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The development of dermal-cartilaginous autografts on the surface of a full-thickness skin defect in rats

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Развитие кожно-хрящевых аутотрансплантатов на поверхности полнослойного кожного дефекта у крыс

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Abstract.
Objectives. To reveal in dynamics the regularities of engraftment and existence on the receptive field of rats skin-cartilaginous autografts obtained from their auricles.
Material and methods. In male Wistar rats, a full-thickness skin defect of 1.2-1.4 cm^2 was created in the interscapular region, which was limited by a plastic security fixation. The animals were cut off each ear, from the skin of the inner surface of which a square site of 1 cm^2 was cut out. It was divided into 9 pieces and distributed on the wound surface. Macroscopic, histological and electron microscopic methods were used to study the engraftment of dermal-cartilaginous autografts.
Results. In 5 days after transplantation on those parts of the autografts where the cartilaginous support was intact, the chondrocyte layer looked almost the same as in the intact auricle structure. On the sites with the damaged lower chondrocytic cell layer, chondrocyte proliferation was observed in 5-10 days. After 30 days, a drop of fat was present in the cytoplasm of many newly formed chondrocytes, which was observed after 100 and 200 days. Autografts after 400 and 600 days remained as organized as autografts after 100 and 200 days.
Conclusions. In heterotopic autotopic autotransplantation of skin-cartilage grafts, cartilage tissue takes root on the receptive bed and remains viable in a size close to the original one for more than 1.5 years. The skin of the inner surface of the auricle, that was part of the autografts, significantly blocked the contraction of the receptive field.
Keywords: skin-cartilage autografts, full-thickness skin defect, receptive field, auricle, chondrocytes.

Резюме.
Цель – выявить в динамике закономерности приживления и существования на рецептивном ложе крыс кожно-хрящевых аутотрансплантатов, полученных с их ушных раковин.
Материал и методы. У крыс-самцов Wistar в межлопаточной области создавали полнослойный кожный дефект площадью 1,2–1,4 $см^2$, который ограничивали охранной камерой. У животных отрезали по ушной раковине, с кожи внутренней поверхности которой вырезали квадратный участок площадью 1 $см^2$. Разделив его на 9 кусочков, распределяли на раневой поверхности. С помощью макроскопического, гистологического и электронно-микроскопического методов изучали приживление кожно-хрящевых аутотрансплантатов.
Результаты. Через 5 суток после трансплантации на тех участках аутотрансплантатов, где хрящевая опора была не повреждена, пласт хондроцитов выглядел практически так, как в составе интактной ушной раковины. На участках с поврежденным нижним слоем хондрацитарных клеток пролиферация хондроцитов наблюдалась через 5-10 суток. Через 30 суток в цитоплазме многих новообразованных хондроцитов присутствовала капля жира, что наблюдалось через 100 и 200 суток. Аутотрансплантаты через 400 и 600 суток оставались организованнными так же, как и аутотрансплантаты через 100 и 200 суток.

Заключение. При гетеротопической аутотрансплантации кожно-хрящевых трансплантатов хрящевая ткань приживается на рецептивном ложе и сохраняется в жизнеспособном состоянии в размерах, близких к исходным, более 1,5 лет. При этом кожа внутренней поверхности ушной раковины, входившая в состав аутотрансплантатов, значительно блокировала контракцию рецептивного ложе.
Ключевые слова: кожно-хрящевые аутотрансплантаты, полнослойный кожный дефект, рецептивное ложе, ушная раковина, хондроциты.

Introduction

Restoration of cartilage tissue in the human body is one of the most important tasks of modern plastic surgery. The need for its solution also arises in the reconstruction of congenital or damaged cartilages of the larynx, nose, and ear [1]. At the same time, the vast majority of surgeons favor autografting over autoplasty [2]. The latter, in turn, makes it desirable to conduct preliminary experiments on animals [3].

Experiments on transplantation of cartilage tissue obtained from mammalian auricles began in the twentieth century. Thus, auricular cartilage from New Zealand rabbits was transplanted under the skin of these animals [4]. It was found that after 4 months, whole pieces of cartilage had taken root in their new location, while shattered cartilage had resorbed. The possibility of using dog auricular cartilage as autografts was studied in the healing of defects of their tubular bones [5]. There are known studies on implanting an artificially made auricle skeleton on the back of rats [3]. However, it was not possible to identify scientific works, where the engraftment of skin-cartilaginous autografts obtained from the auricles of laboratory animals has been studied for quite a long time.

In rats, a layer of chondrocytes covered on both surfaces by thin skin serves as a mechanical support for the auricle. The auricular muscles are present only under the skin of the outer surface of the latter, approximately 2/3 of its area [6]. Because of its location on the body surface, this stratum is available for the fabrication of dermal-cartilaginous autografts, can be used in relevant studies in which such autografts have been observed mainly macroscopically [7, 8].

In addition, we have previously shown the presence of cambial chondrocytes on both surfaces of the cartilaginous support of the auricle, which also suggests that after successful autotransplantation of rat auricular cartilage, it is able to take root in a new place together with the skin and its derivatives [9]. However, in order to confirm this hypothesis there remained the necessity to study the state of skin-cartilaginous autografts transferred to the surface of a full-thickness skin defect using modern methods of morphological study.

In connection with the mentioned, the aim of the conducted research was to reveal in dynamics (with the help of macroscopic, histological and electron-microscopic methods) the regularities of grafting and further existence on the receptive field of rats of skin-cartilaginous autografts obtained from their auricles.

Material and Methods

Forty-three sexually mature male Wistar rats weighing 220-270 g were used in the study. The animals were kept under standard vivarium conditions with free access to food and water. All manipulations with them - removal of wool, suturing of the protective chamber, creation of a full-layer skin defect, collection of tissues for making grafts, their transfer to the receptive bed, dressings, slaughter – were carried out under deep ether anesthesia, which corresponds to GOST 33215-2014 [10] GOST 33216-2014 [11], TCP 125-2008 (02040) «Good laboratory practice» [12].

Before formation of the receptive field in the interscapular region, the wool was removed and the guard cell was sutured to the skin. A 1.2-1.4 cm^2 full-thickness skin defect was created on the skin area inside the chamber by removing a full-thickness skin flap (the subcutaneous muscle was removed along with the skin), the bottom of which was the subcutaneous tissue [7]. The wound surface was covered with gauze and a gauze swab. The plastic security fixation was covered with a lid. The rats were placed in individual cages.

Two days after the formation of a full-thickness skin defect, one auricle was cut off from each animal. Skin was removed from the outer surface of the auricle, and a 1 cm^2 square section was excised from the skin of the inner surface of the organ, which contained the cartilaginous support of the auricle. It was divided into 9 more pieces, which were evenly distributed on the wound surface (Figure 1).

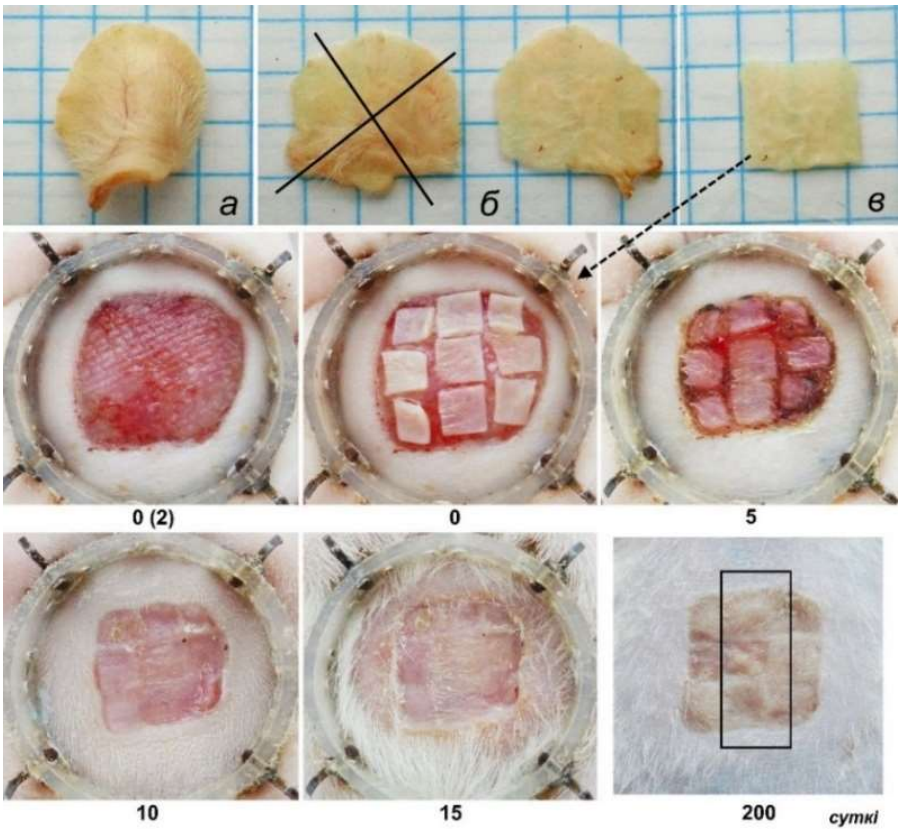

Figure 1 – The top row shows: a severed rat auricle (photo a) placed on caged paper (5×5 mm); it was divided into two layers, of which the inner layer was used later (photo b; the outer layer of skin is crossed out, it was not used); A square piece of 1 cm2 was cut from it (c), which was cut into 9 more pieces and spread evenly over the surface of the full-thickness skin defect (shown by the arrow). An example of how the wound and autografts looked macroscopically on its surface 0-200 days after transplantation is shown in the following 6 photos. It can be seen that autografts significantly inhibit the contraction of the full-thickness skin defect [7]. The numbers below the photo show the number of days since transplantation. The frame in the last photo shows the section of the receptive field that was taken for histologic and electron microscopic examination

Dressings were done daily for the first week, then they were done every 2-3 days thereafter. After 15 days, the guard cell was removed and the rats were labeled and placed in shared cages. After 5, 10, 15, 30, 100, 200, 400 i 600 days the rats were killed. Rectangular pieces of skin measuring 6×12 mm, oriented along the sagittal line, were excised from the receptive field region (Figure 1), along with sections of the cartilaginous plate that was under the skin. Tissues were fixed in a spread state in a formalin-alcohol-acetic acid mixture. After washing in water and dehydration, they were cast in paraffin using the conventional method. We obtained transverse histological sections 4.5 μm thick, oriented parallel to the sagittal axis of the rat body. Sections were stained with hematoxylin and eosin.

The histological organization of dermal-cartilaginous autografts obtained from rat auricles was studied similarly. The structure of the chondrocyte layer was focused on. For electron microscopic study in rats 200 days after transplantation from the receptive field, tissue pieces of 1×2×2×2 mm (in the area where the layers of transplanted chondrocytes were present) were cut out and fixed in 1% osmium fixative on Milonga buffer and poured into araldite. First, semi-thin sections were obtained, on the staining ground (methylene blue) and analysis of which blocks were further trimmed to obtain ultrathin sections. These sections were contrasted with uranyl acetate and lead citrate [13]. The preparations were studied in a JEM-1011 electron microscope.

Results and Discussion

The study of histological sections of the inner layer of the skin obtained after mechanical

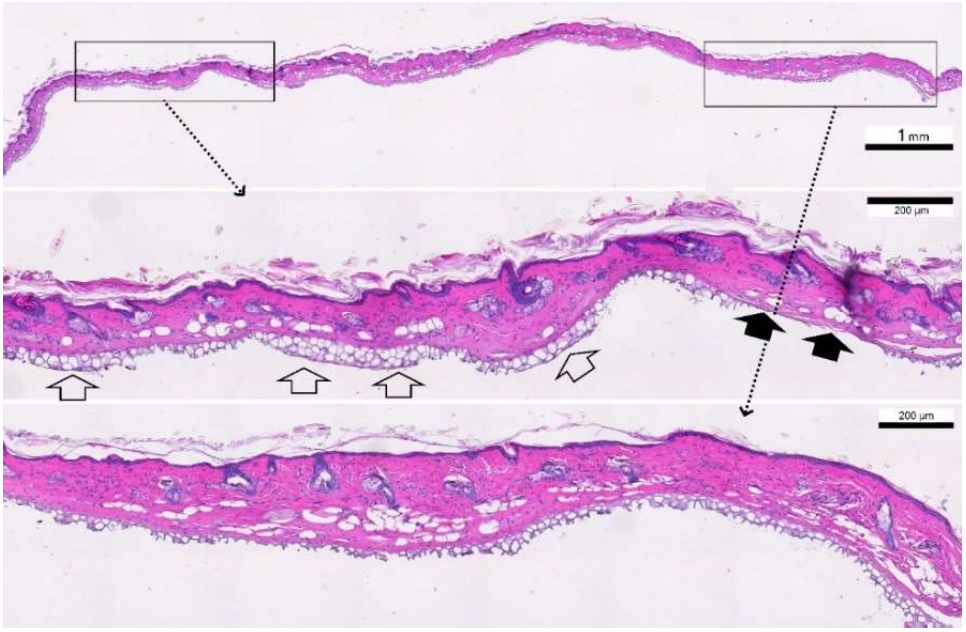

Figure 2 – Inner (ventral) layer of the auricular skin obtained after its detachment.
It can be seen that most of this layer contains epidermis and dermis with skin derivatives, as well as a significant portion of cartilaginous support. This support is often damaged to some degree along its length. Wide contour arrows indicate areas of the auricular layer where it was essentially intact; black broad arrows indicate areas of the graft where the cartilaginous support of the auricle appeared to have been completely removed along with the outer layer of the auricular skin. In other areas, the chondrocyte layer appears partially damaged – chondrocytes that were closer to the skin of the dorsal surface of the auricle are missing, chondrocytes that were closer to the skin of the dorsal surface of the auricle are missing or damaged

separation of the auricle has shown that in addition to the structures characteristic of the skin area of this localization (such structures as epidermis, dermis, hair follicles, skin glands, a thin layer of loose connective tissue), the cartilaginous support of the auricle is also present in this layer. Often the cartilaginous lamina was more or less damaged (this occurred during autograft fabrication), which had a significant impact on how this structure grafted onto the receptive field (Figure 2).

Histologic study of the tissues taken from the receptive field made it possible to see that 5 days after transplantation the epidermis, dermis, and skin derivatives were in a fully viable state as part of the ear autografts that were on the surface of the full-thickness skin defect. At the same time, the chondrocyte layer was preserved in different parts of the autografts to different degrees (which corresponds to the above mentioned phenomenon of partial damage – figure 2). In those parts of the autografts where the cartilaginous support was insignificantly damaged, the chondrocyte layer looked almost the same as it does in the intact auricle. The lower surface of this layer (the former surface of the cartilaginous support adjacent to the skin of the dorsal surface of the auricle) was on the surface of the young granulation tissue of the receptive field. In the same areas of autografts where the chondrocyte stratum was more significantly damaged, areas of stratum fibrosum were present along with groups of chondrocytes.

At this term, in some cases with a damaged chondrocyte layer, an increase in the number of unripe chondrocytes was already observed compared to the inactivated state, and occasionally it was possible to find figures of their mitotic division. This means that the cambial chondrocytes of the cartilaginous support of the auricular cartilage are indeed capable of division, and for it to begin, it probably requires the removal of some of the mature chondrocytes from the stratum, as well as the presence of certain cytokines that young granulation tissue is capable of forming. At 5 days after transplantation, dead chondrocytes were detected in only one case (from 4 slices examined) and in a small section. It was caused by bacterial infectious agents (neutrophilic infiltration was present) that reached the receptive bed either during its formation or during transplantation.

In 10 days after transplantation the cystological picture in general looked similar to the previous one, except that in those places of the transplanted chondrocyte layers, where proliferation of their cambial forms had occurred earlier, there was a newly formed cartilaginous tissue (Figure 3). The cambial forms of chondrocytes were without lipid droplets in the cytoplasm, and special cells in a state of mitotic division were also occasionally found among them.

The cartilaginous tissue in the graft looked similar to the previous one in 15 days after transplantation: the chondrocyte layers had a structure close to the intact state. Masses of chondrocytes were present in areas where stratum injury had occurred, usually still without the single small lipid droplets within some cells that were part of the newly formed chondrocytic masses.

Thirty days after transplantation, the cartilage tissue retained the basic principles of its post-transplant organization as described above. The principal difference from the previous term was that a drop of fat was already present in the cytoplasm of most of the newly formed chondrocytes.

The dermal appearance of autografts and chondrocyte strata on the receptive field at 100 and 200 days after transplantation was generally the same as at 30 days (Figure 4), except that all newly formed chondrocytes had a pronounced centrally located fat droplet in their composition. Histological examination of autografts, including their chondrocytic part, 400 and 600 days after transplantation showed that they remained organized fundamentally the same as autografts 100, 200 days after transplantation.

Thus, in the interval of 30–600 days the changes in the structure of autografts and chondrocyte layer in their composition slowed down so much that we can say that one month after transplantation autografts entered the phase of morpho-functional stabilization (when further structural changes either did not occur or occurred very slowly).

Using electron microscopic examination of 200-day autografts, it was confirmed that the receptive field did indeed contain layers of chondrocytes, folded in most cases from mature chondrocytes with a large centrally located fat droplet, which in places were covered by a fibrous sheath. The chondrocytes within the transplanted cartilage tissue were separated from each other by a space filled with fibrous-grained substance and elastin, which together formed specific envelopes around the cells.

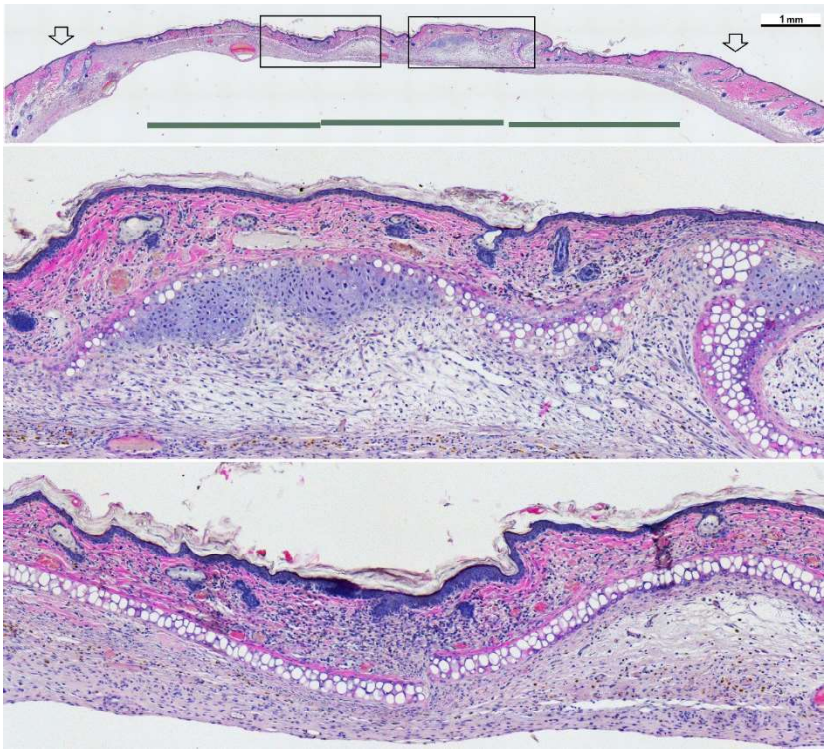

Figure 3 – 10 days after transplantation, at the sites where chondrocyte layers were damaged, the cambial forms of the latter multiplied, forming conglomerates composed of new young chondrocytes (middle photo). Where the chondrocyte layer was only slightly damaged, there are no such formations (bottom photo)

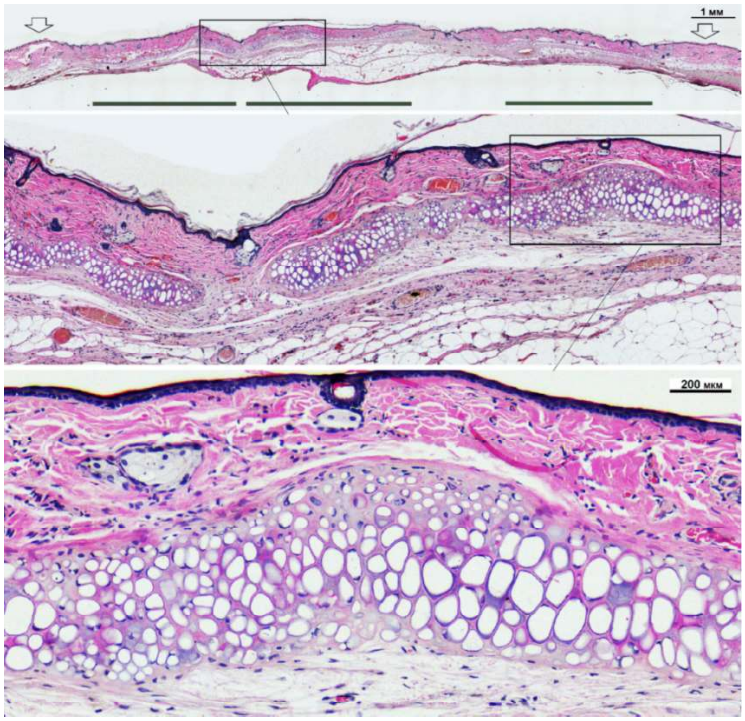

Figure 4 – One of the autografts 200 days after transplantation. It can be seen that in one of its sections the pre-multiplied chondrocytes, arranged in a conglomerate in several layers, have one fat droplet each

In the thickness of the chondrocyte stratum, voids where previously differentiated chondrocytes were located were occasionally embedded, which was an indication that some differentiated chondrocytes could not survive transplantation. As well as in the intact layer of chondrocytes, in the structure of its upper surface (closer to the skin of autografts), many young chondrocytes were detected (the latter were characterized by: smaller size; presence of several small fat droplets in the cytoplasm, which, as a rule, already occupied the central position; high electron density of the cytoplasm; numerous tufts on the cell surface). On the surface of the layer of cartilage tissue adjacent to the reticulate bed, chondrocytes could also be found, which resembled combial cells in their features: small cell size, which is located within the boundaries of the chondrocyte layer; centrally located nucleus; light-colored cytoplasm filled with organelles, among which centrioles are found.

The listed features of combial and juvenile chondrocytes, as well as the presence of chondrocytes themselves, entirely correspond to the structure of the chondrocyte layer in the intact auricle. However, among the less differentiated chondrocytes there were occasionally some that could be located several pieces under one elastic sheath (which was not observed in the intact state). On the lower surface of the chondrocyte layer, the arrangement and structure of differentiated and undifferentiated chondrocytes often looked similar to that at the top. It was covered by a fibrous sheath, behind which there was a loose connective tissue with blood vessels, fibroblasts, and adipocytes characteristic of it. However, there were areas where chondrocytes were unusually loose (compared to the intact state).

A special variant of the structure of the lower surface of the chondrocyte layer was formed by the areas where the line of rupture of the cartilaginous support of the auricle, which occurred during the autograft fabrication, was reliably visible. This line ran along the inferior edges of the ruptured elastic sheaths that surrounded the mature chondrocytes in the intact state (Figure 5). Although more than six months after transplantation, evidence of damage to the chondrocyte layer was still present at the receptive field. This phenomenon probably shows a weak response of macrophages to the presence of organic material in the wound, of which the intercellular matrix of the cartilaginous support of the auricle is constructed.

Macrophages were also present in significant numbers beneath the areas of the chondrocyte layer with the described features. Many of these cells were easy to identify. However, in some cases

Figure 5 – Two sections of the chondrocyte layer where, together with differentiated chondrocytes and granulation tissue of the receptive bed, the edges of the elastin sheaths (shown by arrows) destroyed during autograft fabrication are visible. The upper photo shows signs of more damage (additional voids are present under the elastin sheaths)

(when macrophages penetrated into the elastin cells of chondrocytes, which usually contained young chondrocytes, and filled their cytoplasm with large lipid droplets) it was difficult to determine whether it was a chondrocyte or a macrophage.

Thus, after heterotopic autotransplantation of rat skin-cartilage grafts used in this experiment, cartilage tissue can take root on the receptive bed and remain viable in a size close to the original size for more than 600 days. At the same time, the skin of the inner surface of the auricle, which was included in the autografts, can significantly block the contraction of the receptive bed all this time. Sections of the chondrocyte layer that were not damaged during autograft fabrication and the following transplantation take root at the new site and remain in a virtually intact state.

In this model, chondrocyte proliferation is observed as early as 5–10 days. This process occurs in areas of the cartilage layer of the graft where damage to the lower layer of chondracitic cells has occurred. In our preliminary study devoted to the investigation of the healing of a through hole made in the rat auricle [14], it was revealed that the first manifestations of cambial chondrocyte proliferation could be detected in these animals much later (35 days after the injury) and had, in comparison with the transplantation model, a weakly expressed character. What can explain the difference in the manifestations of regenerative activity of mechanically damaged cartilage tissue of the same injury site?

Answering this question, we must first of all refer to the hypothesis expressed by Seifert A.W. [15] and Brewer, C. M. et al. [16], which states that

myofibroblasts of granulation tissue, which naturally appears at the site of damage to the cartilaginous support of the auricle, inhibited the regenerative potential of cambial chondrocytes. We obtained additional evidence in support of this hypothesis – the dermal part of the autograft, which took root on the surface of the full-thickness skin defect, inhibited the development of granulation tissue and through this – wound contraction. Probably, the consequence of the latter was the possibility of greater realization of the regenerative potential of cambial chondrocytes present in the autograft. The much smaller presence of granulation tissue caused its insignificant inhibitory effects.

Conclusion

On the model of transferring the skin-cartilaginous autografts, made from the auricle of laboratory rats, on the surface of the full-layer skin defect, by means of macroscopic, histological and electron-microscopic methods it has been revealed that these autografts take root in the new place and remain in the viable state for more than 1.5 years. In this case, the cartilaginous support of the auricle remains under the skin of the autografts preferably in a spread out state. Those portions of the chondrocyte stratum that were not damaged during autograft fabrication and subsequent transplantation take root at the new site and remain essentially intact at all times. In the same areas of the chondrocyte layer where the lower row of differentiated cells was damaged, active regenerative processes associated with the proliferation of cambial chondrocytes and their formation of intercellular matrix begin in a few days. As a result of these processes, cartilaginous masses are revealed after 15 days, which replace the damaged areas of the cartilaginous support of the auricle. Thirty days after transplantation, lipid droplets appear in the cytoplasm of a significant portion of newly formed chondrocytes, and after 100 days or more, lipid droplets are present in almost all of them. Damaged areas of elastin sheaths of chondrocytes that appeared on the receptive bed after transplantation were detected by electron microscopic examination even after 200 days.

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References

1. Bulgin DV, Kovtun AL, Reshetov IV, Radomskaya EYu. Prospects of creating artificial human tissues and organs based on the method of three-dimensional bioprinting. Vestn Transplantologii Iskusstv Organov. 2023;25(2):63-81. (In Russ.). doi: 10.15825/1995-1191-2023-2-63-81
2. Onderková A, Kalaskar DM. 3D bioprinting for auricular reconstruction: A review and future perspectives. Int J Bioprinting. 2023;9(6):273-307. doi: 10.36922/ijb.0898
3. Jang CH, Koo YW, Kim GH. ASC/chondrocyte-laden alginate hydrogel/PCL hybrid scaffold fabricated using 3D printing for auricle regeneration. Carbohydr Polym. 2020 Nov:248:116776. doi: 10.1016/j.carbpol.2020.116776
4. Can IH, Atilla P, Cakar AN, Onerci M. An animal study on cartilage healing using auricular cartilage as a model. Eur Arch Otorhinolaryngol. 2008 Mar;265(3):307-11. doi: 10.1007/s00405-007-0455-1
5. Saifzadeh S, Rezazadeh Gh, Ghasemi SM. Role of pinna cartilage autograft on long bone healing in dog: radiographic and biomechanical studies. J Veterinary Res. 2007;61(4):415-21.
6. Raduta AF, Belanovskaya AB, Shatrova VA, Zaloga IV, Ostrovskiy AA. Features of the structure of the auricle of laboratory rats and coniferous mice. Vesn GrDU im Ya Kupaly. Ser 5, Ekanomika Satsyyalogiya Biyalogiya. 2023;13(1):138-49. (In Russ.)
7. Bakunovich AA, Yaroshenko YuU, Raduta AF, Konanov EV, Buko VYu, Ostrovskiy AA. Experimental model for assessing the readiness of the wound surface to accept skin grafts. Izv Nats Akad Nauk Belarusi Ser Med Nauk. 2021;18(3):340-50. (In Russ.). doi: 10.29235/1814-6023-2021-18-3-340-350
8. Bakunovich AA. A model for evaluating the influence of various factors on the performance of skin grafts. Novosti Mediko-biol Nauk. 2021;21(2):11-7.
9. Raduta AF, Ostrovskaya AB. Cambial elements of rat auricular cartilage. V: GrGU im Yanki Kupaly; Yanchurevich OV, Ryzhaya AV, redkol. Zoologicheskie chteniya: sb nauch st, posvyashch 125-letiyu d-ra biol nauk Ivana Nikolaevicha Serzhanina. Grodno, RB: ГрГУ; 2023. P. 239-41. (In Russ.)
10. GOST 33215-2014. Guidelines for the maintenance and care of laboratory animals. Rules of equipment of premises and organization of procedures. Vved. 2016-07-01. Izd ofits. Moscow, RF: Standartinform; 2016. VI, 19 p. (In Russ.)
11. GOST 33216-2014. Guidelines for the housing and care of laboratory animals. Rules for the housing and care of laboratory rodents and rabbits. Vved 2016-07-01. Izd ofits. Moscow, RF: Standartinform; 2016. VI, 16 p. (In Russ.)
12. Good laboratory practice = Nalezhnaya labaratornaya praktyka: TKP 125-2008 (02040). Vved 2008-03-28. Izd ofits. Minsk, RB: M-vo zdravookhraneniya Resp Belarus'; [2008]. IV, 39 p. (In Russ.)
13. Reynolds ES. The use of lead citrate at high pH as an electron-opaque stain in electron microscopy. J Cell Biol. 1963 Apr;17(1):208-12. doi: 10.1083/jcb.17.1.208

14. Raduta AF. Closure of penetrating holes in the auricles of laboratory rats and hamsters. V: Trushel' NA, red. Aktual'nye problemy morfologii na sovremennom etape [Electronic resource]: sb nauch st, posvyashch 85-letiyu kmn, dots SP Yaroshevicha UO «Belorusskii gosudarstvennyi meditsinskii universitet», Minsk, Resp Belarus', okt 2023 g. Minsk, RB: BGMU; 2023. 1 elektron opt disk (CD-ROM). P. 409-13. (In Russ.)
15. Brewer CM, Nelson BR, Wakenight P, Collins SJ, Okamura DM, Dong XR, et al. Adaptations in Hippo-Yap signaling and myofibroblast fate underlie scar-free ear appendage wound healing in spiny mice. Dev Cell. 2021 Oct;56(19):2722-40. doi: 10.1016/j.devcel.2021.09.008
16. Seifert AW, Muneoka K. The blastema and epimorphic regeneration in mammals. Dev Biol. 2018 Jan;433(2):190-199. doi: 10.1016/j.ydbio.2017.08.007

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Литература

1. Перспективы создания искусственных тканей и органов человека на основе метода трехмерной биопечати / Д. В. Булгин [и др.] // Вестн. трансплантологии искусств. органов. 2023. Т. 25, № 2. С. 63–81. doi: 10.15825/1995-1191-2023-2-63-81
2. Onderková, A. 3D bioprinting for auricular reconstruction: A review and future perspectives / A. Onderková, D. M. Kalaskar // Int. J. Bioprinting. 2023. Vol. 9, N 6. P. 273–307. doi: 10.36922/ijb.0898
3. Jang, C. H. ASC/chondrocyte-laden alginate hydrogel/PCL hybrid scaffold fabricated using 3D printing for auricle regeneration / C. H. Jang, Y. W. Koo, G. H. Kim // Carbohydr. Polym. 2020 Nov. Vol. 248. Art. 116776. doi:10.1016/j.carbpol.2020.116776
4. An animal study on cartilage healing using auricular cartilage as a model / I. H. Can [et al.] // Eur. Arch. Otorhinolaryngol. 2008 Mar. Vol. 265, N 3. P. 307–311. doi: 10.1007/s00405-007-0455-1
5. Saifzadeh, S. Role of pinna cartilage autograft on long bone healing in dog: radiographic and biomechanical studies / S. Saifzadeh, Gh. Rezazadeh, S. M. Ghasemi // J. Veterinary Res. 2007. Vol. 61, N 4. P. 415–421.
6. Асаблівасці будовы вушной ракавіны лабараторных пацукоў і іглістых мышэй / А. Ф. Радута [і інш.] // Весн. ГрДУ ім. Я. Купалы. Сер. 5, Эканоміка. Сацыялогія. Біялогія. 2023. Т. 13, № 1. С. 138–149.
7. Эксперыментальная мадэль для ацэнкі гатоўнасці ранавай паверхні да прыняцця скурных трансплантатаў / А. А. Бакуновіч [і інш.] // Изв. Нац. акад. наук Беларуси. Сер. мед. наук. 2021. Т. 18, № 3. Р. 340–350. doi: 10.29235/1814-6023-2021-18-3-340-350
8. Бакуновіч, А. А. Мадэль для ацэнкі ўздзеяння розных чыннікаў на здольнасць скурных трансплантатаў / А. А. Бакуновіч // Новости медико-биол. наук. 2021. Т. 21, № 2. С. 11–17.
9. Радута, А. Ф. Камбіяльныя элементы хрястка вушной ракавіны пацукоў / А. Ф. Радута, А. Б. Астроўская // Зоологические чтения : сб. науч. ст., посвящ. 125-летию д-ра биол. наук Ивана Николаевича Сержанина / ГрГУ им. Янки Купалы ; редкол.: О. В. Янчуревич (гл. ред.), А. В. Рыжая. Гродно : ГрГУ, 2023. С. 239–241.
10. ГОСТ 33215-2014. Руководство по содержанию и уходу за лабораторными животными. Правила оборудования помещений и организации процедур. Введ. 2016-07-01. Изд. офиц. Москва : Стандартинформ, 2016. VI, 19 с.
11. ГОСТ 33216-2014. Руководство по содержанию и уходу за лабораторными животными. Правила содержания и ухода за лабораторными грызунами и кроликами. Введ. 2016-07-01. Изд. офиц. Москва : Стандартинформ, 2016. VI, 16 с.
12. Надлежащая лабораторная практика = Належная лабараторная практыка : ТКП 125-2008 (02040). Введ. 2008-03-28. Изд. офиц. Минск : М-во здравоохранения Респ. Беларусь, [2008]. IV, 39 с.
13. Reynolds, E. S. The use of lead citrate at high pH as an electron-opaque stain in electron microscopy / E. S. Reynolds // J.Cell Biol. 1963 Apr. Vol. 17, N 1. P. 208–212. doi: 10.1083/jcb.17.1.208
14. Радута, А. Ф. Закрыццё скразных адтулін у вушных ракавінах лабараторных пацукоў і акомісаў / А. Ф. Радута // Актуальные проблемы морфологии на современном этапе [Электронный ресурс] : сб. науч. ст., посвящ. 85-летию к.м.н., доц. С. П. Ярошевича УО «Белорусский государственный медицинский университет», Минск, Респ. Беларусь, окт. 2023 г. / под общ. ред. Н. А. Трушель. Минск : БГМУ, 2023. 1 электрон. опт. диск (CD-ROM). С. 409–413.
15. Adaptations in Hippo-Yap signaling and myofibroblast fate underlie scar-free ear appendage wound healing in spiny mice / C. M. Brewer [et al.] // Dev. Cell. 2021 Oct. Vol. 56, N 19. P. 2722–2740. doi: 10.1016/j.devcel.2021.09.008
16. Seifert, A. W. The blastema and epimorphic regeneration in mammals / A. W. Seifert, K. Muneoka // Dev. Biology. 2018 Jan. Vol. 433, N 2. P. 190–199. doi:10.1016/j.ydbio.2017.08.007

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