



# UNIVERSITÀ DEGLI STUDI DI PALERMO

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| <b>DEPARTMENT</b>                   | Biomedicina, Neuroscienze e Diagnostica avanzata   |
| <b>ACADEMIC YEAR</b>                | 2017/2018  |
| <b>MASTER'S DEGREE (MSC)</b>        | MEDICINE AND SURGERY   |
| <b>SUBJECT</b>                      | SYSTEMATIC HUMAN BIOCHEMISTRY  |
| <b>TYPE OF EDUCATIONAL ACTIVITY</b> | A  |
| <b>AMBIT</b>                        | 50423-Struttura, funzione e metabolismo delle molecole d'interesse biologico   |
| <b>CODE</b>                         | 96505  |
| <b>SCIENTIFIC SECTOR(S)</b>         | BIO/10   |
| <b>HEAD PROFESSOR(S)</b>            | LAURICELLA MARIANNA Professore Ordinario Univ. di PALERMO<br>DI LIEGRO ITALIA Professore a contratto in Univ. di PALERMO<br>quiescenza   |
| <b>OTHER PROFESSOR(S)</b>           |  |
| <b>CREDITS</b>                      | 7  |
| <b>INDIVIDUAL STUDY (Hrs)</b>       | 105  |
| <b>COURSE ACTIVITY (Hrs)</b>        | 70   |
| <b>PROPAEDEUTICAL SUBJECTS</b>      | 17447 - CHEMISTRY AND BIOCHEMISTRY - INTEGRATED COURSE   |
| <b>MUTUALIZATION</b>                |  |
| <b>YEAR</b>                         | 2  |
| <b>TERM (SEMESTER)</b>              | 1° semester  |
| <b>ATTENDANCE</b>                   | Mandatory  |
| <b>EVALUATION</b>                   | Out of 30  |
| <b>TEACHER OFFICE HOURS</b>         | <p><b>DI LIEGRO ITALIA</b><br/> Monday 10:00 12:00 Caltanissetta, CEFPAS, padiglione 3, o Palazzo Moncada.<br/> Wednesday 15:00 17:00 Palermo, Viale delle Scienze, Edificio 16 (STEBICEF)<br/> Thursday 15:00 17:00 Palermo, Viale delle Scienze, Edificio 16 (STEBICEF)<br/> Friday 15:00 17:00 Palermo, Viale delle Scienze, Edificio 16 (STEBICEF)</p> <p><b>LAURICELLA MARIANNA</b><br/> Monday 9:00 11:00 SEzione di Biochimica del BIND</p> |

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| <p><b>PREREQUISITES</b></p>      | <p>Knowing the biochemical and molecular bases of cellular activities and understanding the mechanisms that regulate metabolic processes. In particular, the student has to know the biological molecules and the main metabolic processes in which they are involved; knowing and understanding the mode of action of enzymes, the fundamentals of their regulation and catalytic mechanisms, the bases of bioenergetics. The student must already know how to apply his/her knowledge to interpret the behavior of molecules in biological processes and have the ability to understand the molecular mechanisms underlying metabolic processes of life. Finally, he/she should already have to know the molecular mechanisms of action of chemical messengers and the main modes of extracellular signal transduction.</p>  |
| <p><b>LEARNING OUTCOMES</b></p>  | <p>Knowledge and understanding:<br/>Students should learn the biochemical and molecular bases of cellular activities and understand the mechanisms that regulate metabolic processes. For an adequate understanding of the most relevant biological phenomena in medicine, they should understand the unique aspects of the biochemistry of the major tissues and organs and their interactions, also in regard to the biochemical aspects of the most common human diseases. It is essential to achieve a knowledge level which allows full understanding of integrated metabolism, with particular regard to the role of hormones and the nervous system.</p> <p>Applying knowledge and understanding:<br/>Students should be able to apply their knowledge to the study of subjects that follow biochemistry in their curriculum.</p> <p>Making judgements:<br/>They should also be able to express their own opinions about the causes of pathological conditions with evident biochemical bases, and to recommend possible analytic protocols. They should also be able to independently search for relevant scientific information and to analyze it critically.</p> <p>Communication and lifelong learning skills:<br/>Finally, the students should know how to clearly communicate their knowledge and opinions. They are also expected to have developed learning skills which enable them to go on with their studies in an independent way.</p>   |
| <p><b>ASSESSMENT METHODS</b></p> | <p>Oral exam, which consists of an interview aimed at verifying theoretic knowledge and full understanding of the topics addressed in the course, as well as the candidate personal capacity of explain and processing his/her knowledge.</p> <p>In particular, the interview aims at verifying the candidate's ability of systematically integrating the biochemical knowledge concerning single systems/organs into a general view, in order to understand the overall regulation of life processes. This ability is of fundamental importance when considering the health of the organism as a whole, and the biochemical bases of diseases. To further stimulate the personal processing capabilities of the students, they can be invited to dedicate some time, during their preparation, to an issue that particularly attracted their interest, by reading 1-2 recent research/review articles published in international journals. Evaluation of this analysis, when done, will be part of the interview.</p> <p>In order to pass the exam the candidate has to be evaluated with a mark between 18 and 30.</p> <p>Evaluation and criteria:</p> <ul style="list-style-type: none"> <li>-Excellent (ECTS grade A/A+, excellent): Excellent knowledge of the topics of the Integrated Course and their possible applications in the lab. The student shows high analysis-synthesis capability and is able to apply his/her knowledge to solve complex problems. Mark: 30- 30 cum laude</li> <li>-Very good (ECTS grade B, very good): Very good knowledge of the topics of the Course and speaking ability. The student shows good analysis-synthesis capability, and is able to apply his/her knowledge to solve middle-high level problems. Mark: 27-29</li> <li>-Good (ECTS grade C, good): good knowledge of the topics of the course and goof speaking ability. The student is able to apply his/her knowledge to solve middle level problems. Mark: 24 – 26</li> <li>-Satisfactory (ECTS grade D satisfactory): knowledge of the topics of the course is satisfactory but, in most cases, limited to the principal subjects. Acceptable capability to employ the specific language of the matter and to apply knowledge. Mark: 21 – 23</li> <li>-Sufficient (ECTS grade E sufficient): Minimal knowledge of the topics of the Course, often limited to principal subjects. Modest ability to employ the specific language on the matter and to apply knowledge. Mark: 18-20</li> <li>Insufficient: (ECTS grade F, fail): The student does not have an acceptable knowledge of the topics of the Course. The ability to employ the specific</li> </ul> |

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|                               | language of the matter and to apply knowledge is scarce. Exam failed.   |
| <b>EDUCATIONAL OBJECTIVES</b> | The course aims at giving students an integrated knowledge of the main metabolic pathways, active in different organs and tissues of the human organism, and at allowing them to understand the mechanisms responsible for global interactive regulation, under both normal and pathological conditions.  |
| <b>TEACHING METHODS</b>       | Frontal lectures  |
| <b>SUGGESTED BIBLIOGRAPHY</b> | <p>1. Baynes JW., Dominiczack MH. Biochimica per le discipline biomediche, CEA Ambrosiana</p> <p>2. Devlin T.M. Biochimica con aspetti clinici, Ed. Idelson-Gnocchi</p> <p>3. Lieberman M, Marks A.D. Biochimica Medica, seconda edizione, Casa Editrice Ambrosiana</p> <p>4. Siliprandi N., Tettamanti G. Biochimica Medica, Ed. Piccin</p> <p>Inoltre, di consultazione, per l'approfondimento di aspetti specifici:</p> <p>1. Berg J.M., Tymoczko J.L., Stryer L. Biochimica, 5a ed. italiana 2003, Zanichelli</p> <p>2. Nelson D.L., Cox M.M. I Principi di Biochimica di Lehninger, Zanichelli</p> <p>3. Garrett R.H., Grisham C.M. Biochimica, Ed. Zanichelli</p> <p>Nel corso delle lezioni verranno anche fornite fonti bibliografiche specifiche per approfondimenti non presenti nei libri di testo.</p> <p>In addition, a few updated scientific reviews could be suggested on specific topics not covered in the textbook and/or of special interest to the achievement of the educational goals.</p> |

## SYLLABUS

| Hrs | Frontal teaching  |
|-----|---|
| 4   | Biochemistry of protein folding: molecular chaperones. Signal sequences for specific sorting of proteins. Secretory pathways. Mechanisms of protein degradation: the proteasome. Organelle biogenesis.  |
| 6   | Cell proliferation: control mechanisms. Growth factors and their receptors. P21Ras. MAP kinase cascade. Transcription factors. Oncogenes and tumor suppressor genes. pRb and the cell cycle. P53. Cyclins and CDKs: role in the cell cycle. Metastases. Metalloproteinases, TIMPs. Angiogenic and anti-angiogenic factors.  |
| 2   | Apoptosis: cell death receptors; caspase activity. Ceramide and sphingomyelinase. Intrinsic pathway of apoptosis. Role of mitochondria in apoptosis.  |
| 8   | Biochemical aspects of liver function. The liver as a glucostate. Metabolism of fructose. Ketogenesis and ketone bodies metabolism. Primary and secondary bile acids and salts, enterohepatic cycle. Role of cholic acid in formation of micelles, emulsification and digestion of diet lipids. Bilirubin and bilirubin diglucuronide production. Jaundice and its different causes: hemolysis, hepatic distress, stasis of the bile flux. Detoxification reactions: hydroxylation, methylation, conjugation, and elimination. Ethanol metabolism. Effects of alcoholism: deficit of gluconeogenesis, increased synthesis of fatty acids. |
| 6   | Biochemical aspects of renal function and blood pressure regulation. Metabolism of tubular cells. Reabsorption processes: changes in the blood volume and osmotic pressure. Reabsorption of glucose, amino acids and bicarbonate. Renal threshold definition. Amminoacidurie. Production of bicarbonate and ammonia. Role of vasopressin. Aldosterone functions. Renin/angiotensin system. ACE and ACE-inhibitors. Catecholamines and their receptors; alpha- and beta-blockers. Natriuretic hormones. Synergistic effects of catecholamines and angiotensin. Synthesis and degradation of catecholamines.                                |
| 6   | Neurochemistry: brain cell metabolism, with regard to neuronal-glia integration. Brain hexokinase. Amino acid metabolism. Glutamate-glutamine cycle. GABA metabolism. Blood-brain barrier. Metabolism of nucleotides. Axonal transport. Insulin and SNC. Myelin sheath and complex lipids: role in neurotransmission. Mechanism of neurotransmission. Sodium and potassium channels. Calcium channels.  |
| 6   | Neurotransmitters. Synthesis and degradation of acetylcholine. Neuromuscular junction and nicotinic cholinergic synapses. Muscarinic cholinergic synapses. Glutamate receptors. GABA receptors. Receptors for catecholamines. Serotonin. Enkephalins and endorphins. Tetanus and botulism. Short- and long-term memory. Dopamine and cocaine. Myasthenia gravis. Biochemical basis of the main neurodegenerative diseases, with regard to the alterations of protein folding/degradation in prion diseases, in Parkinson's disease and in Alzheimer's Disease. Brain stroke. Schizophrenia.   |
| 6   | Biochemical aspects of muscle function: metabolism of skeletal and cardiac muscle cell. Actin and myosin filaments. Tropomyosin. Biochemistry of muscle contraction. Type I and type II fibers of. Muscular dystrophies: biochemical bases and potential gene therapy. Biochemistry of smooth muscle fiber contraction.   |
| 2   | Blood composition. Erythrocyte metabolism. Formation of 2,3-bisphosphoglycerate (BPG). Methaemoglobin reductase. Glutathione and superoxide anion. Plasma proteins. Conversion of prothrombin to thrombin. Vitamin K. Fibrinogen.   |
| 4   | Biochemistry of the gastro-intestinal tract. Biochemical functions of the stomach in digestion; the proton pump. Production of pepsin. Production of ghrelin. Castle's intrinsic factor. Biochemical functions of intestines. Cholecystokinin. Secretin. Enterokinase. Pancreatic enzymes. Protein digestion. Digestion of carbohydrates and lipids.  |
| 2   | Hormones. Hypothalamus-pituitary axis. Hypothalamic releasing hormones: mechanism of action. Hormones released by the pituitary gland: mechanisms of action.  |

## SYLLABUS

| Hrs | Frontal teaching  |
|-----|---|
| 2   | Growth hormone: mechanism of action; dwarfism; acromegaly; somatomedins; somatostatin. Prolactin. Hypothalamic-pituitary-adrenal axis. ACTH: direct and indirect actions.   |
| 2   | Steroid and thyroid hormone nuclear receptors: c-erbA superfamily; cellular and molecular mechanisms of action. Glucocorticoids: effects on metabolism, anti-inflammatory and immunosuppressive functions. Addison's disease and Cushing 's disease: biochemical bases.   |
| 2   | Synthesis of thyroid hormones. Thyrotropin releasing hormone (TRH). Thyroid stimulating hormone (TSH). Thyroid hormone functions.   |
| 4   | Proinsulin and insulin. IRS. PI-3-K. PDK and PKB (Akt). Insulin-dependent diabetes mellitus and insulinresistance. Insulin resistance and obesity. Metabolic syndrome. Polyol pathway (sorbitol-aldose reductase pathway). Non-enzymatic glycosylation. Diabetic ketoacidosis. Glucagon: effects on metabolism and mechanism of action. |
| 2   | Sex hormones: releasing factors. Gonadotropins: follicle stimulating hormone (FSH) and luteinizing hormone (LH). Estrogen and progesterone. Female sexual cycle. Androgens. Hormones and cancer.  |
| 2   | Calcium metabolism. Vitamin D. Parathyroid hormone (PTH). Calcitonin. Rickets. Osteomalacia.  |
| 2   | Iron and heme metabolism. Major pathologies depending on alterations of iron and heme metabolism. IRE sequences Iron dependent post-transcriptional regulation of expression of proteins involved in iron metabolism.   |
| 2   | Eicosanoids. Prostaglandins, prostacyclins, and thromboxanes. Leukotrienes.   |

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| <p><b>EDUCATIONAL OBJECTIVES</b></p> | <p>The course aims at giving students an integrated knowledge of the main metabolic pathways, active in different organs and tissues of the human organism, and at allowing them to understand the mechanisms responsible for global interactive regulation, under both normal and pathological conditions.</p>  |

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| <b>TEACHING METHODS</b>       | frontal lections   |
| <b>SUGGESTED BIBLIOGRAPHY</b> | <ol style="list-style-type: none"> <li>1. Baynes JW., Dominiczack MH. Biochimica per le discipline biomediche, CEA Ambrosiana</li> <li>2. Devlin T.M. Biochimica con aspetti clinici, Ed. Idelson-Gnocchi</li> <li>3. Lieberman M, Marks A.D. Biochimica Medica, seconda edizione, Casa Editrice Ambrosiana</li> <li>4. Siliprandi N., Tettamanti G. Biochimica Medica, Ed. Piccin</li> </ol> Inoltre, di consultazione, per l'approfondimento di aspetti specifici: <ol style="list-style-type: none"> <li>1. Berg J.M., Tymoczko J.L., Stryer L. Biochimica, 5a ed. italiana 2003, Zanichelli</li> <li>2. Nelson D.L., Cox M.M. I Principi di Biochimica di Lehninger, Zanichelli</li> <li>3. Garrett R.H., Grisham C.M. Biochimica, Ed. Zanichelli</li> </ol> Nel corso delle lezioni verranno anche fornite fonti bibliografiche specifiche per approfondimenti non presenti nei libri di testo. |

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| Hrs | Frontal teaching  |
|-----|---|
| 4   | Biochemistry of protein folding: molecular chaperones. Signal sequences for protein sorting. Secretory pathways. Mechanisms of protein degradation: proteasome. Biogenesis of organelles.   |
| 6   | Cell proliferation: control mechanisms. Growth factors and their receptors. P21Ras. MAP kinase cascade. Transcription factors. Oncogenes and tumor suppressor genes. pRb and the cell cycle. P53. Cyclins and CDKs: role in the cell cycle. Metastases. Metalloproteinases, TIMPs. Angiogenic and anti-angiogenic factors.  |
| 2   | Apoptosis: cell death receptors; caspase activity. Ceramide and sphingomyelinase. Intrinsic pathway of apoptosis. Role of mitochondria in apoptosis. Necroptosis and viral infection.   |
| 4   | Biochemical aspects of liver function. The liver as a glucostate. Metabolism of fructose. Ketogenesis and ketone bodies metabolism. Primary and secondary bile acids and salts, enterohepatic cycle. Role of cholic acid in formation of micelles, emulsification and digestion of diet lipids.   |
| 4   | Bilirubin and bilirubin diglucuronide production. Jaundice and its different causes: hemolysis, hepatic distress, stasis of the bile flux . Detoxification reactions: hydroxylation, methylation, conjugation, and elimination. Ethanol metabolism. Effects of alcoholism: deficit of gluconeogenesis, increased synthesis of fatty acids.  |
| 6   | Biochemical aspects of renal function and blood pressure regulation<br>Metabolism of the tubule cell. Generality of the resorption process. Changes in volume and osmotic pressure of the tubule. Renal threshold. Reabsorption of glucose, amino acids and bicarbonate. Gamma-glutamyl cycle . Amminoaciduria. Ammonia production. Vasopressin and aldosterone functions. Renin and angiotensin. ACE and ACE-inhibitors. Catecholamines and their receptors; alpha- and beta-blockers. Natriuretic hormone. Synergism between catecholamines and angiotensin. Synthesis and degradation of catecholamines. |
| 6   | Neurochemistry: brain cell metabolism, with regard to neuronal-glia integration. Brain hexokinase. Amino acid metabolism. Glutamate-glutamine cycle. GABA metabolism. Blood-brain barrier. Metabolism of nucleotides. Axonal transport. Insulin and SNC. Myelin sheath and complex lipids: role in neurotransmission. Mechanism of neurotransmission. Sodium and potassium channels. Calcium channels.  |
| 6   | Neurotransmitters. Synthesis and degradation of acetylcholine. Neuromuscular junction and nicotinic cholinergic synapses. Muscarinic cholinergic synapses. Glutamate receptors. GABA receptors. Receptors for catecholamines. Serotonin. Enkephalins and endorphins. Tetanus and botulism. Short- and long- term memory. Dopamine and cocaine. Myasthenia gravis. Biochemical basis of the main neurodegenerative diseases, with regard to the alterations of protein folding/degradation in prion diseases, in Parkinson's disease and in Alzheimer's Disease. Brain stroke. Schizophrenia.                |
| 6   | Biochemical aspects of muscle function. Metabolism of skeletal and cardiac muscle cell. Cardiac metabolism in hypoxia and anoxia, heart attack. Actins. Myosins. Troponin. Tropomyosin. Muscle contraction. Type I and type II fibers. Contraction of smooth muscle fibers.   |
| 2   | Blood composition. Erythrocyte metabolism. Formation of 2,3-bisphosphoglycerate (BPG). Methaemoglobin reductase. Glutathione and superoxide anion. Plasma proteins. Conversion of prothrombin to thrombin . Vitamin K. Fibrinogen.  |
| 4   | Biochemistry of the gastro-tube . Biochemical functions of the stomach. Proton pump. Production of pepsin. Cholecystokinin. Secretin. Enterokinase. Pancreatic enzymes. Protein digestion. Carbohydrates Digestion. Lipid digestion.  |
| 2   | Hormones Hypothalamic releasing factors: mechanism of action. The anterior pituitary hormones.  |
| 2   | Growth hormone: mechanism of action, dwarfism, acromegaly, somatomedins, somatostatin. Prolactin  |
| 2   | Hypothalamic-pituitary-adrenal axis. .ACTH: direct and indirect actions. Steroid hormone and thyroid receptors: c-erbA family, cellular and molecular mechanisms of action. Glucocorticoids: effects on metabolism, antiinflammatory and immunosuppressive roles. Addison's disease. Cushing's disease.   |
| 2   | Thyroid hormones: Synthesis and roles. Thyroid stimulating hormone (TSH). Hypothyroidism and hyperthyroidism.   |
| 4   | Proinsulin and insulin, IRS-1, 3-phosphoinositide, PKB. Insulin-dependent diabetes and insulin-independent diabetes. Insulin resistance. Polyalcohol pathway. Non-enzymatic glycosylation. Diabetic ketoacidosis. Glucagon: effects on metabolism and mechanism of action   |
| 2   | Sex hormones: releasing factor. Gonadotropins: follicle stimulating hormone (FSH) and luteinizing hormone (LH). Estrogen and progestin. Androgens. female sexual cycle  |
| 2   | Calcium metabolism. Vitamin D. Parathyroid. Calcitonin. Rickets. Osteomalacia   |

## SYLLABUS

| Hrs | Frontal teaching  |
|-----|---|
| 2   | Iron and heme metabolism. Major pathologies depending on alterations of iron and heme metabolism. IRE sequences Iron dependent post-transcriptional regulation of expression of proteins involved in iron metabolism. |
| 2   | Prostaglandins, prostacyclins, and thromboxanes endoperoxides   |