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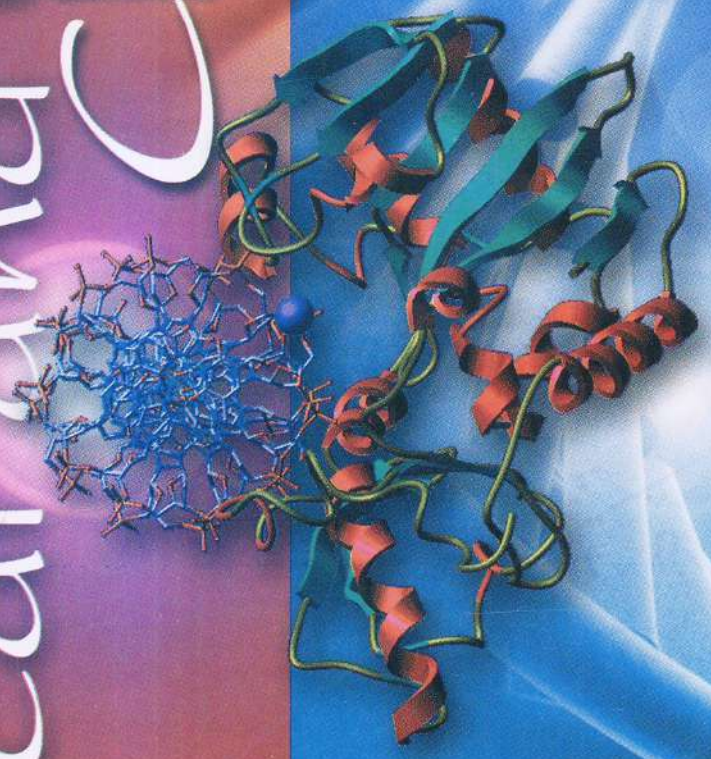

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Інститут фармакології та токсикології НАМН України

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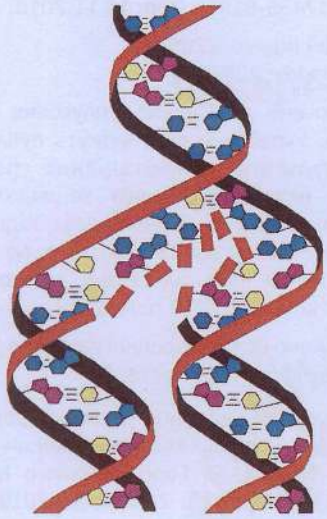
НАУКОВИЙ ЖУРНАЛ



I. Horbachevsky Ternopil National Medical University
Institute of Pharmacology and Toxicology of NAMS of Ukraine

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МАТЕРІАЛИ XII УКРАЇНСЬКОГО БІОХІМІЧНОГО КОНГРЕСУ

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ватці крові (на 32 %, $P<0,05$), збільшення екскреції креатиніну з сечею (на 25 %, $P<0,05$), зростання кліренсу креатиніну (на 40 %, $P<0,05$), зменшення протеїнурії та активності ГГТП в сечі (на 65–74 %, $P<0,05$), порівняно з тваринами, яким не вводили модулятор.

Проведені дослідження засвідчили, що порушення обміну H_2S в нирках є важливим патогенетичним механізмом розвитку діабетичної нефропатії. Використання донорів H_2S покращує фільтрацію в нирках та стан канальцевого апарату при ЦД. Подальші дослідження в цьому напрямі дозволять розширити арсенал фармакологічних засобів для профілактики та лікування діабетичної нефропатії.

ANGIOGENIC REGULATORS AND MMP ACTIVITY IN TROPHIC DIABETIC AND HYPERTONIC ULCERS OF MILD TISSUES

TYKHOMYROV A.A.[1], PETRENKO O.M.[2], KOLOSOVYCH I.V.[2], BEZRODNYI B.G.[2]
[1]PALLADIN INSTITUTE OF BIOCHEMISTRY, NATIONAL ACADEMY OF SCIENCES OF UKRAINE, KYIV;
[2]BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE;
e-mail: artem_tykhomyrov@ukr.net

Chronic wounds are one of the major healthcare problems and represent the highest diagnostic group direct medical cost for the dermatological disease. Chronic ulcers are the common complication of diabetes mellitus and unusual injury in patients with poor-controlled hypertension known as Martorell's syndrome. Diabetic chronic wounds are the result of neuropathies and angiopathies, while Martorell's hypertensive ulcers are ischemic lesions of the skin tissues caused by obstruction of the small arterioles of the medial artery. Wound healing is a complex process that can be divided into a series of stages that include hemostasis, inflammation, proliferation, and remodelling, which are disrupted in diabetes mellitus and contribute to complicated healing. The exact molecular mechanisms of impaired angiogenesis in chronic wounds are still unknown and required detailed investigation. The aim of the present study was to assess levels of two counteracting regulators, angiostatin and vascular endothelial growth factor (VEGF), and matrix metalloproteinases (MMPs) activities in fluids from acute and chronic diabetic wounds of mild tissues and from Martorell's hypertensive ischemic leg ulcer bioptates.

The exudates of chronic wounds from patients with diabetes mellitus type II (n=8) and fluids of acute surgical wounds (n=9) were collected by topical negative pressure (-80–125 mm Hg) (VAC-therapy). The Martorell's ulcer bioptates were taken by five biopsies from different regions of ulcer and histologically normal surrounding (granulating) tissue as a control. Informed written consent was obtained from all patients. Gelatin zymography was used for determination of MMPs activity; angiostatin, plasminogen and VEGF levels were evaluated by western blot. Histological staining was used to assess capillary outgrowth in the wound bed.

In exudates of diabetic wounds, the high levels of plasminogen proteolytical fragments (angiostatins) were determined as compared with the acute wounds-derived fluids. Up-regulation of angiostatin production was also observed in Martorell's ulcer tissue as compared with respective control. Dramatic elevation of MMP-2, -9 activities was observed in exudates of chronic diabetic wounds, unlike that of surgical wounds. Similarly, high levels of MMP-2, -9 and MMP-9 complex activities were detected in Martorell's ulcer tissue. The [angiostatin/plasminogen] ratio in chronic diabetic wounds was 6 times higher compared to that of acute wounds. MMPs are responsible for extracellular matrix degradation and plasminogen cleavage to angiostatins, which specifically inhibit endotheliocyte proliferation, migration, and vessel tube formation. Dramatic elevation of VEGF levels as a compensatory response of ischemic tissues was observed in both ulcer types. However, VEGF overproduction appeared to be unable to provide sufficient reparative angiogenesis in chronic wounds likely due to counteracting action of angiostatins, thus contributing to healing delay. In addition, VEGF up-regulation may have adverse effects on capillary structure, increasing vessel leakage and resulting in haemorrhage and erythematosus. Histological assay demonstrated that evacuation of exudates from the long-term non-healing wounds improved tissue reparation and outgrowth of capillary-like structures at the 10-th day of VAC-therapy.

It has been summarized that chronic wounds of different pathogenesis share common molecular features, such as overactivation of MMP proteolytic activities and imbalance of angiogenesis regulators that could contribute to the restriction of blood vessel recovery and healing delay. Based on the obtained results, elimination of angiogenesis suppressors and inhibition of excessive proteolytic activities in chronic wounds may improve conventional management of skin ulcers for better wound healing outcomes.