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1. THE INVOLVEMENT AND SIGNIFICANCE OF THE TYROSINE N-TERMINAL RESIDUE IN NOCICEPTION PROCESSES

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ABSTRACT
The aim of this study was to investigate the importance of the amino acid tyrosine (Tyr) for the analgesic opioid activity. Different groups of mice or rats were treated with: 1) L-tyrosine (i.p. 200 mg/kg), 2) D-tyrosine (i.p. 200 mg/kg), 3) Tyr-Gly-Gly (i.t. 0.5 mg/rat), 4) Gly-Tyr (i.t. 0.5 mg/rat). Different tests were used to evaluate the anti-nociceptive effect of the substances tested: thermal nociception (hot plate test, plantar test) and mechanical nociception (analgesymeter test). L-tyrosine, but not D-tyrosine, administered intraperitoneal produces a significant anti-nociception, blocked by previous administration of naloxone. Tyr-Gly-Gly, but not Gly-Tyr, elicited analgesic activity antagonized by naloxone. So, the presumption made in the case of atypical opioid peptides, that opioid-like activity at the N-terminal sequence, applies for shorter peptides.

Key words: L-tyrosine, D-tyrosine, Tyr-Gly-Gly, Gly-Tyr, anti-nociceptive effect.

2. THE INCIDENCE OF CARDIOVASCULAR RISK FACTORS IN APPARENTLY HEALTHY YOUNG ADULTS CARDIORISK STUDY: BACKGROUND AND DESIGN

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ABSTRACT
The CARDIORISK study comprised one group of 518 apparently healthy young adults, 375 girls and 143 boys, with a mean age of 20 ± 2.25 years, who attended the first and the second year study at University of Medicine and Pharmacy "Victor Babes" Timisoara.
We assessed the CVD risk factors using 4 methods: (a) the questionnaire method, (b) the measurement of blood pressure, (c) the measurement of several anthropometric parameters, such as body weight, body height, body mass index (BMI) and waist circumference, and (d) the measurement of biochemical parameters such as plasma lipid profile (total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol), and fasting plasma glucose.
Great evidence was obtained that certain lifestyles related to tobacco smoking, physical inactivity, unhealthy diet, and stress had an important incidence in medical young subjects, leading to adverse changes in physiological and biochemical characteristics, that enhance the development of an earlier atherosclerosis in adulthood.

Key words: cardiovascular risk factors, young adult, blood pressure, dyslipidemia

3. BRIEF REVIEW: ROLE OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) IN ANGIOGENESIS

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ABSTRACT
Angiogenesis is a process of new blood vessel development from preexisting vasculature. It plays an essential role in embryonic development, normal growth of tissues, wound healing, the female reproductive cycle (ovulation, menstruation and placental development), as well as a major role in many diseases. Particular interest has focused on cancer, since tumors cannot grow beyond a few millimeters in size without developing a new blood supply. Angiogenesis is also necessary for the spread and growth of tumor cell metastases.
VEGF is a key regulator of physiological angiogenesis during embryogenesis, skeletal growth and reproductive functions. VEGF has also been implicated in pathological angiogenesis associated with tumors, intraocular neovascular disorders and other conditions. The biological effects of VEGF are mediated by two receptor tyrosine kinases (RTKs), VEGFR-1 and VEGFR-2, which differ considerably in signaling properties. VEGF inhibitors are undergoing clinical testing in several malignancies and other diseases.

Key words: VEGF, receptor, physiological angiogenesis, pathological angiogenesis.

4. THYROID HORMONES AND IMMOBILIZATION

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ABSTRACT
Prolonged immobilization, due to the stress generated by it, leads to different modifications of blood parameters, including the thyroid hormones.
The purpose of this study is to monitor the variations in thyroid hormones concentration during the immobilization period.
A group of 15 immobilized patients were taken into this study, who were hospitalize in a specialty department due to fractures of the inferior members, without suffering from other diseases or complications of the fractures. Venous blood samples were taken in the first day of immobilization, and T_4 and TSH determinations were performed. The same determinations were performed in the 14^{th} day of immobilization. A significant increase of T_3 was noticed ($p<0.05$) after the immobilization period, while the levels of T_4 and TSH were not significantly decreased.
The variation of thyroid hormones level during immobilization depends on the period of time this immobilization is required. Compared to the increase of thyroid secretion that occurs in short time immobilization (4-6 days), in long time immobilization (14-25 days), which leads to specific changes in lipids metabolism, a decrease of thyroid hormones concentration is noticed, which can be explained by reduced stimulation of thyroid gland, as an adaptive response to the decreased body physical load.

Key words: immobilization, thyroid hormones, TSH, T_3, T_4.

5. EFFECTS OF ZOPICLONE ON BLOOD GLUCOSE LEVEL AND SERUM LIPIDS IN STREPTOZOTOCIN –INDUCED DIABETES IN RATS

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ABSTRACT
In rats with streptozotocin-induced diabetes (65mg/kg, i.v., repeated for five days), the blood glucose level, serum total cholesterol, serum triglycerides and free glycerol were increased, whereas the free fatty acids (FFA) level was decreased, zopiclone (2.5 mg/kg – 5.0 mg/kg – 10.0 mg/kg i.p., for five days) very significantly decreased blood glucose and serum lipids level, elevated by the administration of streptozotocin. In the same time, zopiclone increased the level of FFA. It is hypothesized that the anti-diabetic effects of benzodiazepines and zopiclone are due to the stimulation of peripheral type of benzodiazepine receptors.

Key words: rats, streptozotocin, diabetes, zopiclone, blood glucose, serum lipids.

6. ANGIOGENESIS SIGNIFICANCE IN RENAL CARCINOMAS PROGNOSTIC

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ABSTRACT
Angiogenesis represents one of the important factors of tumor proliferation (8). Theoretically, an intense neovascularization allows a rapid tumor growth, while the decrease of angiogenesis process will reduce or even stop the neoplazic growth (5).
In our study we tried to establish a correlation between tumor angiogenesis and the prognostic of renal carcinomas. A number of 43 patients were monitored, which had operated renal tumors, in the Department of Urology of the County Hospital 1 Timisoara. The surgical treatment performed was total nefrectomy. The surgical excision pieces were processed by the Morphopathology Laboratory of County Hospital 1 Timisoara and the Histopathology Laboratory of the Department of Morphopathology from University of Medicine and Pharmacy "Victor Babes" Timisoara. In order to reveal the angiogenesis, the tissue samples were processed by usual methods (paraffin inclusion, several sections were made, hematoxylin-eosin staining), and by special methods of immunohistochemistry for CD31, using CD31 DACO monoclonal antibody; for revealing we used the DACO peroxidase system LSAB2, the chromogen being DAB.
From the 43 tumors, 9 of them were well differentiated in G_1, 27 of them in G_2, and 7 tumors were weakly differentiated in G_3. The relative vascular density determined by microscopy, showed the highest values in case of G_1renal carcinomas, of 27.35. The lowest vascular density, of 4.95, was achieved for the less differentiated carcinomas. For G_2 tumors, the relative vascular density was 11.98. The relative vascular density assessed by immunohistochemical reaction to CD31, indicates an inverse proportionality between the tumor differentiation degree and vascular density (13).

Key words: angiogenesis, neovascularization, renal carcinoma, immunohistochemistry.

7. P53 EXPRESSION IN HODGKIN LYMPHOMA – A TUMORAL PROGRESSION INDEX?

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ABSTRACT
P53 protein suffers mutations at malignant cells level, becoming stable and accumulating at these cells level, thus, could be revealed by immunohistochemical methods. 64 hospitalized in Hematology Department of City Hospital Timişoara cases of Hodgkin's disease were studied. The p53 expression was immunohistochemical semi quantitative evaluated using clone DO7 as monoclonal antibody and LSAB2-Peroxidase/DAB system for visualization.
In our study, p53 expression isn't associated with disease progression, nor with histological type, because weak positive (-/+) interval into were situated the majority of cases is irrelevant for all histological type or stage association. Depending by literature data too, we recommend giving up to p53 expression determination including as tumor proliferation index in Hodgkin's lymphomas.

Keywords: Hodgkin's lymphoma, p53, tumor progression.

8. THE INFLUENCE OF CORONARY RISK FACTORS ON THE PROGRESSION OF AORTIC STENOSIS

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ABSTRACT
The aim of the present study was to identify the prevalence of aortic valve abnormalities in an elderly group, the clinical factors associated with degenerative aortic valve disease and to analyze the influence of the risk factors of atherosclerosis on the progression of mild aortic stenosis.
The study was made on 386 elderly patients (age over 65 years), of which there are 218 men (60%) and 168 women (40%). 270 cases (70%) had normal valves, 95 cases (25 %) presented aortic sclerosis and 19 cases (5%) aortic stenosis (3 severe AS and 16 mild AS).
The progression of mild aortic stenosis (increase in peak systolic gradient across the aortic valve/year) was studied on 16 patients with mild aortic stenosis. Progression was statistical significant associated to age, current cigarette smoking, systemic hypertension, diabetes mellitus, high LDL and low HDL cholesterol.
The patients with LDL cholesterol ≥125 mg/dl received treatment with statins. The statins reduced the mean serum LDL cholesterol from 182 ± 20 to 116 ± 11 mg/dl ($p < 0.001$), increased the mean serum HDL cholesterol from 41 ± 9 to 45 ± 9 mg/dl ($p<0.001$) and reduced the mean serum triglycerides from 135 ± 45 to 118 ± 40 mg/dl ($p<0.001$).
The conclusion of the study is that mild aortic stenosis is influenced by the following independent risk factors: smoking ($p<0.0001$), hypertension ($p<0.0001$), LDL cholesterol ≥ 125 mg% ($p<0.001$), HDL cholesterol ≤ 35 mg ($p<0.001$), diabetes mellitus ($p<0.001$) and the use of statins (inverse association, $p < 0.001$).

Key words: aortic stenosis, progression, coronary risk factors.

9. BOOK REVIEW: CHEMOINFORMATICS IN DRUG DISCOVERY

Tudor I Oprea

Weinheim, Germany: Wiley-VCH Verlag GmbH & Co. KGaA, 2004, xxii + 493 pp. ISBN 3-527-30753-2, Vol 23 in series Methods and Principles in Medicinal Chemistry;
Series editors: R Mannhold, H Kubinyi, G Folkers

Intersection between two large domains, chemistry and informatics, is as old as information technology itself. There were created many data bases comprising an enormous amount of information about many chemical compounds and dedicated software for applications in chemistry were developed. However, the term "chemoinformatics" is quite new, being introduced in 1998 by Franck Brown, who defined it as "*the mixing of information resources relevant in the drug discovery process, to transform data into information and information into knowledge for the intended purpose of making better decisions faster in the area of drug lead identification and organization"*.
Chemoinformatics has a central concept: chemical information and the definition presented above intends to cover all possible operations related to it: design, creation, organization, storage, retrieval, analysis, visualization and use. The present volume on "Chemoinformatics in Drug Discovery" covers all these important aspects in a systematic manner.
The editor, Tudor Oprea, is now Professor of Biochemistry and Molecular Biology at University of New Mexico School of Medicine in Albuquerque. He did his studies in Timisoara and had his Ph.D. thesis supervised by Francisc Schneider. He was a post-doctoral fellow at Washington University and Los Alamos National Laboratory, and then worked six years for Astra Zeneca in Sweden. In 2002 he received the Hansch Award from the QSAR and Modeling Society. With such a sound background in both medicine and chemistry and a solid experience in research, he put his fingerprint on this volume not only as author but also by arranging hierarchically the chapters, driving the reader

in an attractive way from the theoretical background in the first part to the practical applications in last part.

The book starts with an excellent introduction by Garland Marshall followed by four sections. The first one is focused on *Virtual Screening* and lead discovery, covering aspects of screening set design, algorithmic engines and pharmacophore-based virtual screening. The second section, *Hit and Lead Discovery* refers to various performant *in silico* technologies. In the third section, *Databases and Libraries,* data collection and mining using chemical databases are discussed in the context of chemical libraries. Finally, in the last section, *Chemoinformatics Applications*, specific applications and examples are collected, bringing together industrial and academic perspectives. The volume concludes with another excellent account, by Dan Abraham, on drug discovery.

We can trace across the book, as a red thread, the progression from hit identification to lead generation, then to lead optimization up to candidate drug nomination. A large variety of chemoinformatics tools and strategies serve this purpose. All these new procedures underline the progress in preclinical drug discovery process as well as its needs for novel technologies and for integrated informatics support. The huge span, from atomic level in drug-receptor binding up to pharmacokinetics profiling, is likely to lead towards a better path for drug discovery.

The book is written in an excellent academic style. Even the level is advanced; it is accessible also from introductory level. The transition between chapters is smoth and the contents cover a large variety of items, being recommended not only to biochemists, pharmacologists and bioinformaticians but also to researchers in neighboring fields.

I join the opinion of the series editors who remarked Tudor Oprea's enthusiasm to organize the volume and work with such a fine selection of authors from several research centers in USA, Germany, France, UK, Switzerland, Sweden and Romania.

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