Al-Farabi Kazakh National University
Higher School of Medicine
Department of Fundamental Medicine

Regulomics and metabolomics

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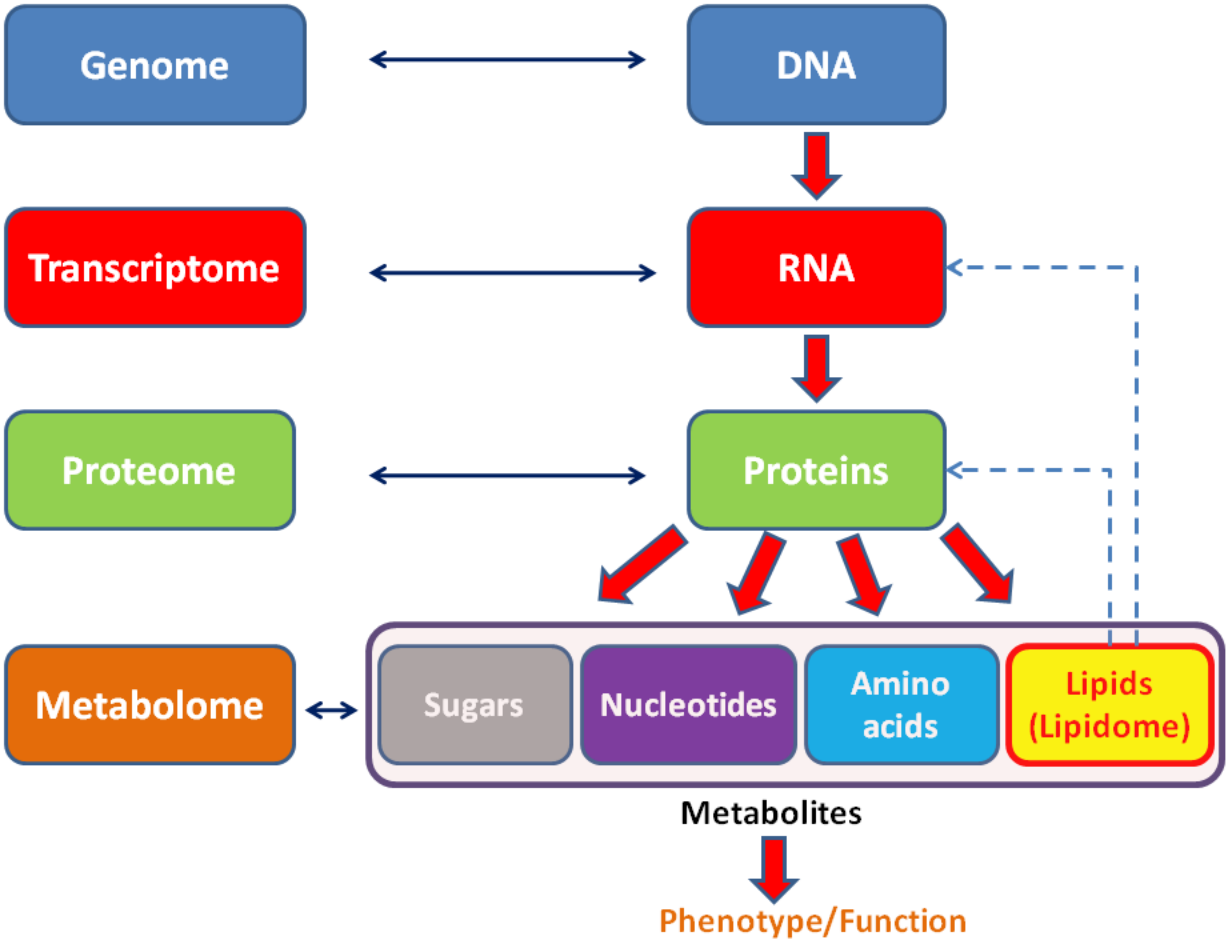
LEARNING OUTCOMES
As a result of the lesson you will be able to:

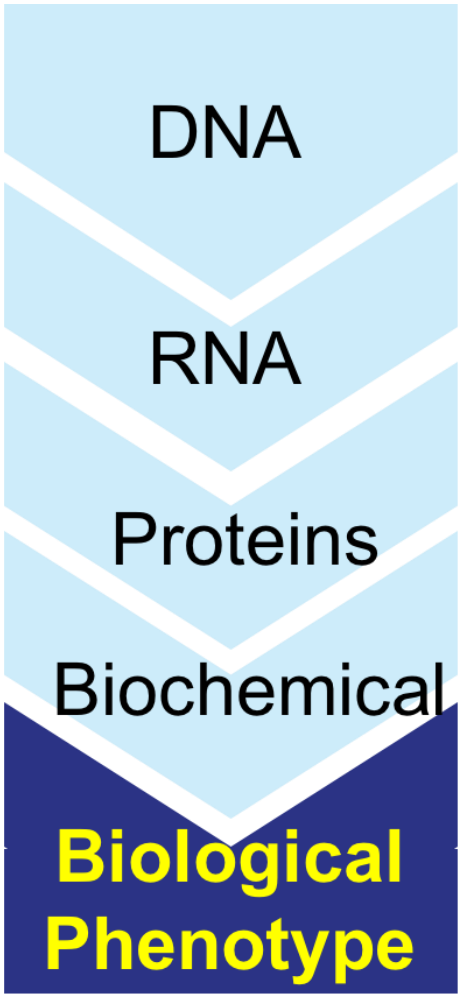
- 1. Give the definition to the terms “metabolites”, “metabolism”, “regulome”, “regulomics”, “metabolome”, “metabolomics”.
- 2. Explain the mechanisms of enzyme activity regulation, give the specific examples.
- 3. Briefly describe the metabolism of all organic and non-organic substances in human organism (metabolism of proteins, carbohydrates, lipids, minerals, salts and water) and its regulation (hormonal, neural and biochemical).
- 4. Characterize the methods of researching the metabolism.
- 5. Explain how metabolic disturbances connected with different human diseases, give the specific examples.

Definitions

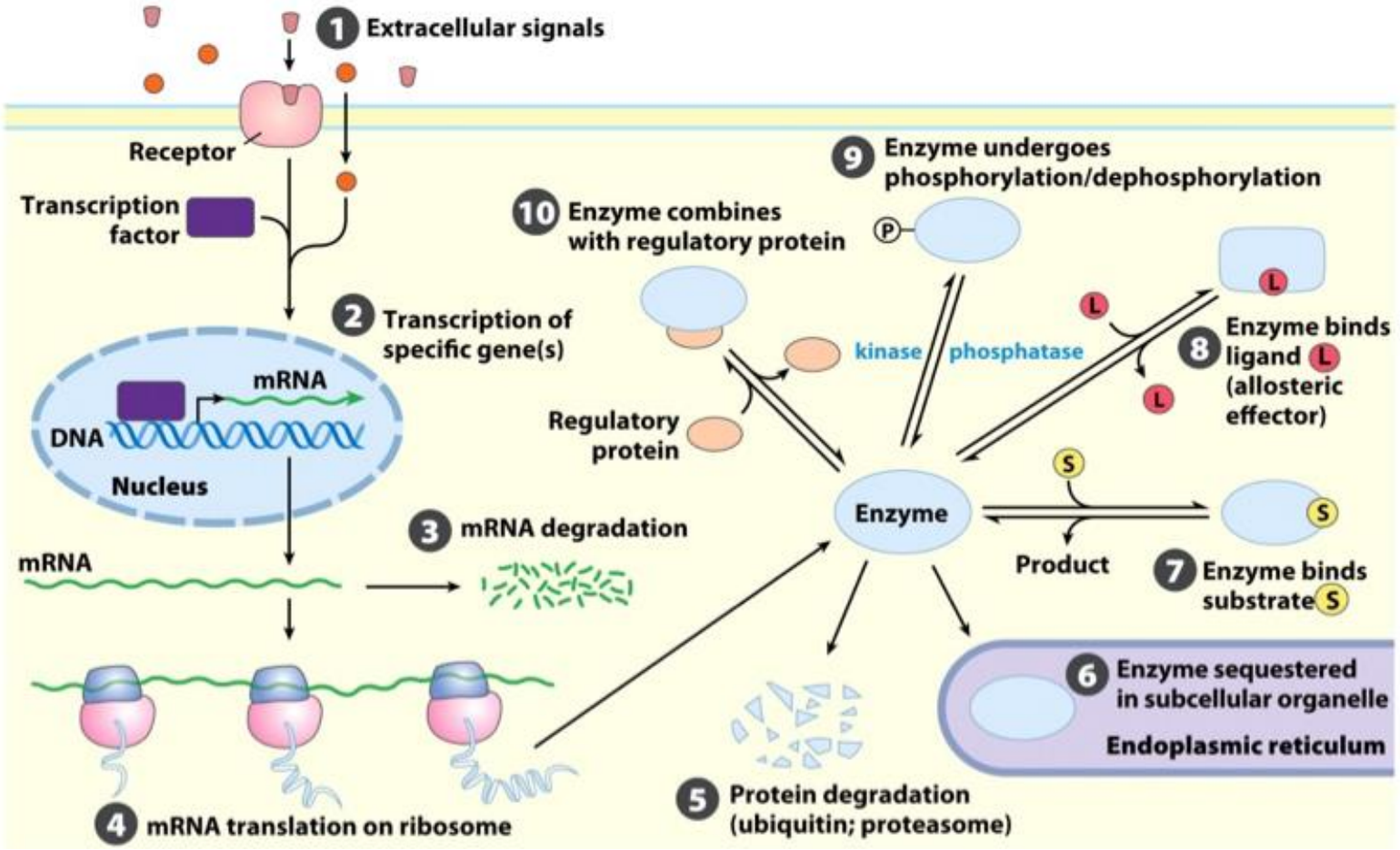
Metabolomics is the scientific study of chemical processes involving **metabolites**, the small molecule substrates, intermediates and products of cell **metabolism**. Specifically, metabolomics is the "systematic study of the unique chemical fingerprints that specific cellular processes leave behind", the study of their small-molecule metabolite profiles.[1] The **metabolome** represents the complete set of metabolites in a biological cell, tissue, organ or organism, which are the end products of cellular processes.[2] Messenger RNA (mRNA), gene expression data and proteomic analyses reveal the set of gene products being produced in the cell, data that represents one aspect of cellular function. Conversely, metabolic profiling can give an instantaneous snapshot of the physiology of that cell,[3] and thus, metabolomics provides a direct "functional readout of the physiological state" of an organism.[4] One of the challenges of systems biology and functional genomics is to integrate genomic, transcriptomic, proteomic, and metabolomic information to provide a better understanding of cellular biology.



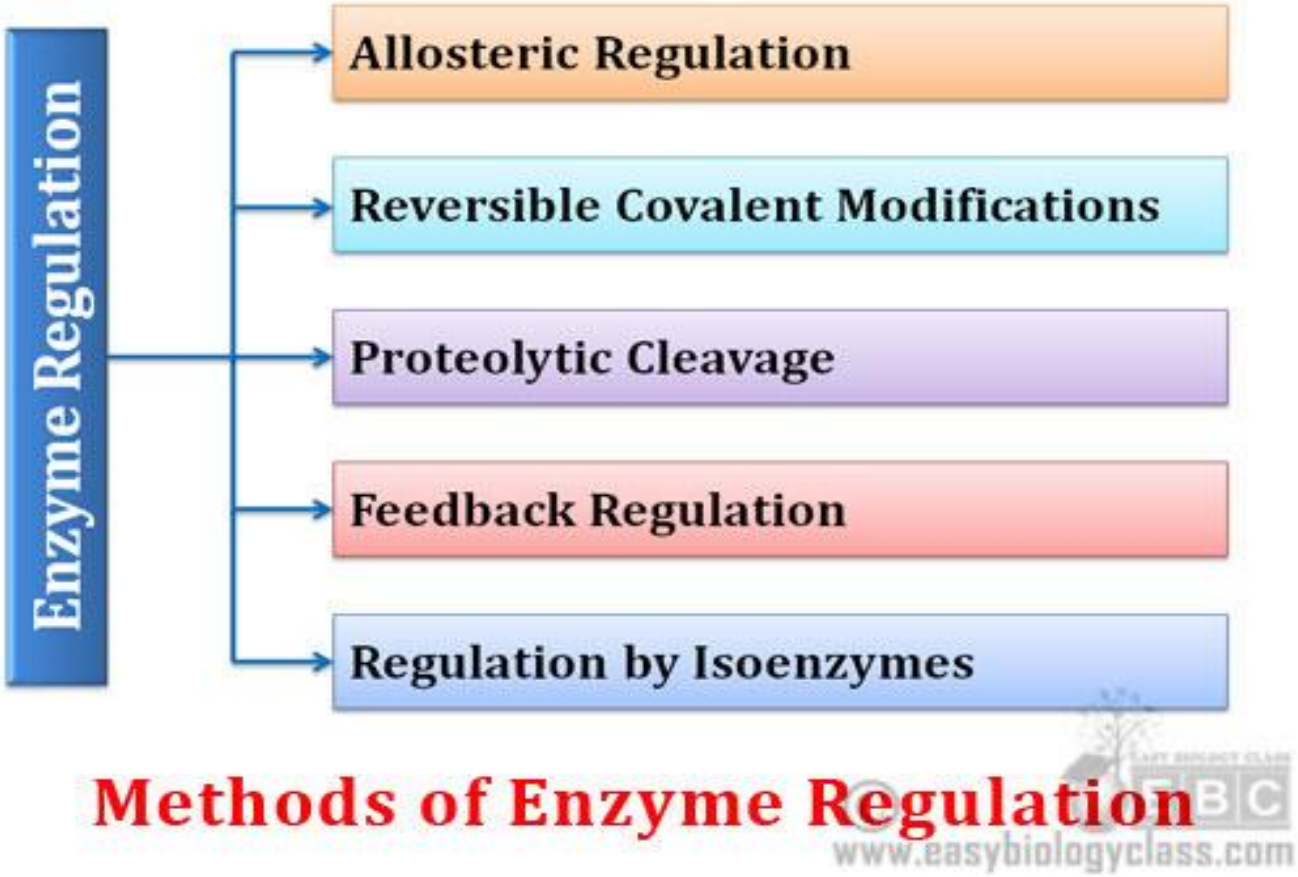
https://en.wikipedia.org/wiki/Lipidomics#/media/File:Metabolomics_schema.png



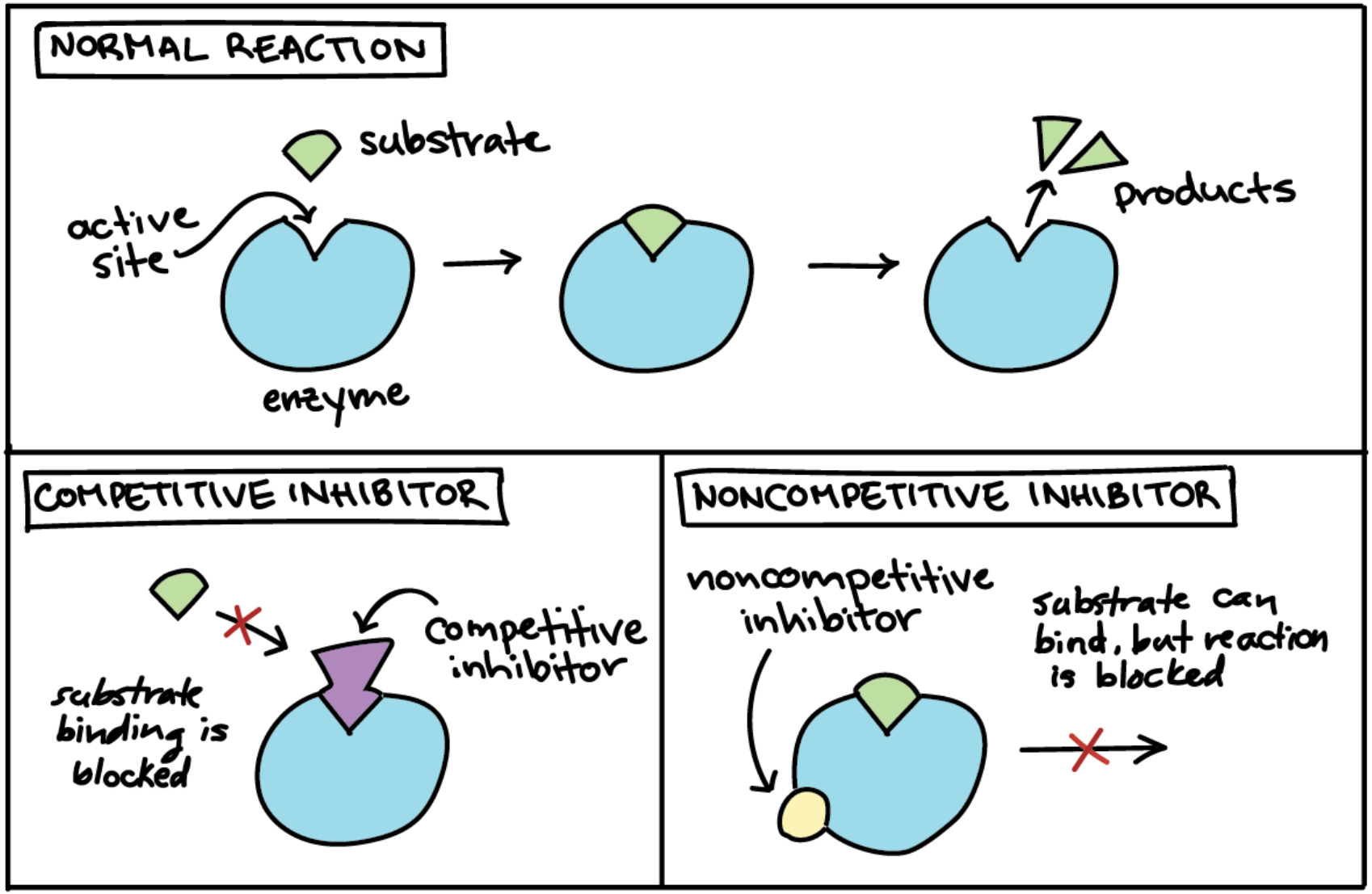
https://en.wikipedia.org/wiki/Metabolomics#/media/File:The_central_dogma_of_biology_showing_the_flow_of_information_from_DNA_to_the_phenotype._Associated_with_each_stage_is_the_corresponding_systems_biology_tool_from_genomics_to_genomics_to_metabolomics.png



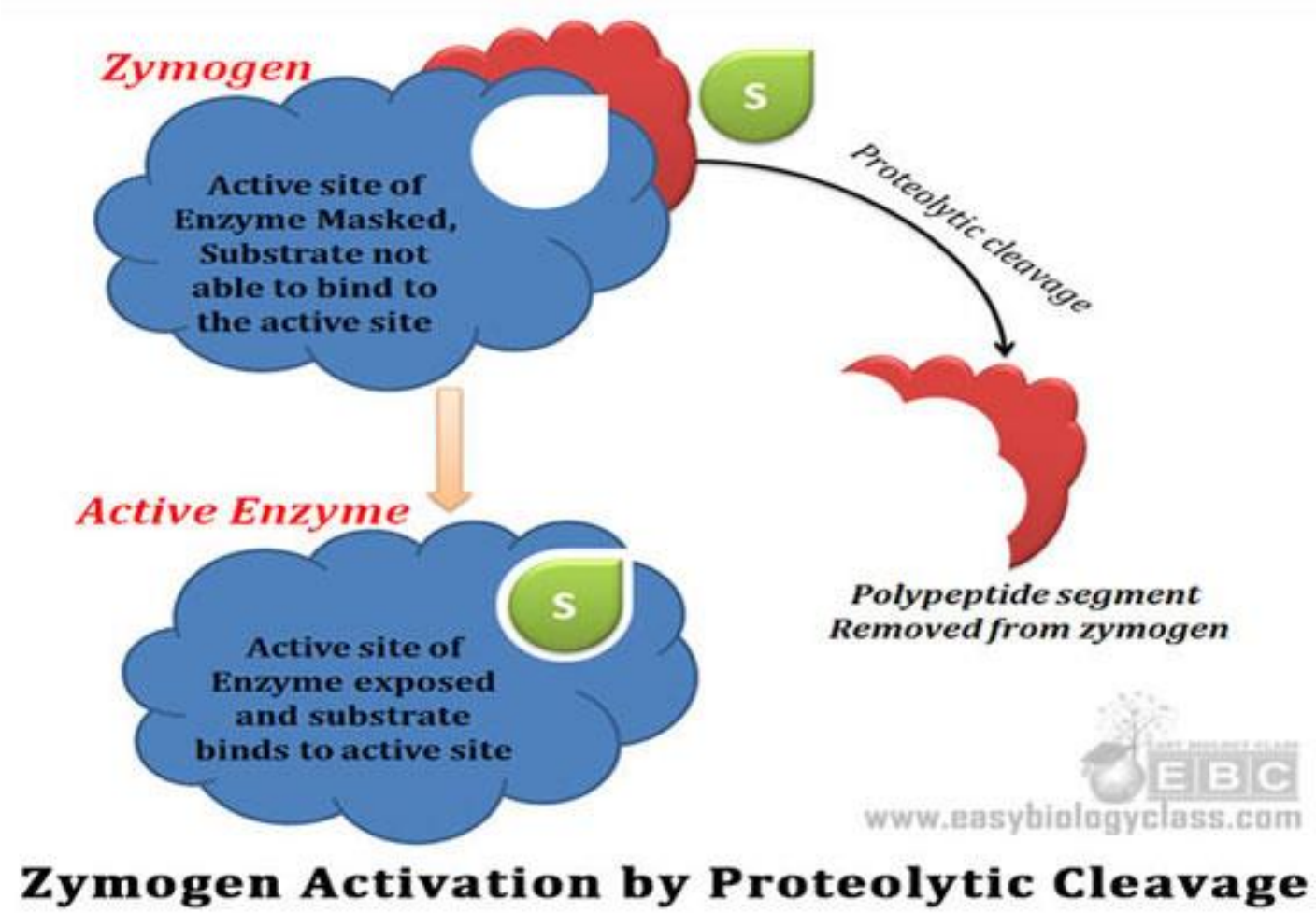
Enzyme Regulation
chegg.com



Regulatory Enzyme and Enzyme Regulation
easybiologyclass.com

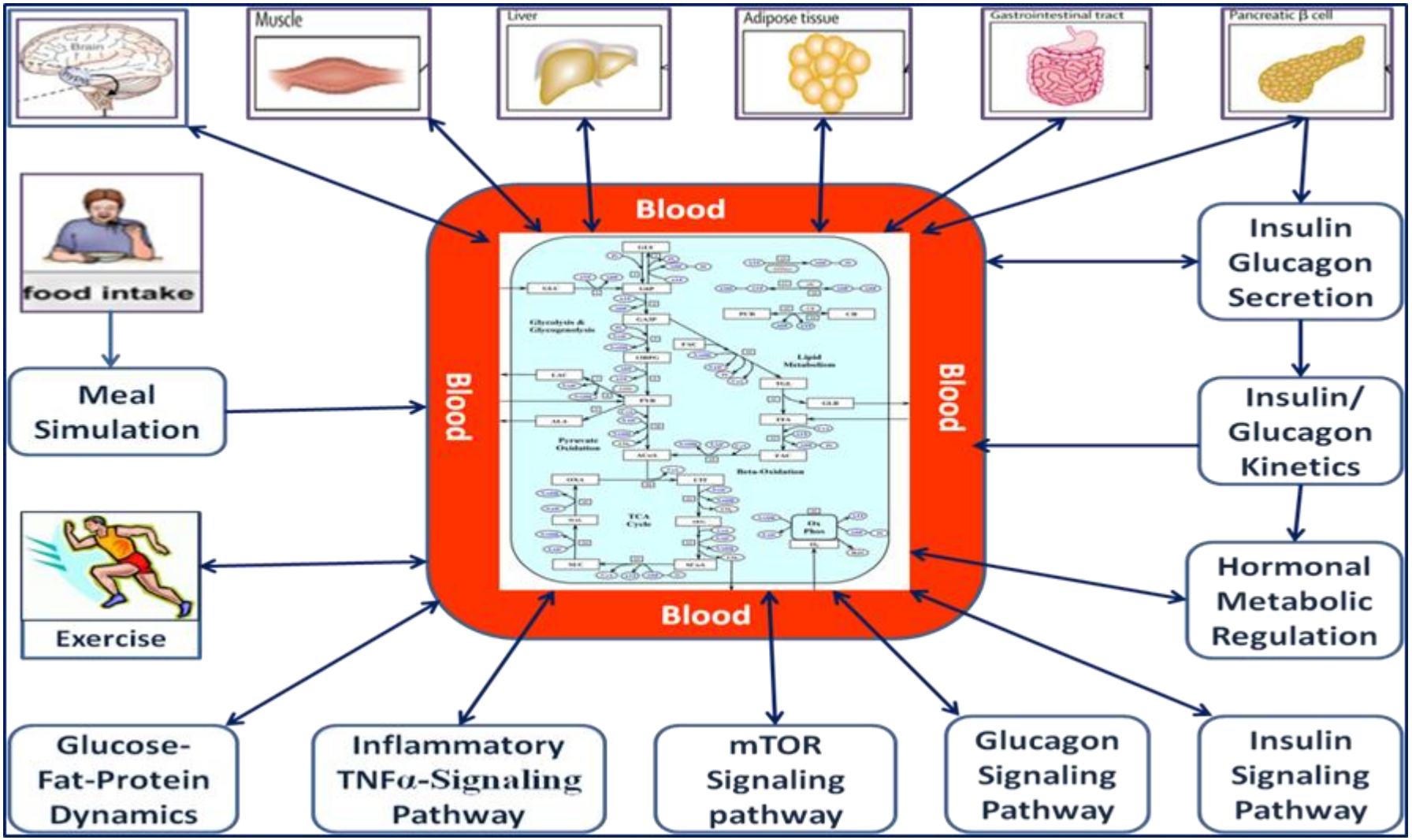


Enzyme regulation (article) | Khan Academy
khanacademy.org

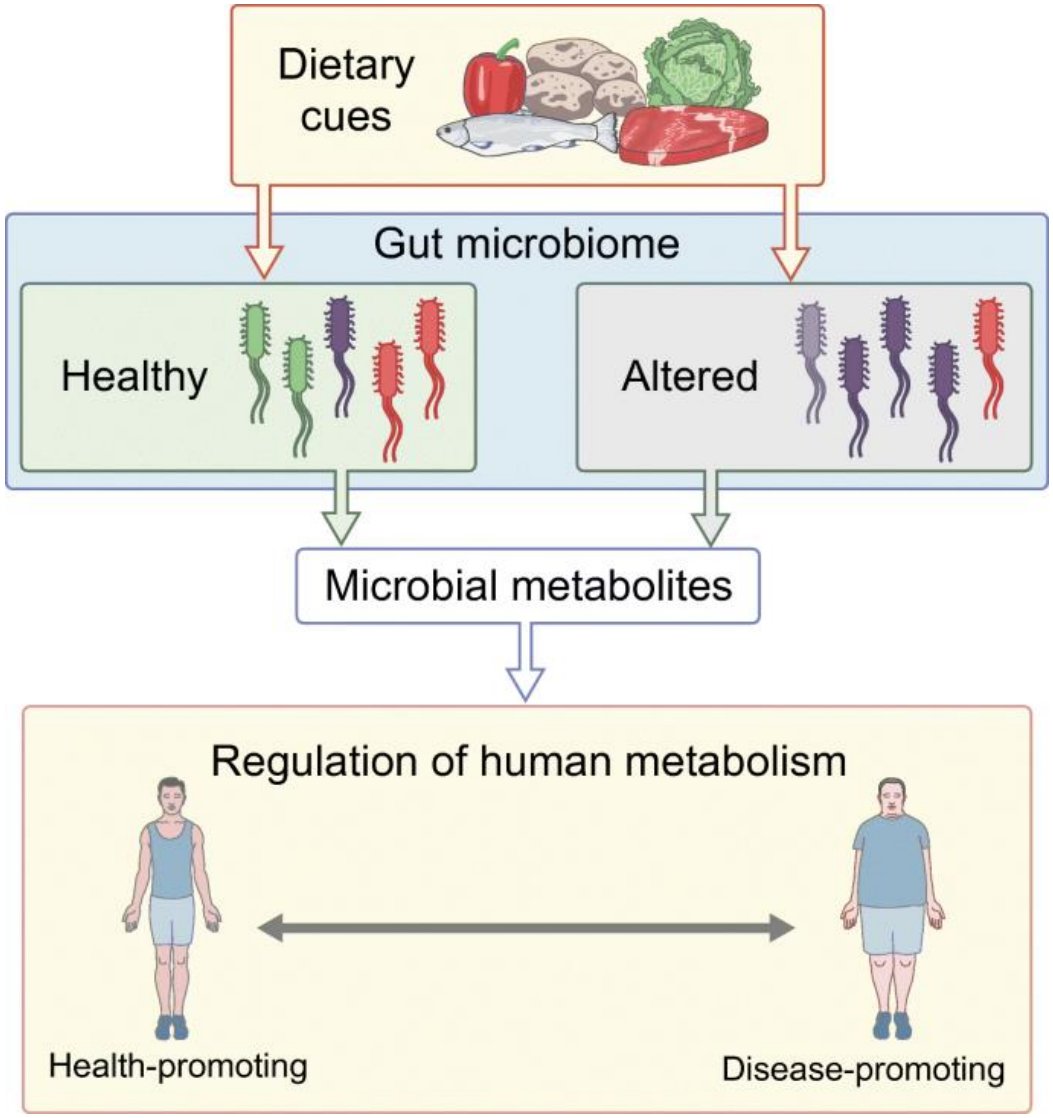


Zymogen Activation by Proteolytic Cleavage

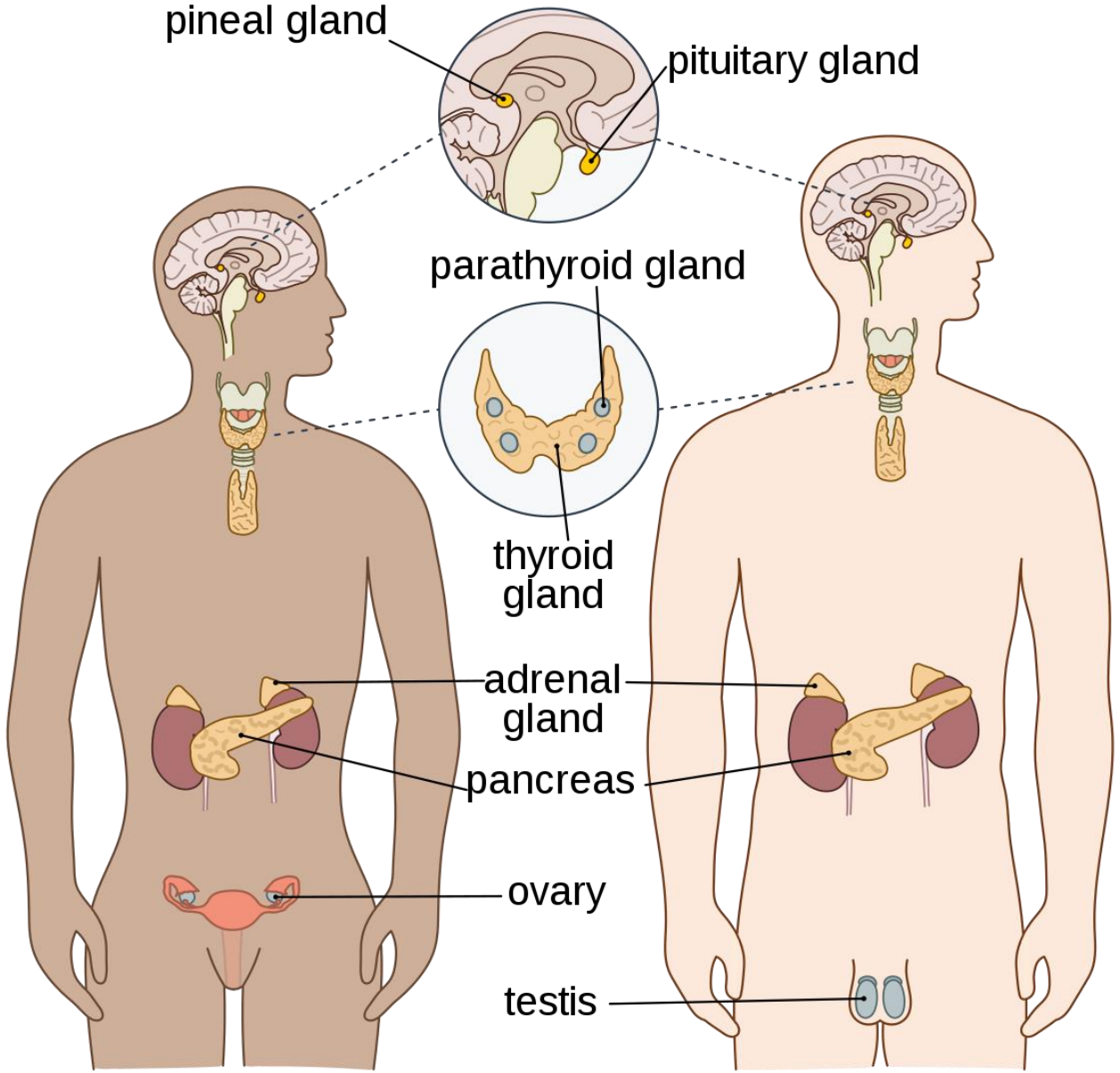
Regulatory Enzyme and Enzyme Regulation
easybiologyclass.com



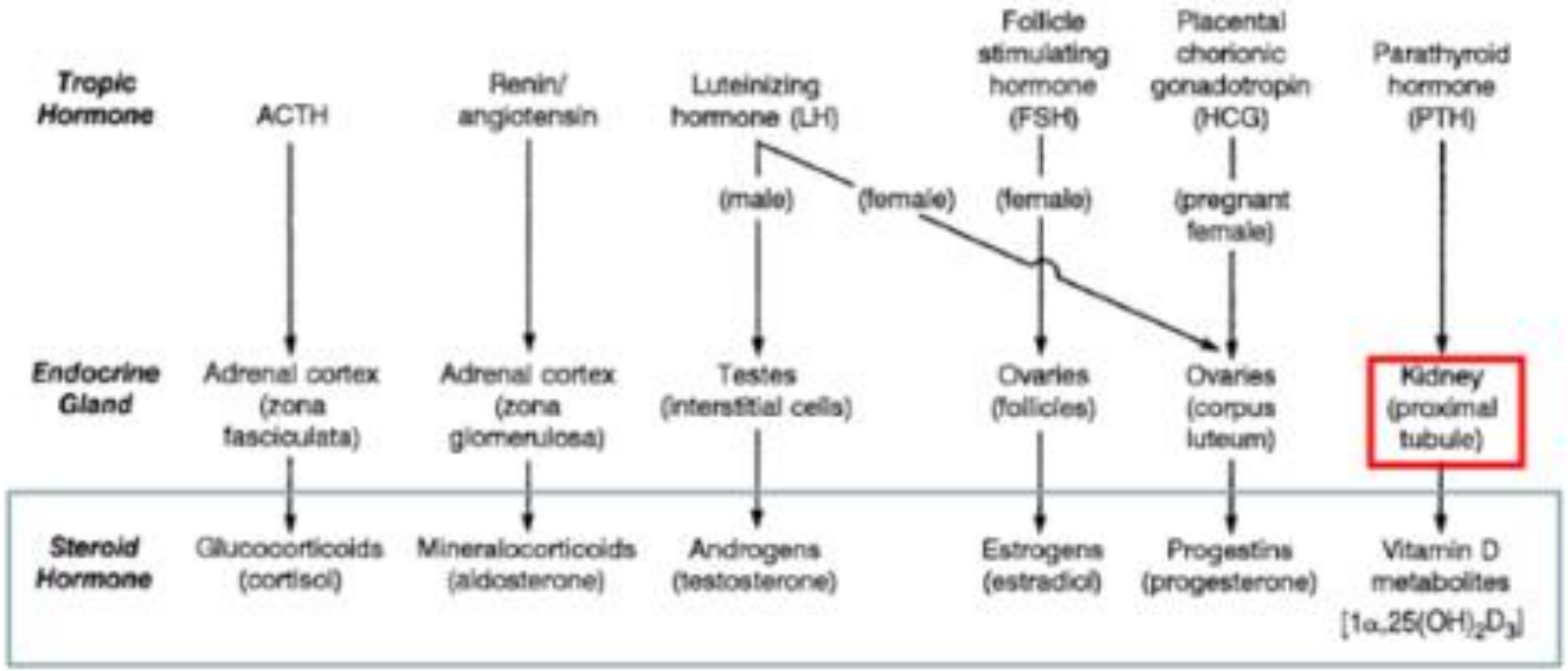
Human Metabolism
che.iitb.ac.in



Intestinal microbial metabolites in human metabolism and type 2 diabetes
x-mol.com



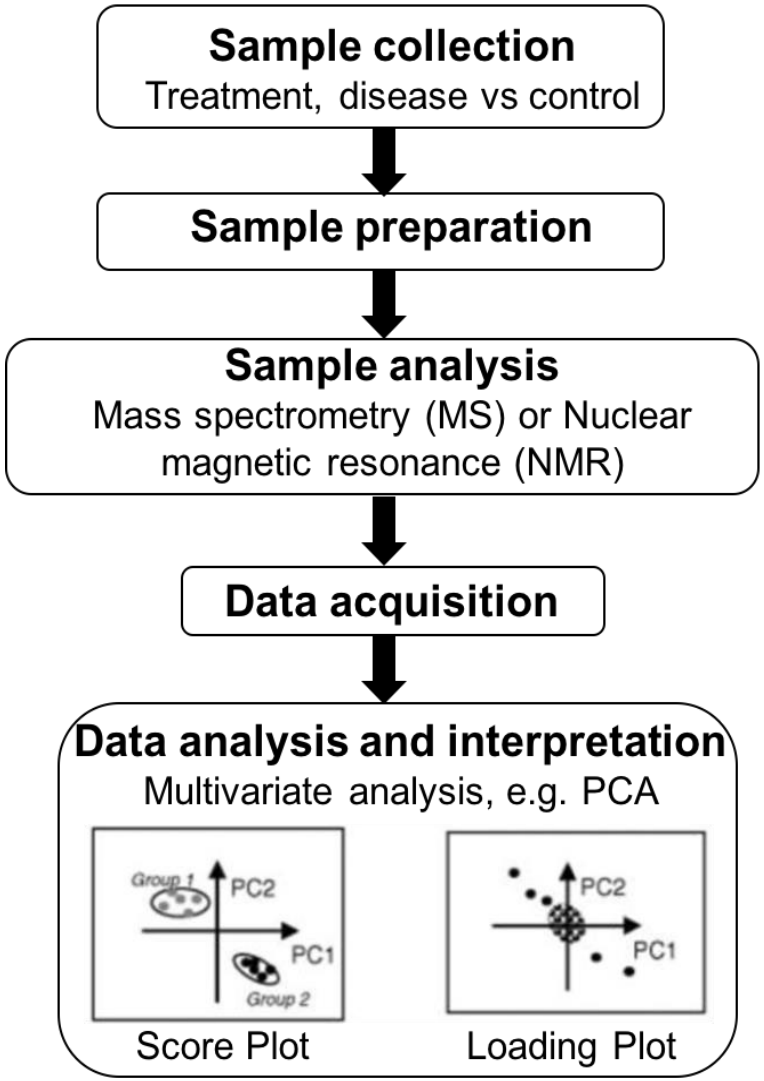
Endocrine system - Wikipedia
en.wikipedia.org



mineralocorticoids are those in which effects on Na+ and K+ excretion predominate

glucocorticoids are those in which effects on glucose and protein metabolism predominate

Hormonal regulation of human metabolism
quizlet.com



https://en.wikipedia.org/wiki/Metabolomics#/media/File:Key_stages_of_a_metabolomics_study.png

Technology	Advantages	Disadvantages
GC-MS	▪ Quantitative (with calibration) ▪ Modest sample volume (0.1-0.2mL) ▪ Good sensitivity (LOD = 0.5 μM) ▪ Large body of software and databases for metabolite identification ▪ Detects most organic and some inorganic molecules ▪ Excellent separation reproducibility ▪ Compatible with gases and liquids	▪ Destructive (sample not recoverable) ▪ Requires sample separation ▪ Slow (20—40 min per sample) ▪ Cannot be used in imaging ▪ Not compatible with solids
LC-MS	▪ Superb sensitivity (LOD = 0.5 nM) ▪ Small sample volumes (10–100 μL) ▪ Very flexible technology ▪ Detects most organic and some inorganic molecules ▪ Can be used in metabolite imaging (MALDI or DESI) ▪ Compatible with solids and liquids	▪ Destructive (sample not recoverable) ▪ Not very quantitative ▪ Higher start-up cost (>$300,000) ▪ Slow (15–40 min per sample) ▪ Usually requires separation ▪ Not compatible with gases
NMR spectroscopy	▪ Superb sensitivity (LOD = 0.5 nM) ▪ Small sample volumes (10–100 μL) ▪ Very flexible technology ▪ Detects most organic and some inorganic molecules ▪ Can be used in metabolite imaging (MALDI or DESI) ▪ Compatible with solids and liquids	▪ Not sensitive (LOD = 5 μM) ▪ High start-up cost (>US$1 million) ▪ Large instrument footprint ▪ Cannot detect or identify salts and ▪ inorganic ions ▪ Cannot detect non-protonated compounds ▪ Requires larger sample volumes (0.1–0.5 mL)

https://en.wikipedia.org/wiki/Metabolomics#/media/File:Comparison_of_most_common_used_metabolomics_methods.png

Name	Main Application	Specific Features	User interface
Meta XCMS	Importing XCMS ouutput	Post processing of XCMS for comparison of multiple classes and visualizing statistical analyses	R language and GTK
XCMS	Processing LC-MS raw data	R module for data processing, including feature detection and peak alignment	R language
XCMS2	Importing tandem mass spectrometry (MS/MS) raw data	Processing of tandem mass spectrometry data for metabolite identification and structural characterization	Plug-in of R language
MetAlign	Importing many common formats, including Masslynx, Xcalibour, and the old-style HP/Agilent format of GC-MS/LC-MS data	Interface-driven data processing program. Includes baseline correction, smoothing, feature detection and alignment	Local Application (GUI)
LIMSA	Data processing/mass spectrometric lipidome data	Tool finds and integrates peaks in a mass spectrum and matches the peaks with a user-supplied list of expected lipids	Local Application (GUI)
MZmine	Data processing of MS data	Modular framework for processing, visualizing and analyzing mass spectrometry-based molecular profile data	Local Application (GUI)
MetDAT	Statistical analysis, database searching, pathway visualization	A modular and workflow-based free online pipeline for mass spectrometry data processing, analysis and interpretation	Web

https://en.wikipedia.org/wiki/Metabolomics#/media/File:Software_List_for_Metabolomic_Analysis.png

References

1. Daviss B (April 2005). "Growing pains for metabolomics". The Scientist. 19 (8): 25–28.
2. Jordan KW, Nordenstam J, Lauwers GY, Rothenberger DA, Alavi K, Garwood M, Cheng LL (March 2009). "Metabolomic characterization of human rectal adenocarcinoma with intact tissue magnetic resonance spectroscopy". Diseases of the Colon and Rectum. 52 (3): 520–5. doi:10.1007/DCR.0b013e31819c9a2c. PMC 2720561. PMID 19333056.
3. Villate, Aitor; Nicolas, Markel San; Gallastegi, Mara; Aulas, Pierre-Antoine; Olivares, Maitane; Usobiaga, Aresatz; Etxebarria, Nestor; Aizpurua-Olaizola, Oier (2020-12-09). "Review: Metabolomics as a prediction tool for plants performance under environmental stress". Plant Science. 303: 110789. doi:10.1016/j.plantsci.2020.110789. ISSN 0168-9452. PMID 33487364.
4. Hollywood K, Brison DR, Goodacre R (September 2006). "Metabolomics: current technologies and future trends". Proteomics. 6 (17): 4716–23. doi:10.1002/pmic.200600106. PMID 16888765. S2CID 14631544.