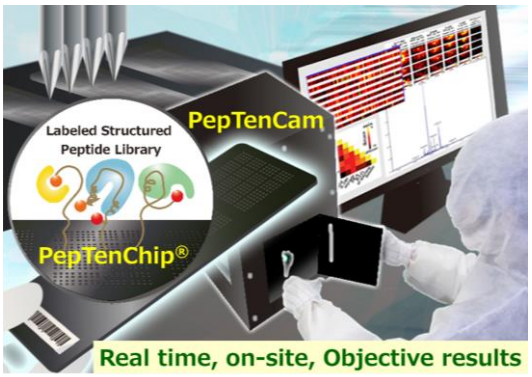
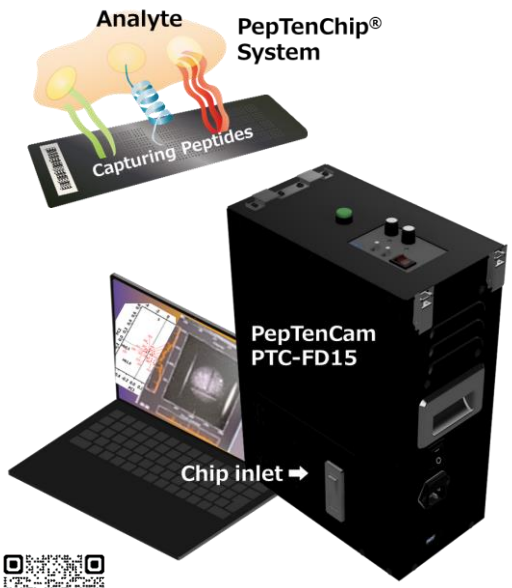
HiPep Laboratories focusing on bio-molecular recognition for healthcare in the next generation, Looking for Exits: licensing out/collaboration

New Products, PepTenChip® System: Biodetection technology with novel principles, Disease-marker independent, giving objective diagnostics





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The 4 key technologies for PepTenChip® system have been completed: *de novo* designed labeled structured peptides as capture molecules; amorphous carbon, novel chip substrates; array technology; a detector for on-site use/maintenance free, PepTenCam. Most attempts for the protein-chip development have been failed and withdrew, due to the sensitivity and reproducibility by immobilization, instead solution assays such as ELISA were the mainstream. The PepTenChip® system does not involve detection of specific molecules in a 1:1 manner, but it's detection principle is different (PAT: JP, US & EU). The structural changes of analyte are reflected in the fluorescence intensity changes of capture peptides in a dose dependent manner. This changes can be visualized as a pattern designated a "Protein Fingerprint". Datamining is carried out by statistical analyses : multivariate analyses.

Discovery of undefined materials related to diseases can be possible. PepTenChip® can be repeatedly used (not disposable), Class I Medical device; noninvasive diagnostics; on-site "Point of Care". Objective results can be given not dependent on clinicians personal skill. Some clinical applications are underway: (1) Precancer diagnostics for early detection using gastric juice, classification of gastric precancerous lesions; (2) Multiple sclerosis (MS), of which cause as well as positive disease markers are unknown, discrimination in MS and related diseases using human spinal fluid for objective indicators. The preliminary results are evaluated by expert clinicians as useful information in making treatment decisions.

Representative publications for Biodetection by microarrays, PepTenChip®

Tominaga, Y., et.al., *Bioorganic & Medicinal Chemistry,* 26, 3210-3216, 2018; https://doi.org/10.1016/j.bmc.2018.04.049

Tominaga, Y., et.al., *Bioorg. Med. Chem. Lett.* 25, 611-615, 2015.

https://doi.org/10.1016/j.bmcl.2014.12.009

Nokihara, K. et.al., *Prion,* 8, 117-118, 2014; https://doi.org/10.4161/pri.27961

Kasai, K., et.al., *FEBS Lett.,* 586, 325-329, 2012; https://doi.org/10.1016/j.febslet.2012.01.012

Usui, K., et.al., *Biopolymers(Peptide Science),* 76, 129-139, 2004; https://doi.org/10.1002/bip.10568

Takahashi, M., et. al., *Chemistry and Biology*, 10, 53-60, 2003; https://doi.org/10.1016/S1074-5521(02)00308-3

Reviewed: Nokihara K, et.al., *Peptide Science 2018*, Futaki, S. and Matsuzaki, K. (Eds), pp 20-21, 2019.

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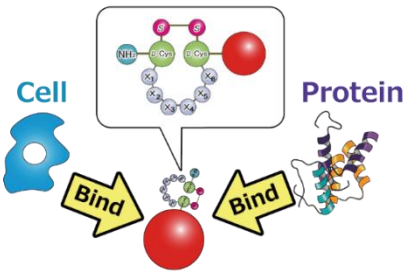
New Products with new technologies for drug development

OPOB: Discovery tools, high quality one cyclic peptide immobilized on one gel-type bead, and high throughput sequencing

Instead of chip-substrates, peptides are immobilized on gel-type beads, one compound on one bead, ca. 80 pico mol peptide/bead

P/N : CP24OB, diversity 24^6 : *ca* 200 million: 19 natural & 5 non- proteogenic amino acids, cyclic with *D*-Cys

NEW P/N : CP12FB: OPOB focusing on drug-likeness and allowing rapid deconvolution (PAT.P), **diversity: 3 million** overcoming limitations in ribosomal system such as displays

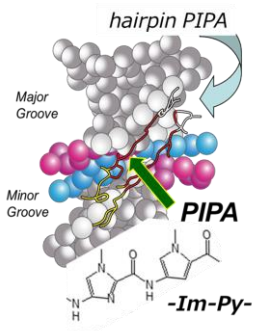


https://hipep.com/?p=3284

Representative publications

Sasaki, T., et.al., Chemical Biology & Drug Design, 00, 1–9, 2023; https://doi.org/10.1111/cbdd.14331
Nokihara, K., et.al., Amino Acids, 48, 2491-2499, 2016; https://doi10.1007/s00726-016-2269-1
Hirata, A. and Nokihara, K., Tetrahedron Lett. 55, 4091-4094, 2014: https://doi.org/10.1016/j.tetlet.2014.05.086

PIPA, Polyamides with Pyrrole and Imidazole as major building unites, sequence specific binding to dsDNA, novel gene control drug candidates



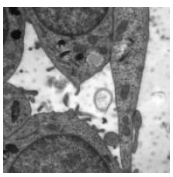
Middle sized drugs such as peptide, designable & difficult to prepare, although HiPep established: Assembly, purification and QC. PIPA blocks binding of transcription factors inhibiting gene expression, can control expression of gene. Peptide Vehicle (THL, 55, 4091, 2014) DDS and DNA-modification alkylation of the target DNA. DNA visualization by labelled PIPAs. No-toxicities have been found, 3-4 weeks passed through urine (∼100%) ; Target diseases: not possible by small molecules or antibodies. A list of synthetic PIPAs as reagents for clinical applications published

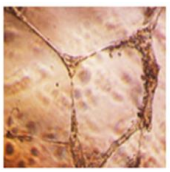
http://hipep.jp/pdf/catalog/R002E.pdf https://hipep.com/?p=2834

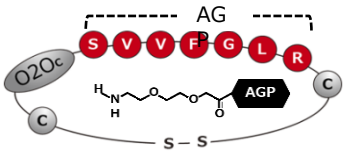
Pioneer work by P. Dervan 1998 : *Science, 282, 111, Nature, 391, 468.*

Sasaki, A., et. al., Scientific Reports, 6, 29261, 2016. https://doi.org/10.1038/srep29261
Hirata, A., et.al., J. Am. Chem. Soc., 136, 11546, 2014; https://doi.org/10.1021/ja506058e

AGP: Peptides exhibiting angiogenic and cell-adhesion properties, longer lasting AGP for transplantation as new drug candidates in regenerative medicine







Structure activity relationship had been elicited. NGF and/or bFGF have been used to give certain effects, although infiltration has been observed. AGP showed no such effects, but the duration of actions has been relatively shorter and not enough for complete engraftment. Focusing on longer half-life time novel AGP has been developed (PAT.P). Assay using human cells, human umbilical vein endothelial cells, with quantitative evaluation were accomplished. Stability was tested in cell lysate and human serum. Cyclic AGPs contribute directly to neovascularization, no linear fragments were generated in cell culture. https://hipep.com/?p=1559

PAT. US, JP, EU; Hamada Y, et.al., BBRC, 310, 153–157, 2003; https://doi.org/10.1016 /j.bbrc.2003.09.001
Tominaga, Y. and Nokihara, K., Int. J. Pep. Res. & Ther, 28, 95-98, 2022. https://doi.org/10.1007/s10989-022-10404-2
Tominaga, Y., et.al., BMC, 28, 115685, 2020; https://doi.org/10.1016/j.bmc.2020.115685