Organic chemistry in protein modification and analysis

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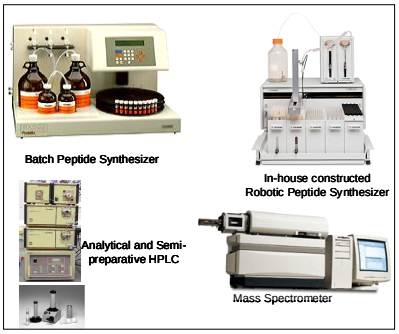
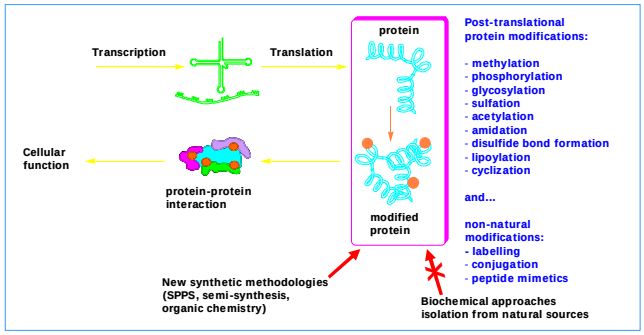


Protein modifications and their role in governing biological processes



Synthetic method	Peptide chain lenght n= number of AA
Peptide synthesis in solution	n<10
Solid Phase Peptide Synthesis (SPPS)	n<40
Native Chemical ligation (NCL)	n<200
Expressed Protein Ligation (EPL)	n>500

Native Crustacean Hyperglycemic Hormone (CHH) : a peculiar primary sequence

Glp-Val-Phe-Asp-Gln-Ala-Cys-Lys-Gly-Ile-Tyr-Asp-Arg-Ala-Ile-Phe-Lys-Lys-Leu-Asp-Arg-Val-Cys-Asp-Asp-Cys-Tyr-Asn-Leu-Tyr-Arg-Lys-Pro-Tyr-Val-Ala-Thr-Thr-Cys-Arg-Gln-Asn-Cys-Tyr-Ala-Asn-Ser-Val-Phe-Arg-Gln-Cys-Leu-Asp-Asp-Leu-Leu-Leu-Ile-Asp-Val-Val-Asp-Glu-Tyr-Ile-Ser-Gly-Val-Gln-Ile-Val-NH_2

- N-terminal pyroglutamic acid
- Phe residue in position 3 can be either L-Phe or D-Phe with different effects on bioactivity
- C-terminus amidated
- Three disulfide bonds

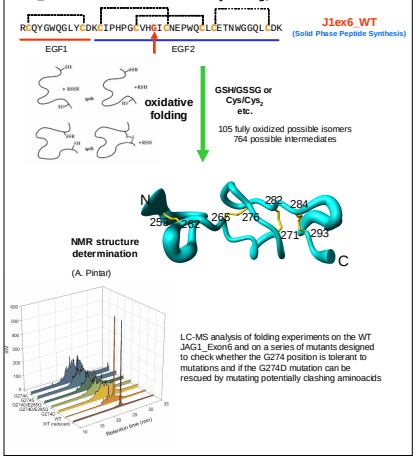
SPPS and native chemical ligation approaches enable D-Phe, Glp and C-term amide modifications

CHH_1-38_thioester (4 peptides: combinations of Glp/Gln with D/L-Phe)
Glp-Val-Phe(D/L)-Asp-Gln-Ala-Cys-Lys-Gly-Ile-Tyr-Asp-Arg-Ala-Ile-Phe-Lys-Lys-Leu-Asp-Arg-Val-Cys-Asp-Asp-Cys-Tyr-Asn-Leu-Tyr-Arg-Lys-Pro-Tyr-Val-Ala-Thr-Thr-COSR

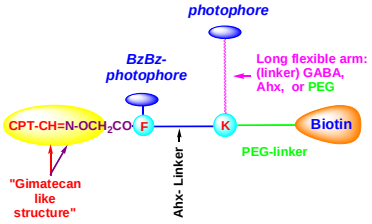
CHH_39-72_amide
Cys-Arg-Gln-Asn-Cys-Tyr-Ala-Asn-Ser-Val-Phe-Arg-Gln-Cys-Leu-Asp-Asp-Leu-Leu-Leu-Ile-Asp-Val-Val-Asp-Glu-Tyr-Ile-Ser-Gly-Val-Gln-Ile-Val-NH_2

Investigating the effects of the G274D mutation in human Jagged-1

JAG1_Exon 6 encodes an autonomously folding, EGF-like structural unit

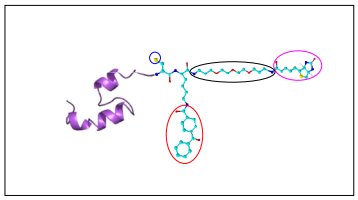


Gimatecan containing reagents for fishing protein interaction partners

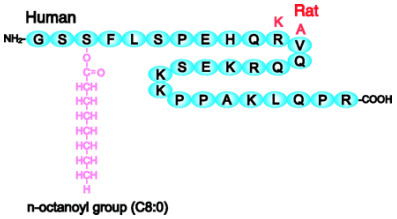


Human Parathyroid Hormone (hPTH1-34)

hPTH[1-34]→Cys(H)- Lys(BzBz)NH(CH2)3PEG2 (CH2)3 -NH(Biotinyl)



Ghrelin: a peptide isolated from the stomach consisting of 28 amino acids and n-octanoylated at Ser3, which is essential for its biological activities.



Peptides from JAGGED1, HES1 and ID2 proteins involved in NOTCH signaling pathway:

SPPS of JAG1 C-term domain peptides for understanding the effect of potential Phosphorylation sites on PDZ interaction:

J1C24 Ac-NWTNKQDNRDLESAQSLNRMEYIV
J1C24pS Ac-NWTNKQDNRDLESAQpSLNRMEYIV
J1C24pSY Ac-NWTNKQDNRDLESAQpSLNRMEpYIV

SPPS of HES1_ORANGE domain (52 aa) for biophysical studies:

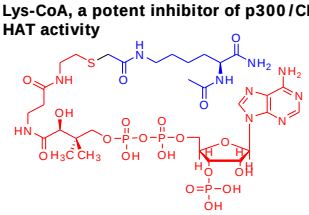
STDPSVLGKYRAGFSEAMNEVTRFLSTAEGVNTEVRTRLLGHLAN AMTQINA

bHLH domain of HES1 (SPPS+NCL, 69aa) and HLH domain of ID2 (SPPS, 41 aa) for protein-protein and protein-DNA interaction studies:

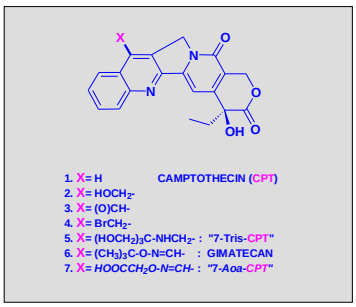
HES1_bHLH:
KPKTASEHRKSSKPIMEKRRRARINESLSCLKTLILDALKKDSSRHSKLEKAD ILEMTVKHLRNLQRAQ

ID2_HLH:
LYNMNDCYSKLKELVPSIPQNKKVSKMEILQHVIDYILDLQ

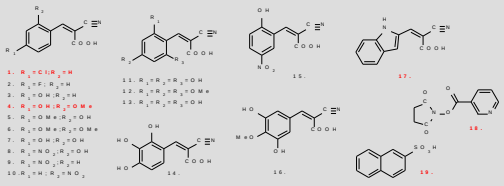
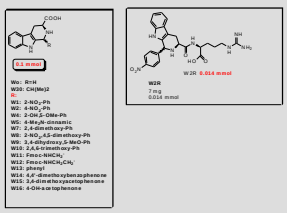
Lys-CoA, a potent inhibitor of p300/CBP HAT activity



Ac-Lys($COCH_2$-CoA)-NH_2



Synthesis and Purification of new and common MALDI matrix molecules



2,3,4,9-Tetrahydro-1H-β-carboline derivatives as potential inhibitors of alternative splicing