptides could discriminate structural changes of prion proteins and may inhibit or promote PrP^{Sc} generation. The interaction of these designed peptides with infectious prion obtained from mouse brain and infected mice brain homogenate has been investigated. Furthermore, by using our novel assay method to monitor structural conversion of recombinant bovine prion protein, we have found the responsible peptides for the structural conversion from bovine brain extracts. These peptide libraries are useful tool for research on protein-structural disease.

Prion protein [Homo sapiens]

1 manlgcwmlv lfvatwsdlg lckkrpkpgg wntggsrypg qgspggnryp pqggggwgqpp
61 hggwgqphg ggwgqphggg wgqphggwg qgggthsqwn kpskpktnmk hmagaaaaga
121 vvglggyvl gsamsrpiih fgdsyedry renmhrypnq vyyrpmdeys nqnnfvhdvc
181 nitikqhtvt tttkgenfte tdkmmervv eqmctqyer esqayyqrgs smvlfssppv
241 illisflif ivg



Reference

Kasai, K., Hirata, A., Ohyama, T., Nokihara, K., Yokoyama, T., Mohri, S. Novel assay with fluorescence-labelled PrP peptides for differentiating L-type atypical and classical BSEs, and scrapie, *FEBS Lett.* **2012**, 586, 325-329.

Characteristic differences of prions may account for the conformational diversity of the pathogenic isoform of prion protein (PrP^{Sc}). We applied a protein detection procedure by using fluorescent labeled peptides for detecting PrP^{Sc}. Five prion protein (PrP) related peptides were found to change significantly their fluorescent intensities with prion-affected animal samples. Their reactivity was different among atypical L-BSE, classical BSE and scrapie. The pull-down assay revealed that they precipitated PrP^{Sc} specifically. These findings suggest that fluorescent intensity changes depend on peptide PrP^{Sc} binding. This novel approach may distinguish the fine structural differences in PrP^{Sc}, which were not detected by the pull-down assay.

Hirata, A., Yajima, S., Yasuhara, T., Nokihara, K. Structural Conversion Rate Changes of Recombinant Bovine Prion by Designed Synthetic Peptides, *Int. J. Pept. Res. Ther.* **2012**, 18, 1-9.

An understanding of structural changes and self-assembly of proteins are thought to involve specific peptide-peptide interactions and it will contribute to the development of therapeutic agents and diagnosis for the detection of conformational diseases such as bovine spongiform encephalopathy or human Creutzfeldt-Jakob disease. We hypothesize that certain peptides may contribute to the conformational change of prion proteins. In contrast to the known effects of beta-sheet breaker peptides, we suggest a possible reverse phenomenon may exist in which certain peptides may induce or enhance putative beta-sheet structures. Hence designed human prion protein related peptides may be useful tools for the investigation of this hypothesis. Our paper describes the discovery of prion-related peptides which influence structural conversion of recombinant bovine prion protein.

Nokihara, K., Yajima, S., Hirata, A., Sogon, T., Yasuhara, T. Characterization of peptides obtained from digests of bovine brain which accelerate structural conversions of the recombinant bovine prion protein, *FEBS Lett.* **2013**, 587, 673-576.

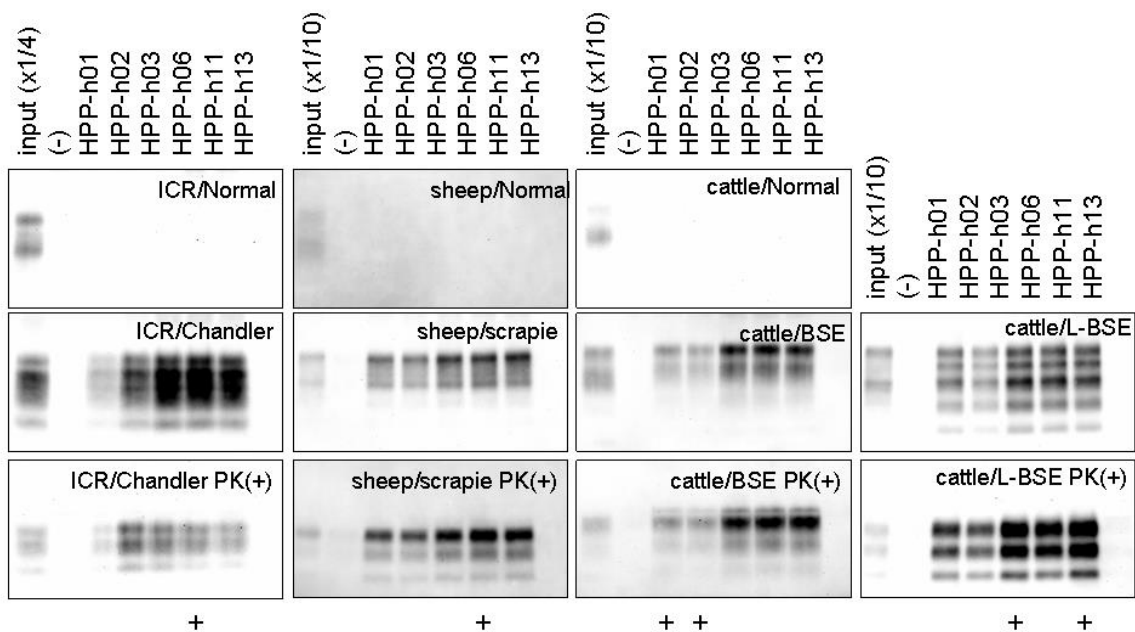
プリオンタンパク質関連ペプチドライブラリー

背景：平成19年度～23年度までの5年間、(独)農業・食品産業技術総合研究機構生物系特定産業技術研究支援センター「生物系産業創出のための異分野融合研究支援事業」を進めました。当該研究成果にもとづいて構築した「ヒトプリオンペプチド断片ペプチドライブラリー」をご提供させていただきます。弊社では、BSE等プリオン病の発症前診断を可能とするバイオチップの開発研究を行い、プリオン株の種類を判別する新しいアッセイ方法も確立しました。さらに、プリオンタンパク質の構造変換速度に影響を与えるペプチドを発見しました(論文参照)。近年、プリオンタンパク質がアルツハイマー病において神経細胞を損傷させる際の原因物質候補として注目されており、分子レベルでの研究が進められております。プリオンタンパク質の断片ペプチドは、人獣共通感染症としてのプリオン病の治療薬や診断ツールとして重要なだけでなく、今後罹患率が高まると予想されている、アルツハイマー病の治療薬の開発・研究にもお役に立てるものと考えております。

参考文献

Kasai, K., Hirata, A., Ohshima, T., Nokihara, K., Yokoyama, T., Mohri, S. Novel assay with fluorescence-labelled PrP peptides for differentiating L-type atypical and classical BSEs, and scrapie, *FEBS Lett.* **2012**, 586, 325-329.

プリオンタンパク質関連ペプチドライブラリーのうち、h01/02は定型BSE感染牛、h03/11は非定型BSE感染牛、h06はスクレイビー感染羊・マウス脳乳剤と特異的に反応した。一方、プルダウンアッセイでは上記の5ペプチドはすべての異常プリオン蛋白質(PrP^{Sc})と結合し、プリオンの由来や種特異性は認められなかった(図)。また、これらのことから、上記ペプチドを用いたアッセイでは、プリオンの種類、具体的には定型BSE(C-BSE)、非定型BSE(L-BSE)、スクレイビーのPrP^{Sc}について識別することができることが判明した。



Hirata, A., Yajima, S., Yasuhara, T., Nokihara, K. Structural Conversion Rate Changes of Recombinant Bovine Prion by Designed Synthetic Peptides *Int. J. Pept. Res. Ther.* **2012**, 18, 1-9.

プリオンタンパク質(PrP)関連ペプチドライブラリーを利用したPrPの構造変換解析を行った。蛍光強度解析から明らかになったことは、構造変換が始まるまでの時間(ラグタイム)に差があるという点であった。興味深いことに、PrPにおいてToxic領域として知られている部分を含むペプチドは、ラグタイムが短くコンビナントウシPrP(rbPrP)の構造変換を早期に誘起することが明らかとなり、Toxicityとの相関を伺わせる結果であった。これらの結果から、ペプチドの種類によりラグタイムに多様性があることから、rbPrPとペプチドとの相互作用に同様の多様性があることを示唆している。すなわち、これらのペプチドを組み合わせることで、バイオチップにおいて蛍光強度をバーコード化し、PrPの構造変換を検出することが十分可能であることを示した。

Nokihara, K., Yajima, S., Hirata, A., Sogon, T., Yasuhara, T. Characterization of peptides obtained from digests of bovine brain which accelerate structural conversions of the recombinant bovine prion protein, *FEBS Lett.* **2013**, 587, 673-676.

Nokihara, K., Yajima, S., Hirata, A. Design and syntheses of peptides which induce or enhance structural changes of recombinant bovine prion protein (rbPrP) and discovery of peptides from bovine brain which accelerate structural conversions of rbPrP, *Prion.* **2014**, 8, 117-118.

N末端Ac, C末端ビオチン
 N末端FAM, C末端ビオチン
 N末端TAMRA, C末端ビオチン
 N末端TAMRA, C末端アミド
 N末端TAMRA, C末端システイン

N-termini Ac, C-termini Biotin
 N-termini FAM, C-termini Biotin
 N-termini TAMRA, C-termini Biotin
 N-termini TAMRA, C-termini Amide
 N-termini TAMRA, C-termini Cysteine





Prion protein related peptide library

Seq.	Modification	P/N
Hamster PrP 113-141	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-PC01-AB HPP-PC01-FB HPP-PC01-TB HPP-PC01-TA HPP-PC01-TC
Mouse PrP 23-33	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-PC02-AB HPP-PC02-FB HPP-PC02-TB HPP-PC02-TA HPP-PC02-TC
Mouse PrP 98-110	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-PC03-AB HPP-PC03-FB HPP-PC03-TB HPP-PC03-TA HPP-PC03-TC
Mouse PrP 136-158	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-PC04-AB HPP-PC04-FB HPP-PC04-TB HPP-PC04-TA HPP-PC04-TC
Human PrP 23-30	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-PC05-AB HPP-PC05-FB HPP-PC05-TB HPP-PC05-TA HPP-PC05-TC
Human PrP 19-30, C2S	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-PC06-AB HPP-PC06-FB HPP-PC06-TB HPP-PC06-TA HPP-PC06-TC
Human PrP 100-111	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-PC07-AB HPP-PC07-FB HPP-PC07-TB HPP-PC07-TA HPP-PC07-TC
Human PrP1-12 KKR, C6S	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h01-AB HPP-h01-FB HPP-h01-TB HPP-h01-TA HPP-h01-TC
Human PrP 11-25, C2S	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h02-AB HPP-h02-FB HPP-h02-TB HPP-h02-TA HPP-h02-TC
Human PrP 21-35, C2S	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h03-AB HPP-h03-FB HPP-h03-TB HPP-h03-TA HPP-h03-TC
Human PrP 31-45	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h04-AB HPP-h04-FB HPP-h04-TB HPP-h04-TA HPP-h04-TC
Human PrP 41-55	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h05-AB HPP-h05-FB HPP-h05-TB HPP-h05-TA HPP-h05-TC

Seq.	Modification	P/N
Human PrP 51-65	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h06-AB HPP-h06-FB HPP-h06-TB HPP-h06-TA HPP-h06-TC
Human PrP 61-75	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h07-AB HPP-h07-FB HPP-h07-TB HPP-h07-TA HPP-h07-TC
Human PrP 71-85	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h08-AB HPP-h08-FB HPP-h08-TB HPP-h08-TA HPP-h08-TC
Human PrP 81-95	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h09-AB HPP-h09-FB HPP-h09-TB HPP-h09-TA HPP-h09-TC
Human PrP 91-105	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h10-AB HPP-h10-FB HPP-h10-TB HPP-h10-TA HPP-h10-TC
Human PrP 101-115	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h11-AB HPP-h11-FB HPP-h11-TB HPP-h11-TA HPP-h11-TC
Human PrP 111-125	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h12-AB HPP-h12-FB HPP-h12-TB HPP-h12-TA HPP-h12-TC
Human PrP 121-135	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h13-AB HPP-h13-FB HPP-h13-TB HPP-h13-TA HPP-h13-TC
Human PrP 131-145	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h14-AB HPP-h14-FB HPP-h14-TB HPP-h14-TA HPP-h14-TC
Human PrP 141-155	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h15-AB HPP-h15-FB HPP-h15-TB HPP-h15-TA HPP-h15-TC
Human PrP 151-165	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h16-AB HPP-h16-FB HPP-h16-TB HPP-h16-TA HPP-h16-TC
Human PrP 161-175	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h17-AB HPP-h17-FB HPP-h17-TB HPP-h17-TA HPP-h17-TC





プリオンタンパク質関連ペプチドライブラリー

Sequence	Modification	P/N	Sequence	Modification	P/N
Human PrP 171-185, C179S	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h18-AB HPP-h18-FB HPP-h18-TB HPP-h18-TA HPP-h18-TC	Human PrP 211-225, C214S	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h22-AB HPP-h22-FB HPP-h22-TB HPP-h22-TA HPP-h22-TC
Human PrP 181-195	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h19-AB HPP-h19-FB HPP-h19-TB HPP-h19-TA HPP-h19-TC	Human PrP 221-235	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h23-AB HPP-h23-FB HPP-h23-TB HPP-h23-TA HPP-h23-TC
Human PrP 191-205	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h20-AB HPP-h20-FB HPP-h20-TB HPP-h20-TA HPP-h20-TC	Human PrP 231-242 KKR	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h24-AB HPP-h24-FB HPP-h24-TB HPP-h24-TA HPP-h24-TC
Human PrP 201-215, C214S	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h21-AB HPP-h21-FB HPP-h21-TB HPP-h21-TA HPP-h21-TC	Human PrP 241-252 KKR	N-termini Ac, C-termini Biotin N-termini FAM, C-termini Biotin N-termini TAMRA, C-termini Biotin N-termini TAMRA, C-termini Amide N-termini TAMRA, C-termini Cysteine	HPP-h25-AB HPP-h25-FB HPP-h25-TB HPP-h25-TA HPP-h25-TC

注文番号	アミノ酸配列 *凝集性が高く難精製ペプチドであったが、自社開発の手法で精製できた。カウンターイオンはTFA
HPP-P01	MLGSAMSRPIIHFG (human PrP129-142)
HPP-P02	GLGGYMLGSAMSRPIIHFG (human PrP124-142)
HPP-P03	GAAAAGAVVGLGGYMLGSAMSRPIIHFG (human PrP114-142)
HPP-P04	MKHMAGAAAAGAVVGLGGYMLGSAMSRPIIHFG (human PrP109-142)
HPP-P05	GQGGGTHSQWNKPSKPKTNMKHMAGAAAAGAVVGLGGYMLGSAMSRPIIHFG (human PrP90-142)
HPP-P06	KTNMKHMAGAAAAGAVVGLGLG (human PrP106-126)
HPP-P07	SRPIIHFGSDYEDRYRENM (human PrP135-154)
HPP-P08	HRYPNQVYRPMDEYSNQNNFVHD (human PrP155-178)
HPP-P09	ITIKQHTVTTTKG (human PrP182-195)
HPP-P10	ETDVKMMERVVEQM (human PrP200-213)
HPP-P11	ITQYERESQAYYQRG (human PrP215-229)
HPP-P12	RGSSMVLFSPPVILLISFLIVG-RR (human PrP228-253 RR)
HPP-SH	YSNQNNF-VNITIKQHTVTTTKG-NH ₂ [human PrP(169-175)+(180-195)]
HPP-A01	DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIAT (Amyloid β 1-43)
HPP-A02	DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA (Amyloid β 1-42)
HPP-A03	DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV (Amyloid β 1-40)
HPP-A04	LVFFAEDVGSNKGAIIGLMVGGVVIA (Amyloid β 17-42)
HPP-A05	AEDVGSNKGAIIGLMVGGVVIA (Amyloid β 21-42)
HPP-A06	LVFFAEDVGSNKGAIIGLMVGGVV (Amyloid β 17-40)
HPP-A07	DAEFRHDSGYEVHHQKLVFF (Amyloid β 1-20)

single ￥200,000/peptide~

5 ￥150,000/peptide~

10 ￥120,000/peptide~

20 ￥90,000/peptide~

50 ￥50,000/peptide~

all ca ￥30,000/peptide~

Each peptide is 1 mM in DMSO 100 mL stock solution

*1.5 mL microtube

Upon request tailor made sequence; Lyophilized peptides; aliquoted in a 96 well-plate can be available.

単品 ￥200,000/peptide~

5種 ￥150,000/peptide~

10種 ￥120,000/peptide~

20種 ￥90,000/peptide~

50種 ￥50,000/peptide~

全種 ca ￥30,000/peptide~

各種1 mM peptide in DMSO

100 mL ストックソリューション

*1.5 mL マイクロチューブに分注

■粉末サンプルでの提供も可能、価格はご希望の量に合わせて都度見積

■96 ウエルタイタープレートへの分注も対応

*We have developed novel purification methods for structured peptides, such as peptides having difficult sequences. Refer also Column Information www.hipep.jp/eng.

*Counter ion of peptide is TFA

■ 標識化酸配列改変の場合は、弊社受託合成規定を適用 (お見積)

■ 単なる依頼による受託作業ではなく、研究の上流から下流までを視野に入れた研究者の立場からの支援が可能

■ 必要に応じ秘密保持契約等を締結。共同・受託研究開発 (契約料+成功報酬/成果は共有)、コンサルテーション (成果はクライアントが保有) も対応

