Universidad de Chile

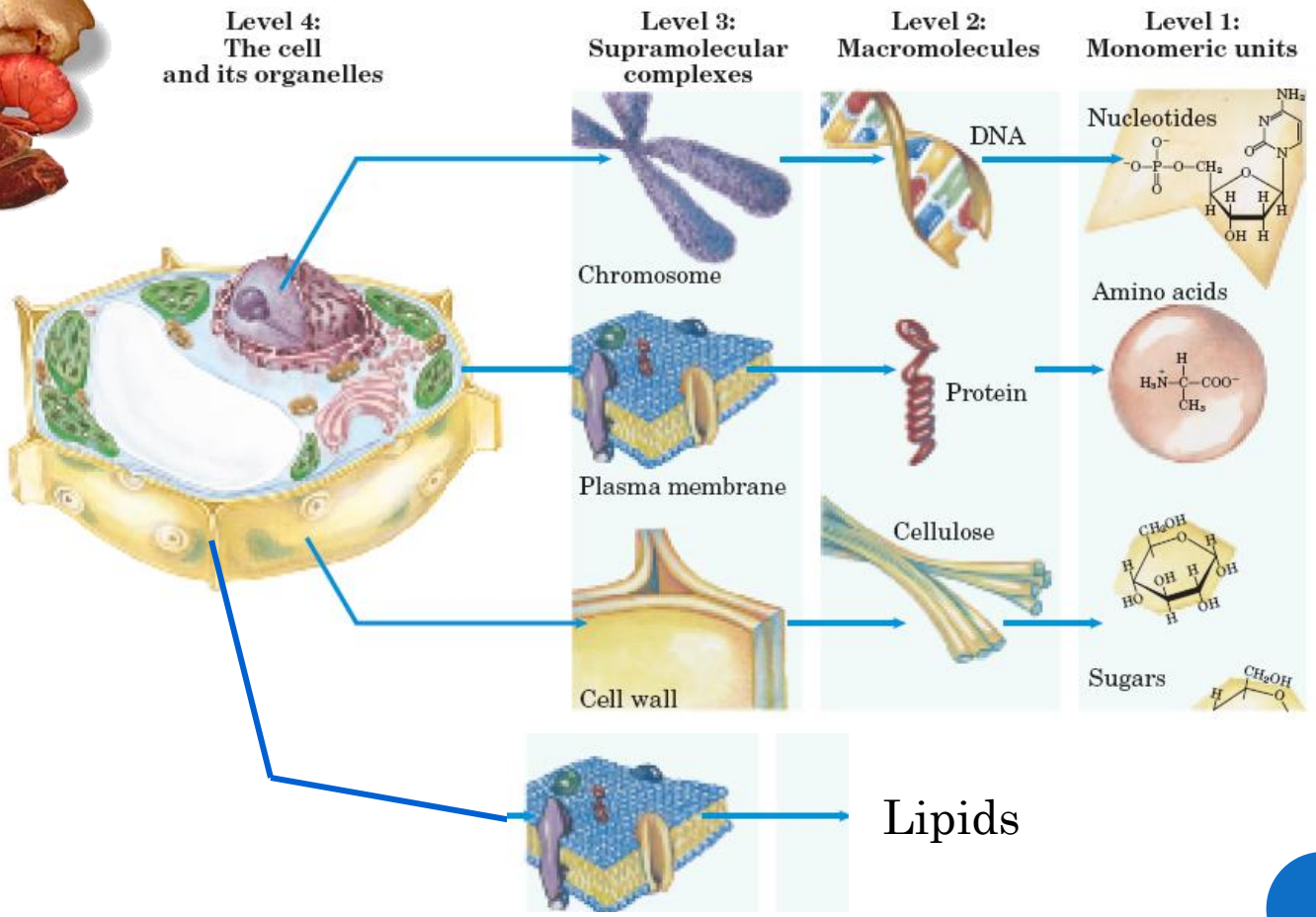
Aminoácidos y Biopéptidos

Horacio Maldonado Lorca, MSc.

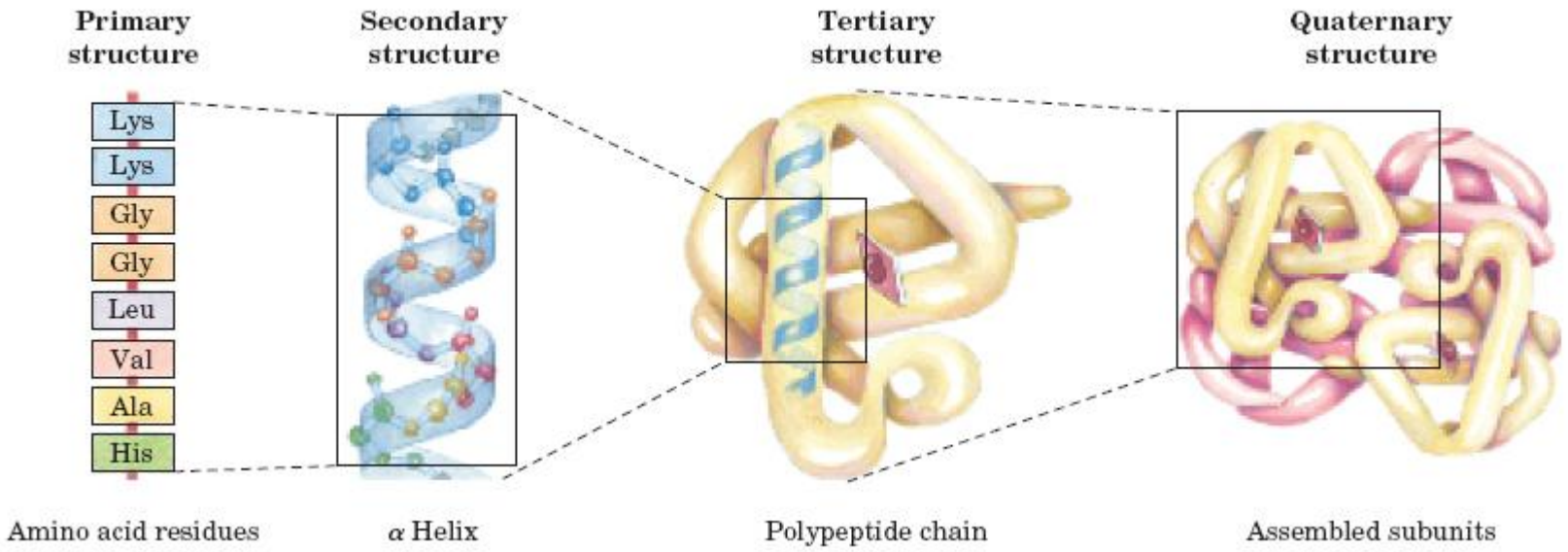
Laboratorio de Comunicaciones Celulares
Centro de Estudios Moleculares de La Célula
Facultad de Medicina
Universidad de Chile

hmaldo@Ciq.uchile.cl

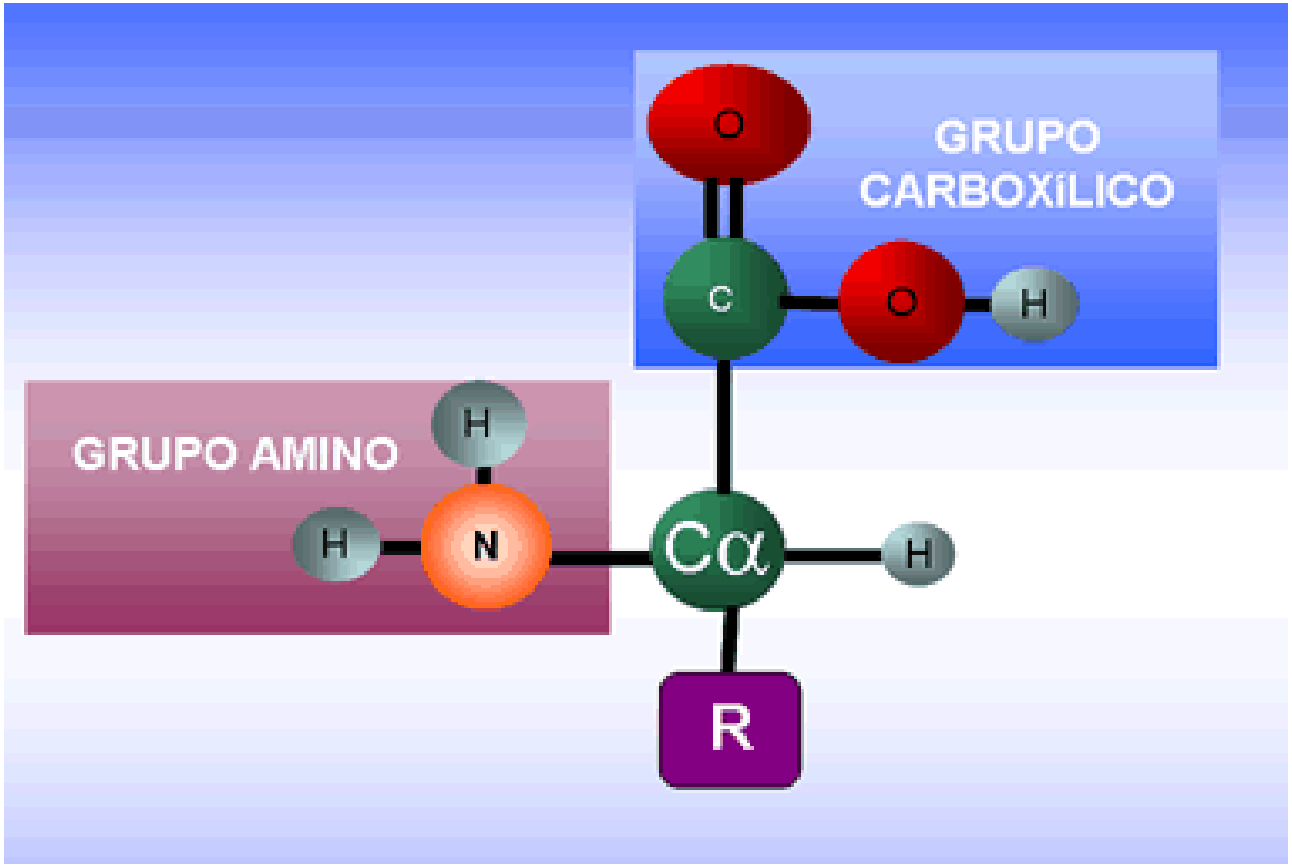
Todas las células compuestas por 4 Macromoléculas



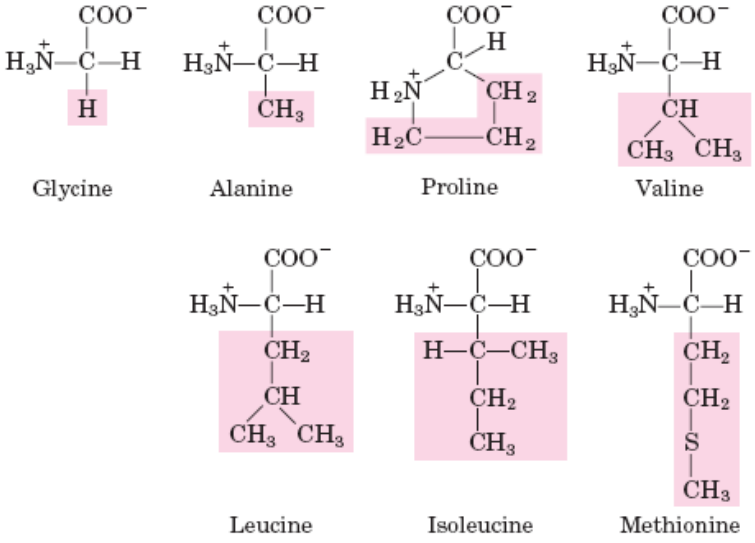
Aminoácidos Bloques fundamentales de las Proteínas



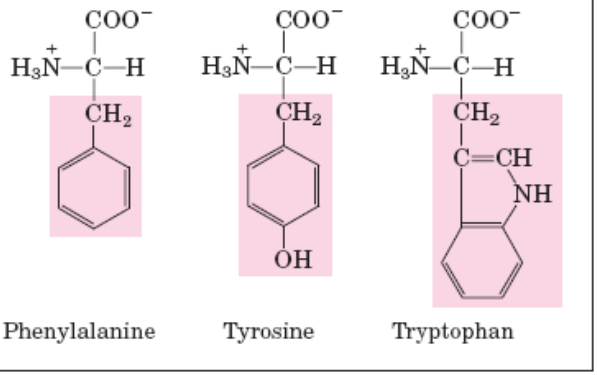
AMINOÁCIDO



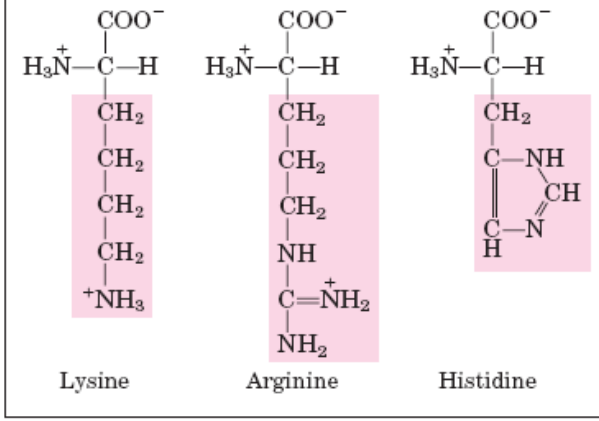
Nonpolar, aliphatic R groups



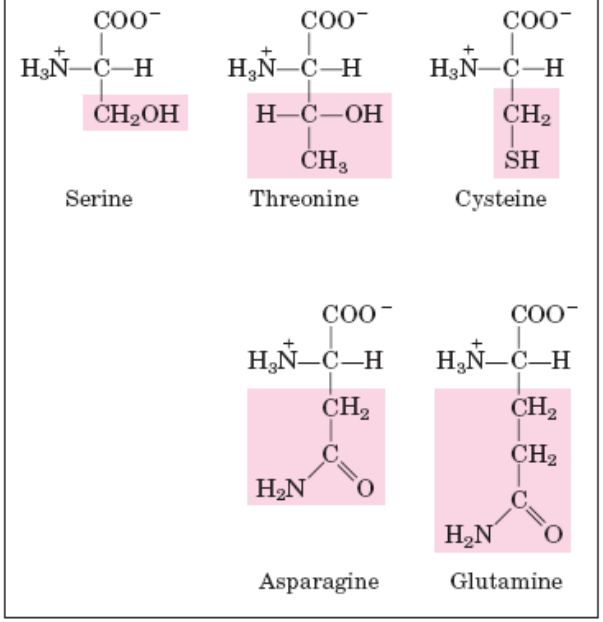
Aromatic R groups



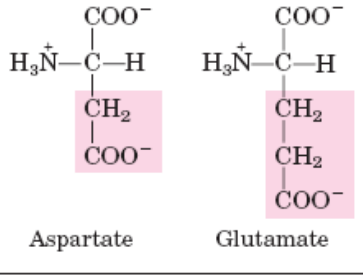
Positively charged R groups



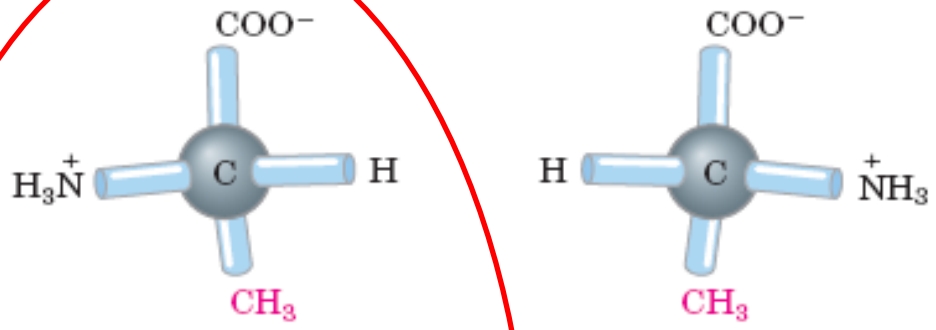
Polar, uncharged R groups



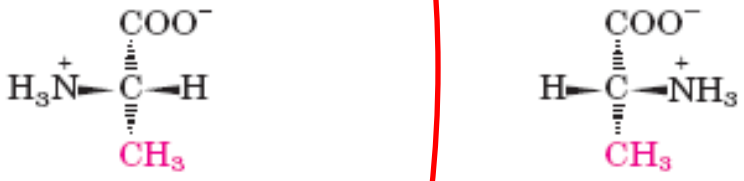
Negatively charged R groups



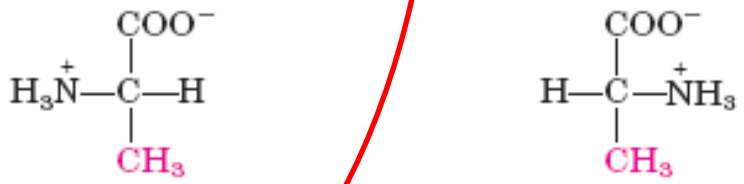
Conformación



(a) L-Alanine D-Alanine



(b) L-Alanine D-Alanine



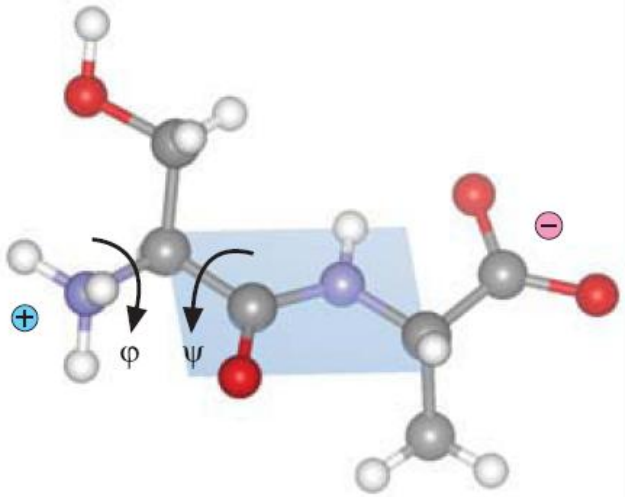
(c) L-Alanine D-Alanine

TABLE 3.15
Percentage (%) by Weight of Amino Acid in a Food Protein

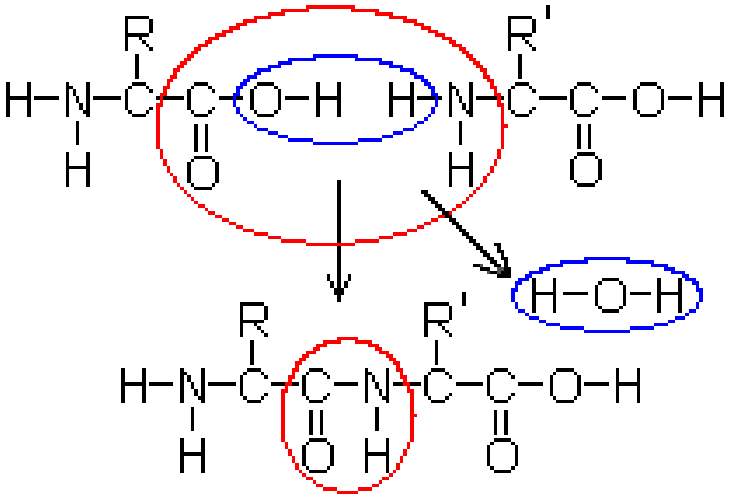
	Protein							
Amino Acid	Egg White	Tuna	Beef	Chicken	Whey	Casein	Soy	Yeast
Alanine	6.6	6.0	6.1	5.5	5.2	2.9	4.2	8.3
Arginine	5.6	6.0	6.5	6.0	2.5	3.7	7.5	6.5
Aspartic acid	8.9	10.2	9.1	8.9	10.9	6.6	11.5	9.8
Cystine	2.5	1.1	1.3	1.3	2.2	0.3	1.3	1.4
Glutamic acid	13.5	14.9	15.0	15.0	16.8	21.5	19.0	13.5
Glycine	3.6	4.8	6.1	4.9	2.2	2.1	4.1	4.8
Histidine[a]	2.2	2.9	3.2	3.1	2.0	3.0	2.6	2.6
Isoleucine[a]	6.0	4.6	4.5	5.3	6.0	5.1	4.8	5.0
Leucine[a]	8.5	8.1	8.0	7.5	9.5	9.0	8.1	7.1
Lysine[a]	6.2	9.2	8.4	8.5	8.8	3.8	6.2	6.9
Methionine[a]	3.6	3.0	2.6	2.8	1.9	2.7	1.3	1.5
Phenylalanine[a]	6.0	3.9	3.9	4.0	2.3	5.1	5.2	4.7
Praline	3.8	3.5	4.8	4.1	6.6	10.7	5.1	4.0
Serine	7.3	4.0	3.9	3.4	5.4	5.6	5.2	5.1
Threonine[a]	4.4	4.4	4.0	4.2	6.9	4.3	3.8	5.8
Tryptophan[a]	1.4	1.1	0.7	1.2	2.2	1.3	1.3	1.6
Tyrosine	2.7	3.4	3.2	3.4	2.7	5.6	3.8	5.0
Valine[a]	7.0	5.2	5.0	5.0	6.0	6.6	5.0	6.2

[a] Essential amino acids.

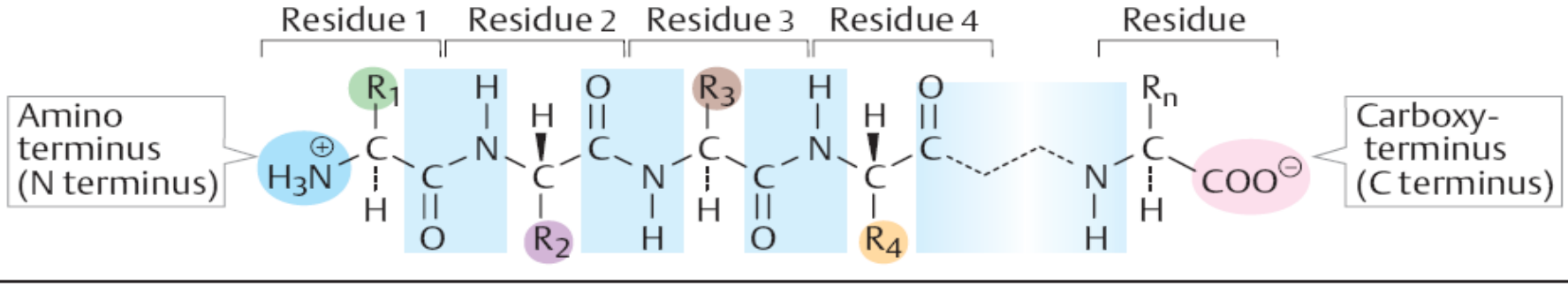
A. Peptide bonds

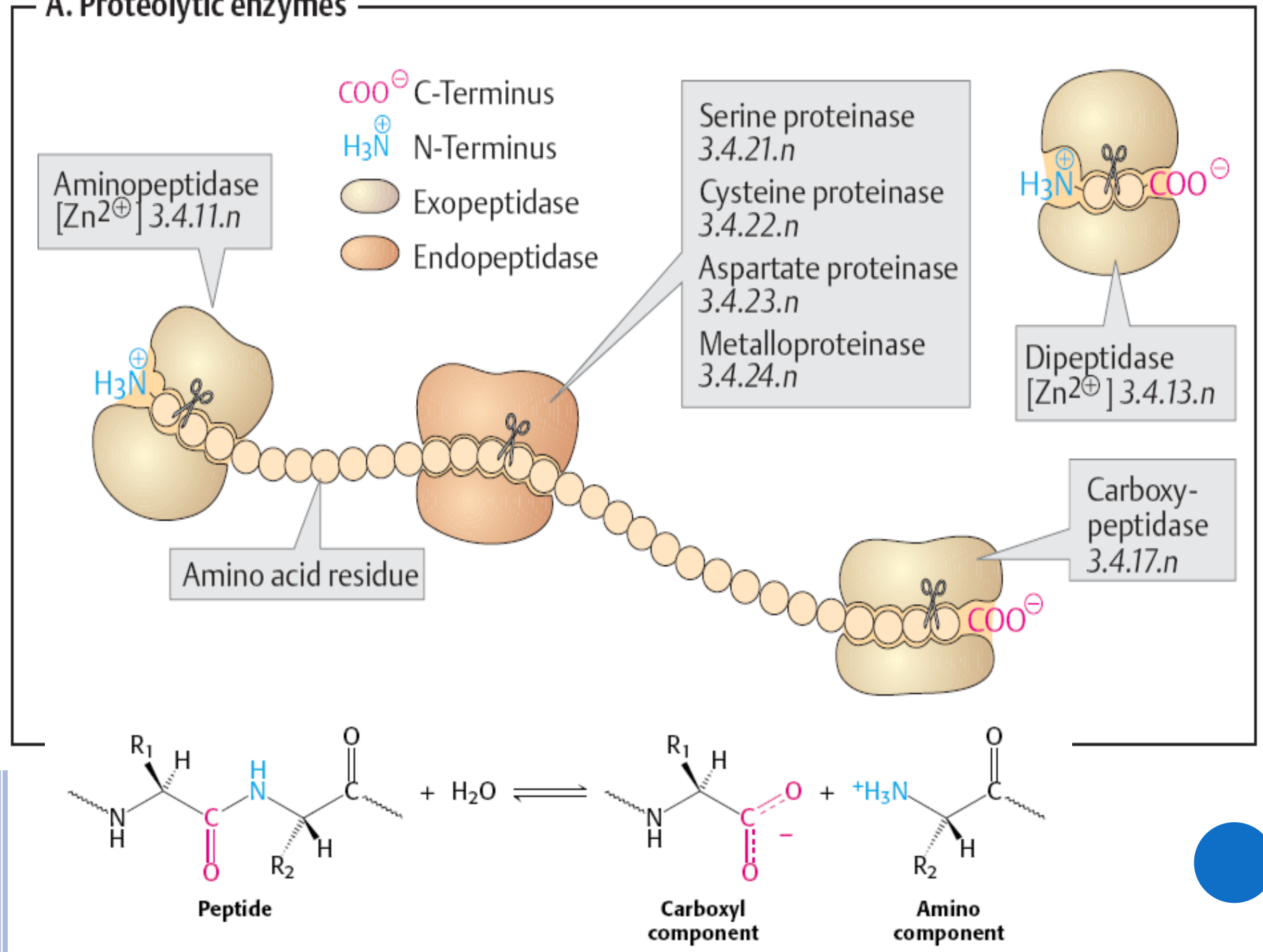


Seryl alanine
(Ser-Ala, $^{\oplus}H_3N$-Ser-Ala-$COO^{\ominus}$, SA)

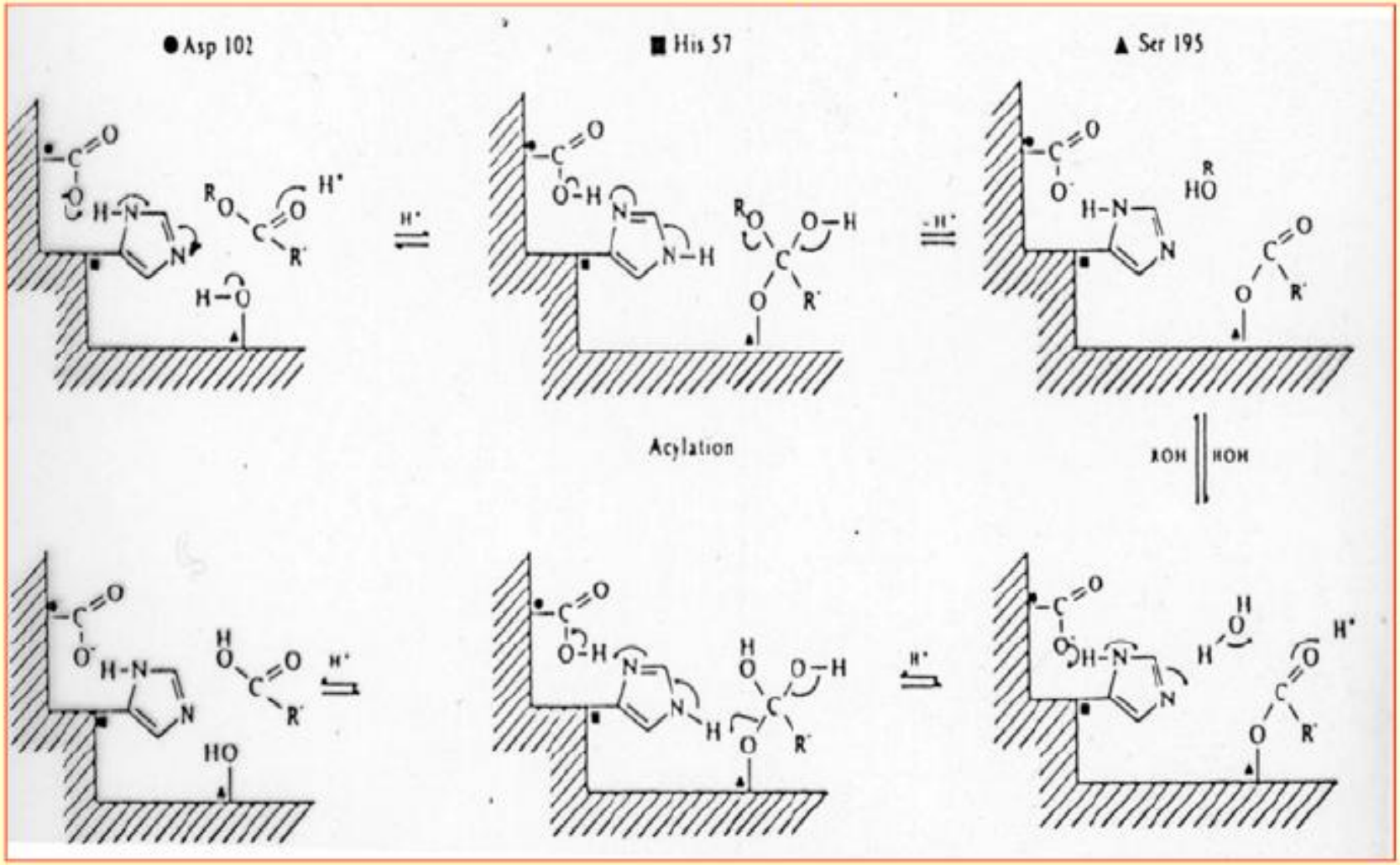


C. Peptide nomenclature




A. Proteolytic enzymes
COO⊖ C-Terminus
H3N⊕ N-Terminus
Exopeptidase
Endopeptidase
Aminopeptidase [Zn2⊕] 3.4.11.n
Serine proteinase 3.4.21.n
Cysteine proteinase 3.4.22.n
Aspartate proteinase 3.4.23.n
Metalloproteinase 3.4.24.n
H3N⊕ COO⊖
Dipeptidase [Zn2⊕] 3.4.13.n
Amino acid residue
Carboxy-peptidase 3.4.17.n
COO⊖
Peptide
Carboxyl component
Amino component

Reacción catalizada por quimotripsina. Catálisis nucleofílica y ácido básica

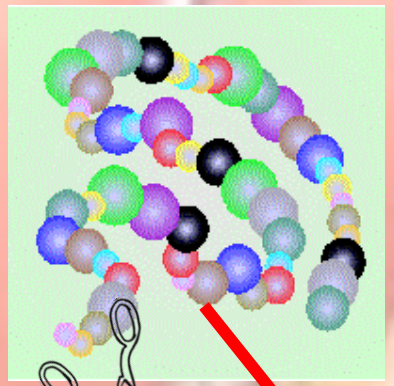


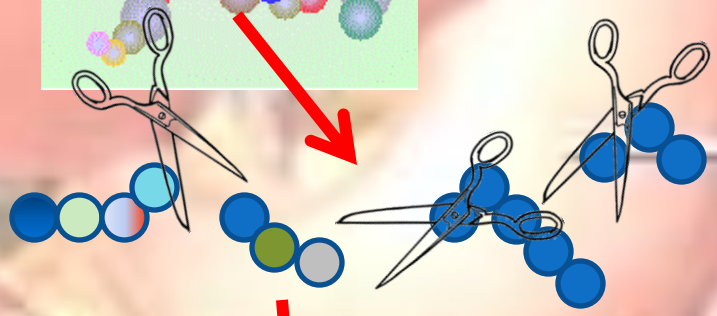
Biopéptidos Alimenticios y Nutriofármacos

Fragmentos específicos de las proteínas de la dieta que además de su valor nutrimental tienen una actividad biológica y regulan procesos fisiológicos

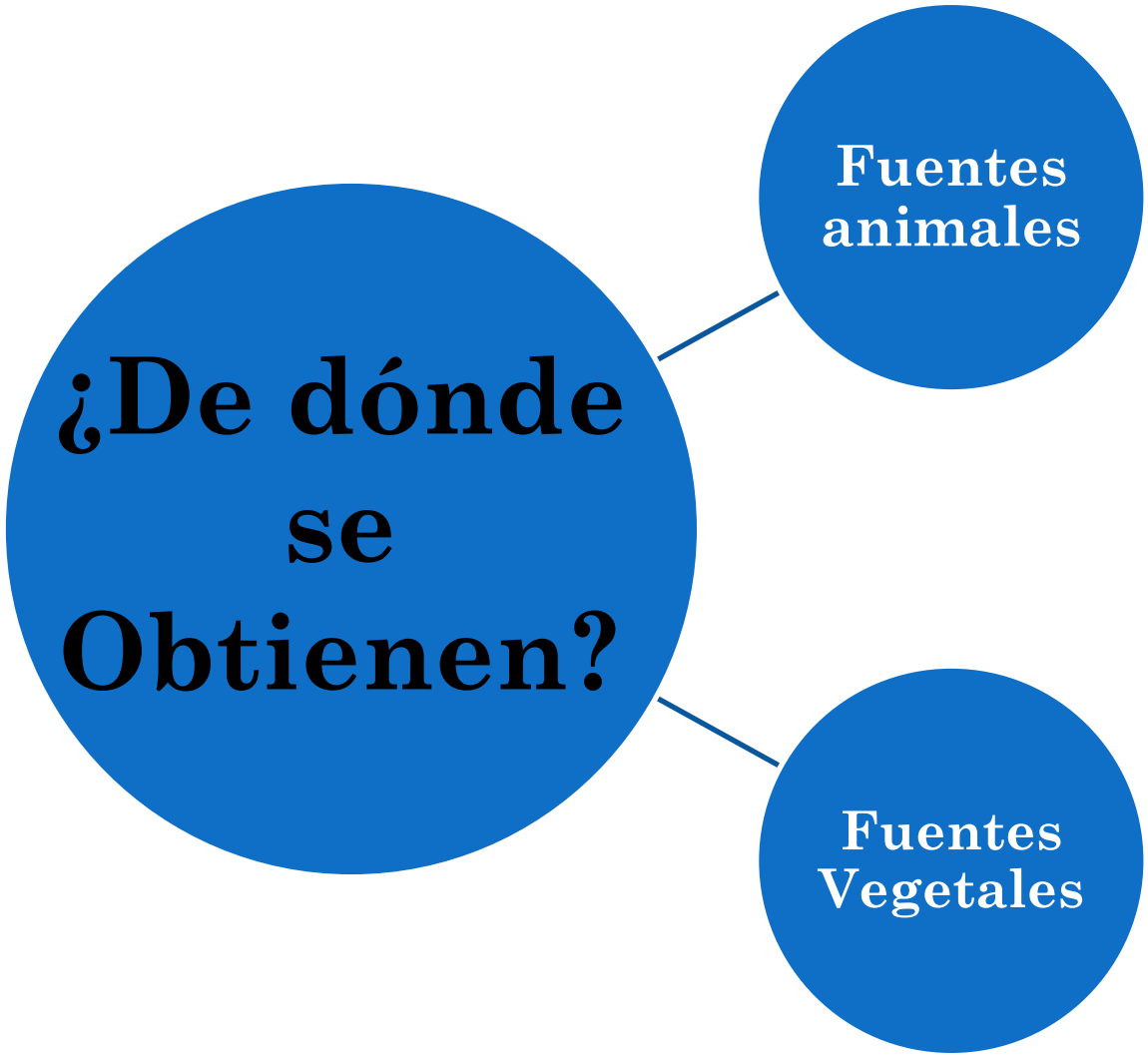
Su función fisiológica puede ejercerse mediante su absorción a nivel del intestino y transportados por la circulación sanguínea, o localmente en el tubo digestivo.

¿Que son?





Ingreso torrente sanguineo y destinación a blanco



- Leche
- Huevo
- Plasma
- Musculo de Pescado

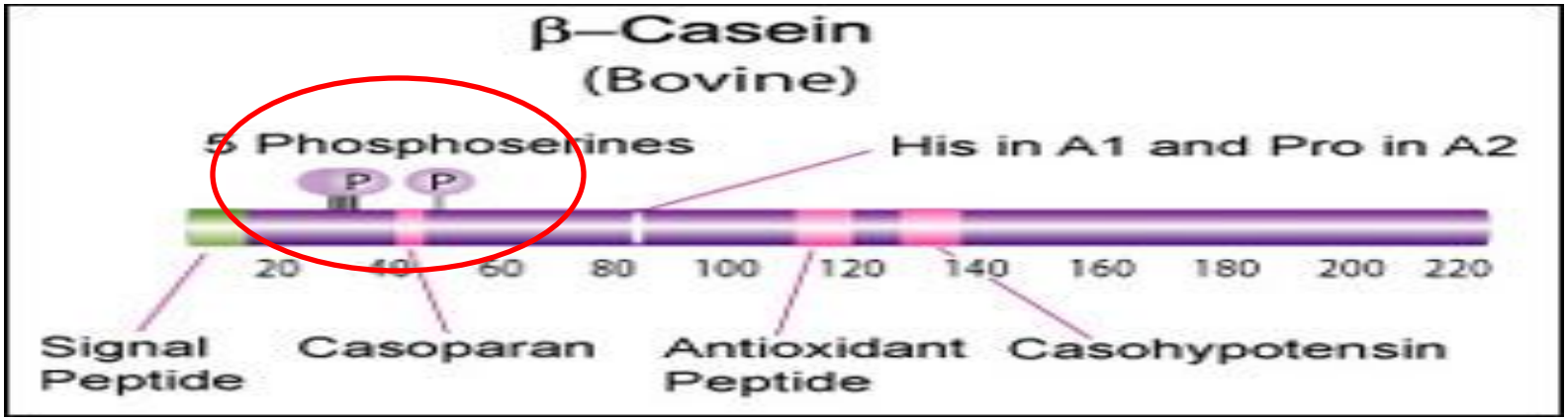
- Soya
- Garbanzo
- Girasol
- Colsa
- Lupino

Tabla 1. Péptidos bioactivos y sus efectos beneficiosos para el organismo

Péptidos	Efecto beneficioso
Inmunomoduladores	Estimulan la respuesta inmune
Inhibidores del enzima convertidor de angiotensina	Reducen el riesgo de padecer enfermedades cardiovasculares
Antioxidantes	Previenen enfermedades degenerativas y envejecimiento
Reguladores del transito intestinal	Mejoran la digestión y absorción
Reguladores de la proliferación intestinal	Reducen la proliferación de tumores cancerígenos
Antimicrobianos	Reducen el riesgo de infecciones
Hipocolesterolémicos	Reducen el riesgo de padecer enfermedades cardiovasculares
Anticoagulantes	Reducen los riesgos de padecer trombos

Actividad biológica de los péptidos de diferentes fuentes

Caseíno-Fosfopéptidos (CPPs) primeros péptidos bioactivos descubiertos (Mellander 1950)



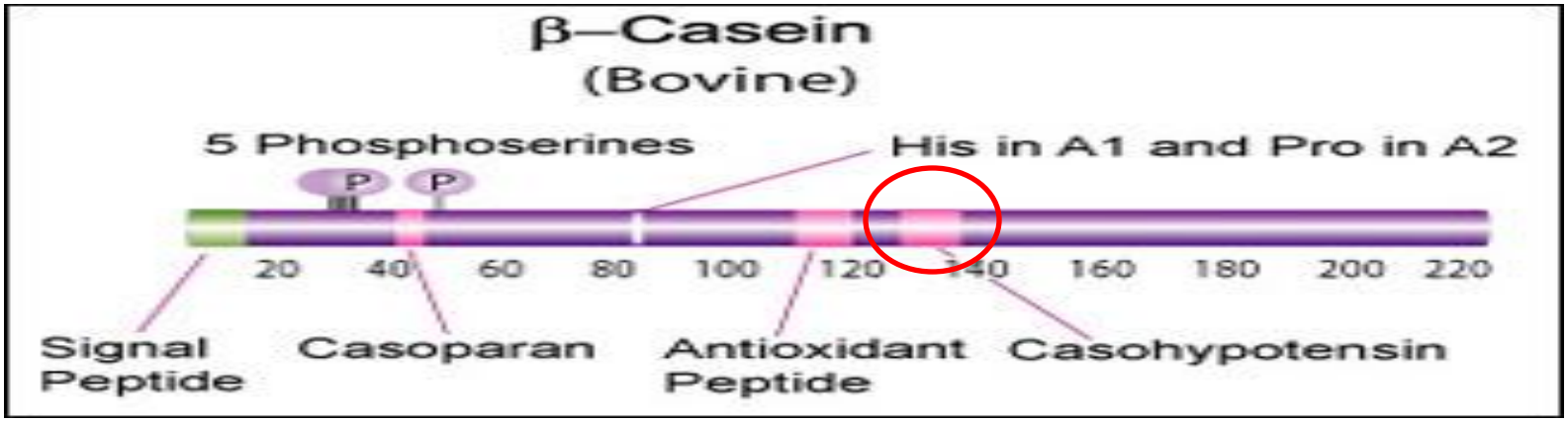
Péptido que presenta fosforilación provenientes de la caseína (αs1, αs2 y β-caseína) de la leche bovina

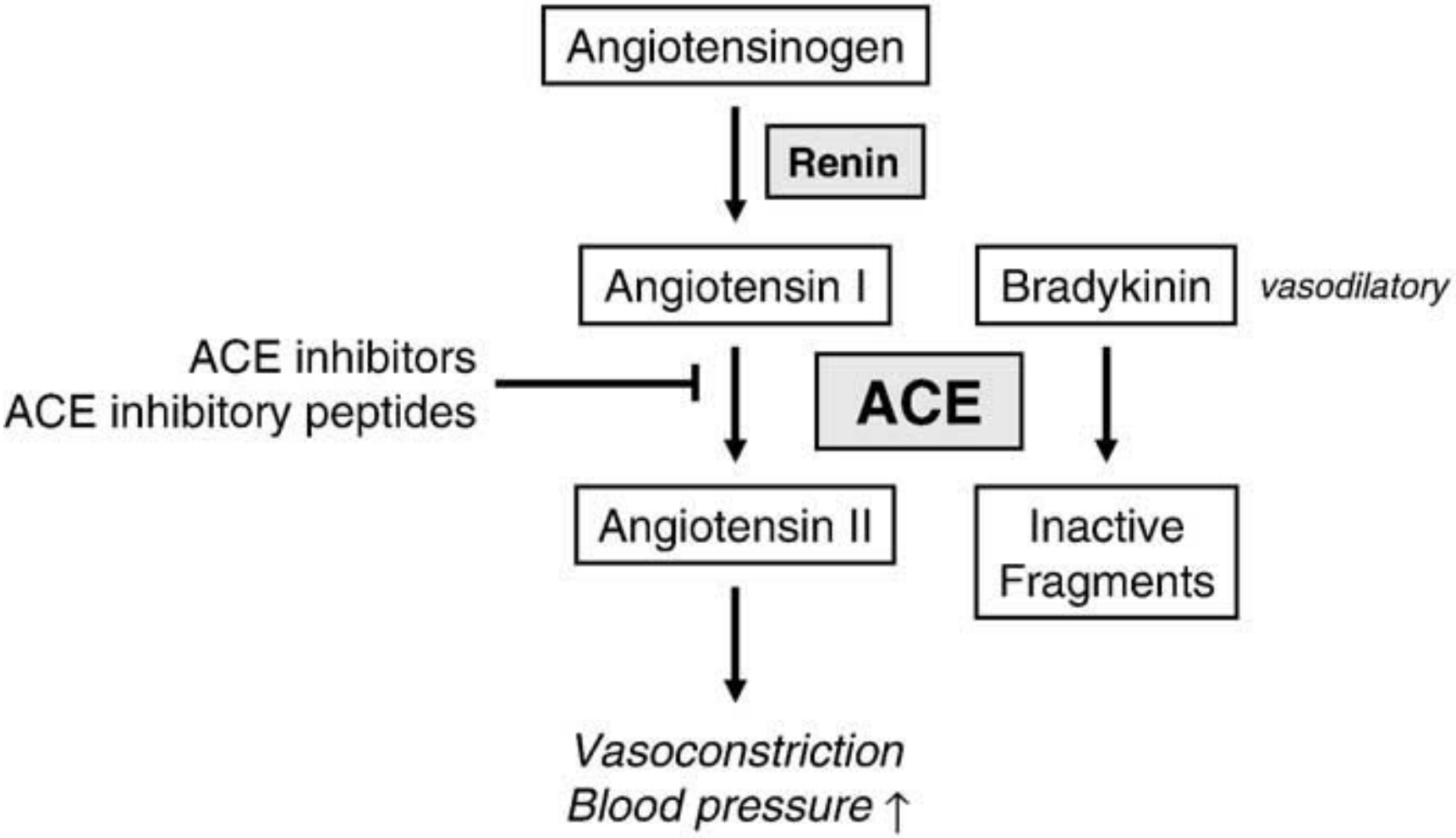
Observó que aumentaba la calcificación de Huesos
de forma independiente de la Vitamina D

Acción : CBPs pueden formar organofosfatos solubles y estos pueden transportar diferentes minerales , especialmente calcio


Blood pressure
Cholesterol levels
Morphine like action
Beta Casein
Gut absorption
Neurological conditions
Gut mobility
Immune response

CASEÍNAS Y PRESIÓN ARTERIAL




Angiotensinogen
Renin
Angiotensin I
Bradykinin
vasodilatory
ACE inhibitors
ACE inhibitory peptides
ACE
Angiotensin II
Inactive Fragments
Vasoconstriction
Blood pressure ↑

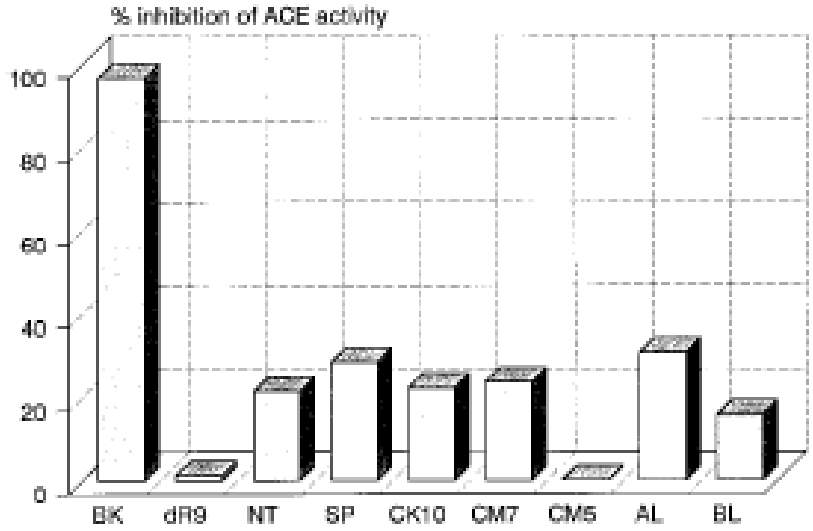


FIGURE 2 Inhibition of ACE activity by endogenous and milk protein derived peptides, respectively, at a 100 μmol/L concentration. The data represent the percentage of inhibition of activity compared with control (no peptide inhibitor present).[13] BK: bradykinin (RPPGFSPFR); dR9: desArg^9-bradykinin; NT: neurotensin (pyroELYENKPRPYIL); SP: substance P (RPKPQQFFGLM·NH_2); CK10: β-casokinin-10 (sequence 18); CM7: β-casomorphin-7 (sequence 2); CM5: β-casomorphin-5 (sequence 3); AL: α-lactorphin (sequence 7); BL: β-lactorphin (sequence 8).

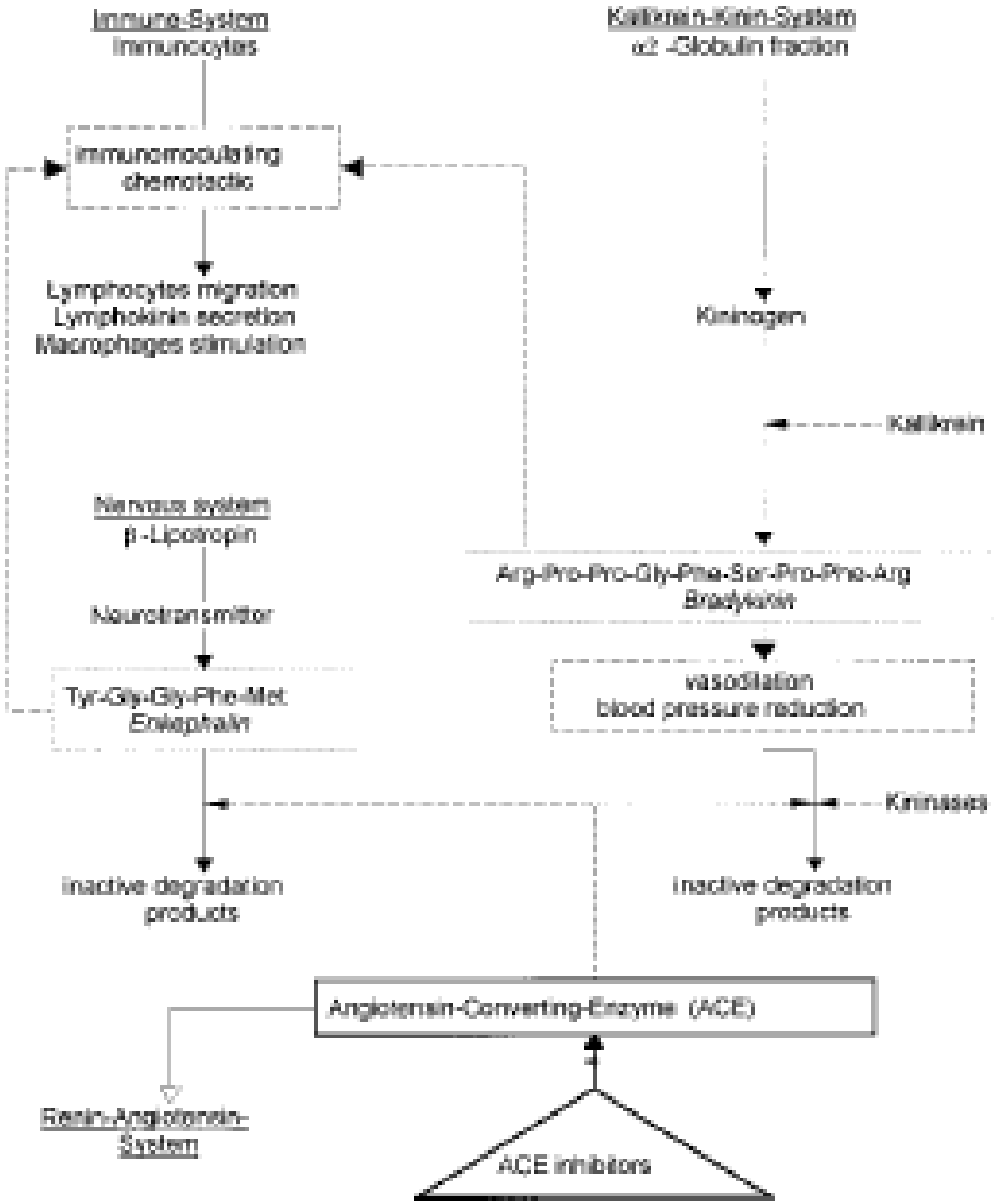
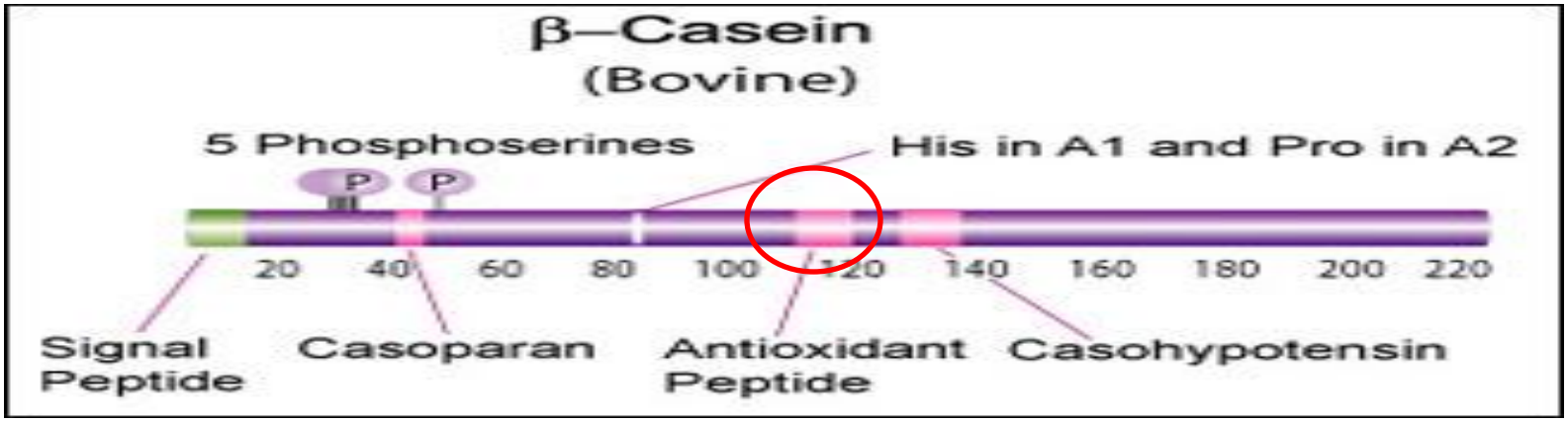


FIGURE 3 Endogenous ACE inhibitors as well as food-derived peptides, like casokinins, may modulate several systems for regulation of blood pressure, immune defense, and neuroendocrine information transfer in the organism. Renin–angiotensin system (not outlined): ACE catalyzes the liberation of the dipeptide HL from the C-terminus of angiotensin I, which is released from angiotensinogen by renin, and thereby generating angiotensin II (ERVYIHPF), which is one of the most potent vasoconstrictor agents known.

Acciones antioxidantes



ACCIONES ANTIOXIDANTES

Source of peptides	Characteristic[a]	Preparation	Activity
Rice endosperm protein	FRDEHKK and KHDRGDEF	Five different proteases, Neutrase was the most effective	Inhibition of autooxidation, DPPH, superoxide and hydroxyl radical-scavenging activity
Peanut kernels protein	Molecular weight 3–5 kDa	Different proteases esperase was the most effective	Reducing power, Inhibition of human LDL oxidation, DPPH radical-scavenging and metal-chelating activity
Algae protein waste	VECYGPNRPQF	Pepsin	Hydroxyl, superoxide, peroxyl, DPPH and ABTS radicals scavenging activity, protective effects on DNA and prevention of cellular damage
Peptide from frog skin	LEELEEELEGCE	Alcalase, neutrase, pepsin, papain, α-chymotrypsin and trypsin	Inhibition of lipid peroxidation, DPPH, hydroxyl, superoxide, peroxyl radical scavenger
Sunflower protein	Hydrolysate with 37% DH, enriched in certain amino acids, such as histidine and arginine	Pepsin and pancreatin	Copper-chelating activity
Alfalfa leaf protein	Molecular weight <1000 Da	Alcalase	Reducing power, radical chelating and scavenging activities
Zein hydrolysate	Contains up to 6.5% free amino acids and the rest short peptides (<500 Da)	Pepsin, pancreatin and alcalase	Radical chelating and scavenging activities
Corn gluten meal	Peptides fraction of 500–1500 Da, 41.12% hydrophobic amino acids and ~12.7% aromatic amino acids	Alcalase	Lipid peroxidation, reducing power, scavenging activity
Peanut protein	Not specified	Alcalase	Inhibition of linoleic acid autoxidation, radical-scavenging activity, reducing power, and inhibitor of liver lipid oxidation
Yam ichyoimo tubers	Not specified	Autolysis and enzymatic digestion (trypsin, pepsin, papain)	Inhibition of linoleic acid oxidation, radical-scavenging activity
Soy protein fractions	Peptides with molecular weight of <10 kDa	Ultrafiltration and hydrolysis by Flavourzyme	Antioxidant activity in emulsion, radical scavengers, reducing power

La composición aminoacídica brinda características anti oxidantes

Aromatic AAs (Tyr, His, Trp, Phe)	Converting radicals to stable molecules by donating electron, while keeping their own stability via resonance structure Improving the radical-scavenging properties of the amino acids residues [76]
Hydrophobic AAs	Enhancing the solubility of peptide in lipid which facilitates accessibility to hydrophobic radical species and to hydrophobic PUFAs [6,75,89], Gly as hydrogen donor [75]
Acidic and basic AAs	Carboxyl and amino groups in the side chains as chelator of metal ions [90], as hydrogen donor
Cysteine	SH group as radical scavenger [72], protecting tissue from oxidative stress, improving the glutathione activity [83]

Producción de biopéptidos

La aplicación de tecnologías en el procesamiento debe enfocarse en dos aspectos importantes: (a) mantener al máximo la bioactividad durante el procesamiento y almacenamiento de los productos formulados y (b) la liberación de los componentes bioactivos deseados en los sitios requeridos del cuerpo

Vías de entrada a la célula

Possible routes of intact absorption of peptides.

Transportation route	Remarks
Paracellular route	Diffusion through the tight junctions between cells by energy independent passive diffusion process
Passive diffusion	Diffusion through transcellular by energy independent passive diffusion process
Via transporter	Exit of some peptides from the enterocyte into the portal circulation via a peptide transporter located intestinal basolateral membrane
Endocytosis	Binding of molecules to the cells and their absorption into cell via vesiculization
Lymphatic system	Absorption of peptides from interstitial space into the intestinal lymphatic system

¿Como se producen?

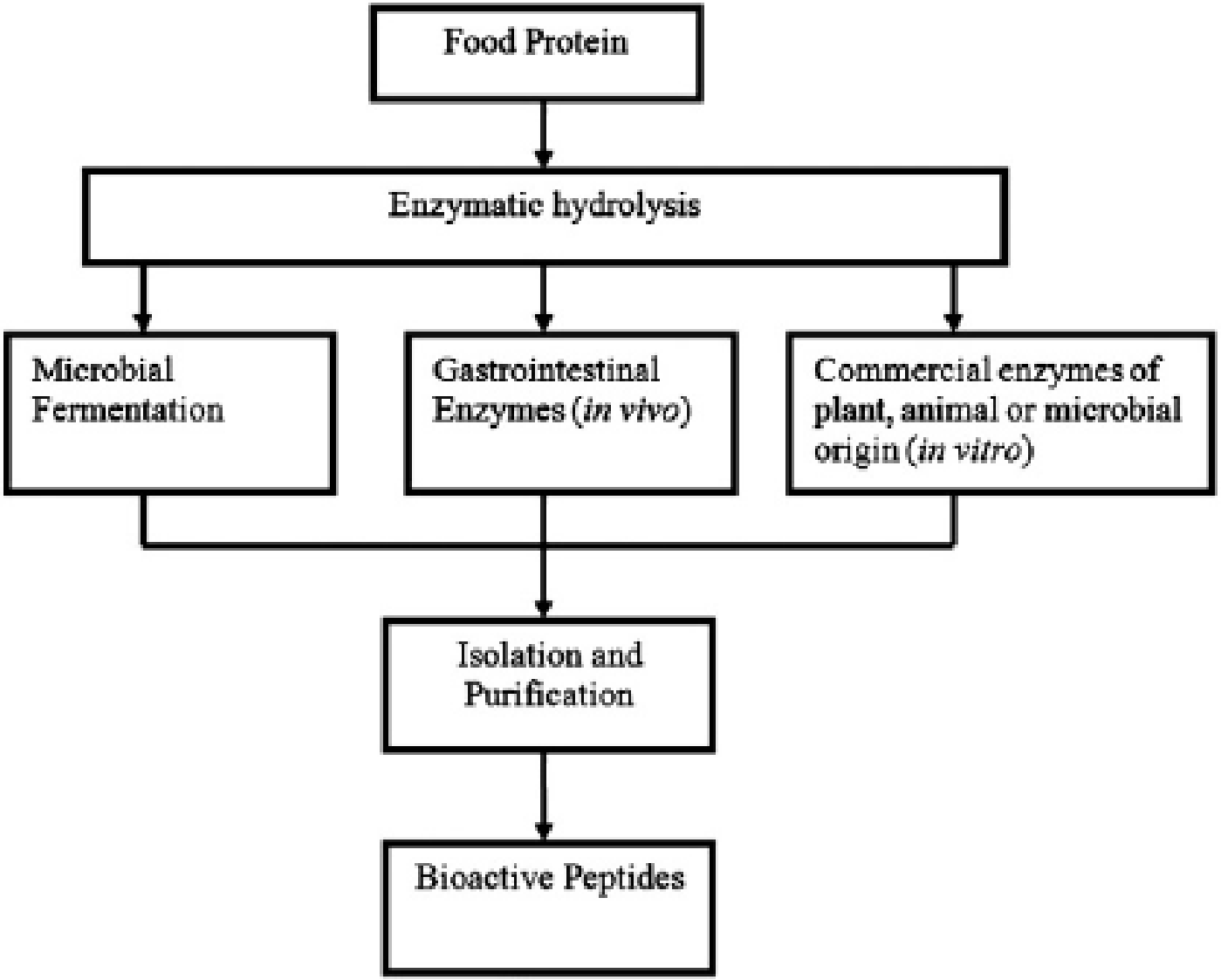
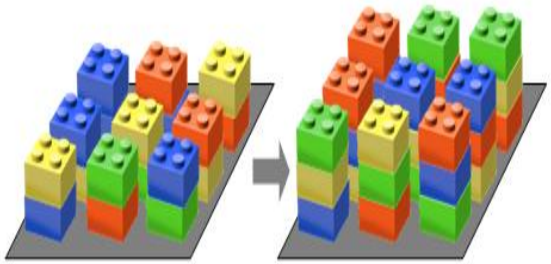
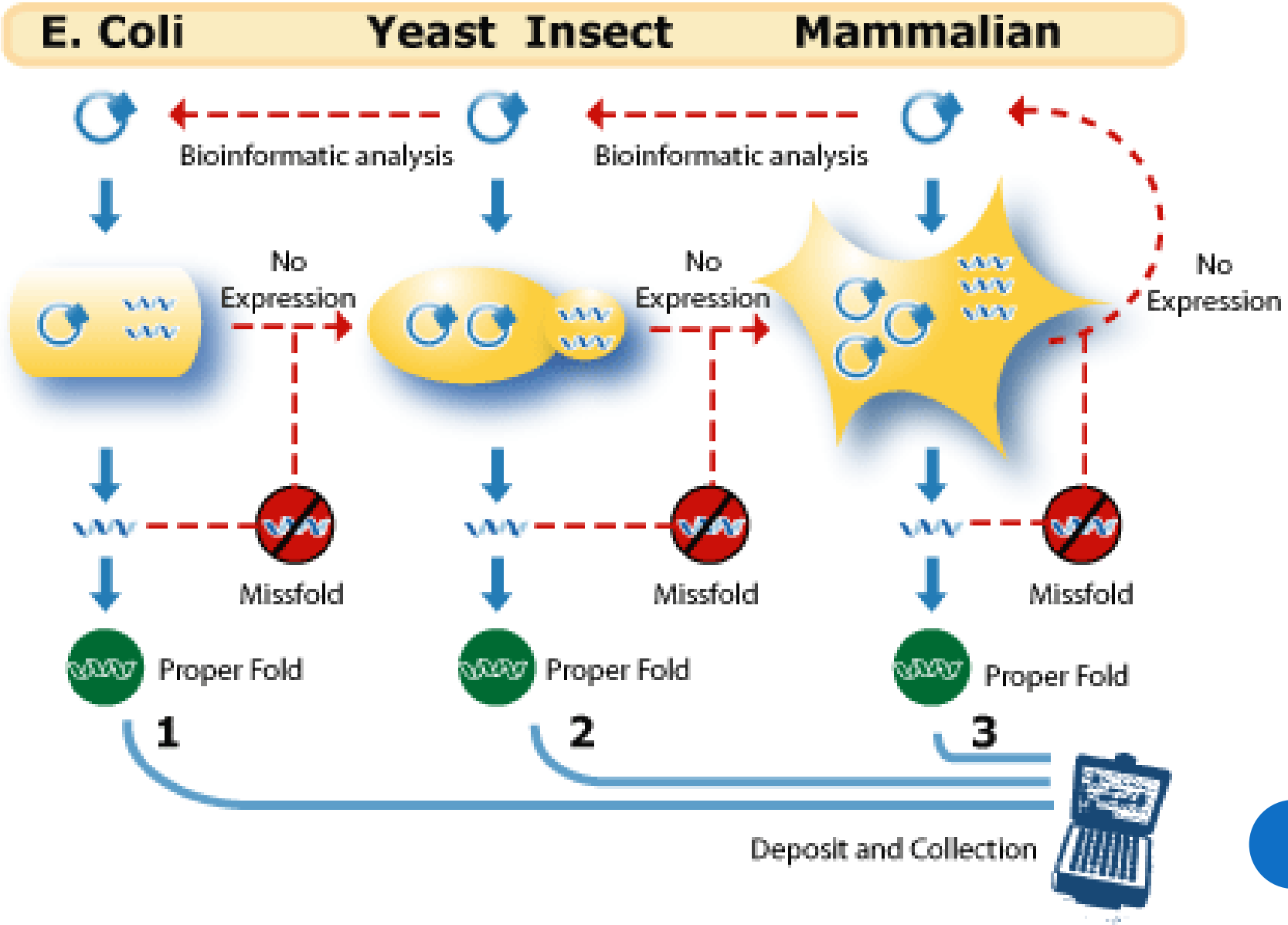


Fig. 1. Production of bioactive peptides.

Nuevas estrategias

Síntesis Química	ADN Recombinante	Síntesis Enzimática
		


E. Coli
Yeast
Insect
Mammalian
Bioinformatic analysis
Bioinformatic analysis
No Expression
No Expression
No Expression
Missfold
Missfold
Missfold
Proper Fold
Proper Fold
Proper Fold
1
2
3
Deposit and Collection

Protein source	Treatment	Peptide	Activity
Casein	Trypsin Trypsin-chymotrypsin Pepsin	Phe-Phe-Val-Ala-Pro Val-Glu-Pro-Ile-Pro-Tyr Gly-Leu-Phe Tyr-Phe-Tyr-Pro-Glu-Leu	ACE-inhibition Immunomodulation Antioxidative
β-lactoglobulin	Trypsin	Ile-Pro-Ala-Val-Phe-Lys Trp-Leu-Ala-His-Lys Ala-Leu-Pro-Met-His-Ile-Arg	Bactericidal ACE-inhibition
Soybean Genetically modified soybean protein	Proteinase S Alcalase Trypsin & chymotrypsin	Leu-Leu-Pro-His-His Low molecular weight peptides Arg-Pro-Leu-Lys-Pro-Trp	Antioxidative Antihypertensive Antihypertensive
Wheat germ	Alkaline protease	Ile-Val-Tyr	ACE-inhibition Antihypertensive
Rice albumin	Trypsin	Gly-Tyr-Pro-Met-Tyr-Pro-Leu-Pro-Arg	Ileum contracting Immunostimulation

Porcine Skeletal Muscle	Thermolysin	Ile-Thr-Thr-Asn-Pro Thr-Asn-Pro	ACE-inhibition Antihypertensive ACE-inhibition
Gelatin (Alaska Pollack skin)	Alcalase, Pronase E	Gly-Glu-Hyp-Gly-Pro-Hyp-Gly-Pro-His-Gly-Pro-Hyp-Gly-Pro-Hyp-Gly Gly-Pro-Hyp-Gly-Pro-Hyp-Gly-Pro-Hyp-Gly-Pro-Hyp-Gly	Antioxidative
Chicken	Thermolysin	Ile-Lys-Trp Leu-Lys-Pro	ACE-inhibition Antihypertensive
Egg ovalbumin	Chymotrypsin Pepsin Pepsin	Arg-Ala-Asp-His-Pro-Phe Leu-Trp Glu-Arg-Lys-Ile-Lys-Val-Tyr-Leu Phe-Arg-Ala-Asp-His-Pro-Phe-Leu	Vasodilatation ACE-inhibition Antihypertensive Antihypertensive