

## Effect of collagen breakdown products on mast cell activity during reparative regeneration

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Immune system including its effector cells and their products (autocoids and autoantibodies) definitely plays an important part in regulation of tissue regeneration. Collagen-based preparations, whose action is due to peptides that have a stimulating effect on the formation of self collagen and bone restoration, as well as indirectly affecting hemostasis and phagocytosis, have gained considerable interest because of frequent bacterial complications of wound healing. The effect of mast cells on the healing process of the wound surface in rats under the influence of collagen dissolution products was assessed in the present study. According to the results, mast cells were found to be activated on the wound surface under the influence of drugs based on collagen breakdown products, which directly caused an acceleration of the reparative regeneration process.

*Keywords:* regeneration, mast cells, morphology, skin wound, collagen.

Immune system including its effector cells and their products (autocoids and autoantibodies) definitely plays an important part in regulation of tissue regeneration [1]. Over the past few decades, the topic of regeneration of various organs and systems has become widespread in the global scientific community. At the same time, despite scientific and practical progress, the incidence of bacterial complications of wound healing remains high. In this connection, collagen-based preparations, whose action is due to peptides that have a stimulating effect on the formation of self collagen and bone restoration, as well as indirectly affecting hemostasis and phagocytosis, have gained considerable interest [2–3]. The authors of the work previously conducted a series of studies aimed at studying the influence of collagen dissolution products made on the basis of acetic acid and fermented milk complex 1 (FMC 1) on the processes of skin regeneration. It was determined that the use of collagen breakdown products based on FMC 1 reliably shortens the healing time of wounds due to the lower molecular weight [4].

### Objective

To study the effect of mast cells on the healing process of the wound surface, under the influence of collagen dissolution products.

## Materials and methods

The study was conducted on 40 rats — males, whose age was 1.5 years. The experiment was conducted in accordance with the rules for working with laboratory animals. During the experiment under ether anesthesia, a layered conditionally aseptic wound was created, formed by excising a skin flap between the shoulder blades, the size of excised area was  $1 \times 1$  cm [3]. During the study, the animals were divided into two groups: *group I* was control one, in which the wound healing in animals took place spontaneously, under the scab; *group II* was experimental one, where healing was altered by applying collagen dissolution products made on the basis of FMC 1. The substance was applied daily to a gauze bandage and fixed to the wound on animals. The duration of the course was 1 week.

The skin from the wound surface area was sampled. Material sampling was carried out on 1<sup>st</sup>, 3<sup>rd</sup>, 7<sup>th</sup>, and 14<sup>th</sup> days of the experiment. Bioplates were taken under ether anesthesia. To identify the mast cells, a toluidine blue dye with a pH of 5.6 was used for staining. Mast cells were counted in the tissues surrounding the wound, taking into accounts their total number and morpho-functional types. The functional activity of mast cells was assessed using the degranulation index, which is the ratio of the number of degranulated cells to the total number of analyzed cells, expressed as a percentage [5]. The morphometric study was carried out using an OLYMPUS CX 31 microscope with the MEKOS-C software [2]. Statistical processing was performed using the non-parametric Mann-Whitney criterion. The differences between the samples were considered statistically significant provided that  $p \leq 0.05$ .

## Results

In the course of the experiment, it was revealed that during the regeneration process complex intercellular relationships are formed. A certain sequence of occurrence and activation of cells in the wound site was found, affecting the change in the phases of inflammation and proliferation. On the first day, in both groups the mass perish of the cells and degeneration of the fibrous component was determined, which corresponds to the phase of alteration in course of acute inflammation. On the third day, which corresponds to the second phase of the inflammatory process, active migration of mast cells to the focus of lesion and their subsequent degranulation was detected. Moreover, the activity of the mast cell component in animals of the second group was much higher and amounted to  $71.8 \pm 12.4$  cells per 10 fields of view, compared with that of control group reached only  $36.2 \pm 10.2$ . Similar changes were noticed while studying the degranulation index, which amounted 73.8 % in the experimental group and just 56.2 % in control one.

Further, on the 7<sup>th</sup> day, the number of mast cells increased and reached its maximum, while maintaining an advantage in the second group, where the degranulation index continued to increase.

During visual inspection of the wound in animals of the experimental group, surface cleansing was more active, which reduced the inflammatory response and contributed to the earlier appearance of granulation tissue with the active formation of blood vessels. The reduction in the duration of the inflammatory phase and barrier delimitation of the inflammatory process created favorable conditions for proliferative-regenerative reactions, which resulted in the acceleration of granulation tissue maturation, against the

background of pronounced collagenogenesis and the prevalence of mast cells in the cellular component, which indirectly stimulated the activity of fibroblasts. Recently the key-role of mast cell interactions with Treg lymphocytes for orchestrating the inflammation as regards to its reparative phase and fibroplasia has been recognized [6].

On day 14, the number of mast cells and their degranulation index decreased. In the healing area, full-fledged collagen fibers were visualized.

## Conclusion

Thus, under the influence of drugs, based on collagen breakdown products, mast cells were found to be activated on the wound surface, which directly caused an acceleration of the reparative regeneration process.

## References

1. Vasiliev A. G., Churilov L. P., Trashkov A. P., Utekhin V. J. Evolution of the immune system and regulatory effects of antibodies. *Tsitologiya*, 2018, vol. 60, no. 2, pp. 71–80. (In Russian)
2. Alekseeva N. T., Klochkova S. V., Nikityuk D. B. Morphological characteristics of mast cells during skin regeneration. *Orenburgskii meditsinskii vestnik*, 2016, no. 3, pp. 13–16. (In Russian)
3. Alekseeva N. T., Nikityuk D. B., Klochkova S. V. Analytical morphology of reparative regeneration in the skin under the influence of various regional factors. *Zhurnal anatomii i gistopatologii*, 2015, vol. 4, no. 1, pp. 26–37. (In Russian)
4. Baranchugova L. M., Obydenko V. I., Rusaeva N. S. Morphological features of wound regeneration under the influence of collagen dissolution products. *Mezhdunarodnyi nauchno-issledovatel'skiy zhurnal*, 2014, no. 6, pp. 61–63. (In Russian)
5. Bobr O. A., Myadelets O. D., Dubovsky V. V. Dynamics of mast cell population during the wound process in rats subjected to hypobiotic conditions (starvation, hypothermia). *Vestnik Vitebskogo gosudarstvennogo meditsinskogo universiteta*, 2006, no. 4, pp. 1–9. (In Russian)
6. Komi D. E. A., Ribatti D. Mast cell mediated mechanistic pathways in organ transplantation. *Europ. J. Pharmacol.*, 2019, p. 172458.

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