The Role of Donor and Recipient in Tissue Implantation

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The relationships between embryonic stem and cambial cells in the ontogeny were evaluated on the basis of our data on organ embryogenesis and *in vivo* implantation of epithelial tissues and published data. We demonstrated the role of recipient tissues in the implantation process. Aseptic inflammation developing in response to the implant activates proliferation of the adjacent donor tissues. Proliferation and differentiation of the implanted donor tissues correspond to inflammation phases in the focus of implantation, are regulated by factors of the recipient organism, and are histogenetically determined.

Key Words: *tissue implantation; donor; recipient*

The method of tissue therapy is now actively developed in many scientific laboratories. The aim of these investigations is to obtain polypotent stem cells capable of restoring the tissue of any damaged organ.

Embryonic stem cells (ESC) do exists, but it can be obtained only during the first few days of embryogenesis. It early undergoes changes (simultaneously with the development of primordia of functionally different tissues). This process leads to the loss of ESC polypotency. Its capacity to renew tissues is retained during embryogenesis. This can be explained by determination existing during embryogenesis and consisting in realization of genetic information carried by ESC. Cambial cells (CC) can restore tissues only within the parental embryonic primordium. Stromal connective tissue cells cannot differentiate into epithelial cell or cell of other (non-mesenchymal) tissues. During allogeneic transplantation the recipient organism reacts not only to the implanted donor cells, but also to extracts of embryonic tissues [2]. ESC and CC should be studied not as separate, but as interrelated elements. CC are young proliferating and self-maintaining cells retaining the capacity to differentiate into mature cells providing the function of the organ. ESC persist in each organ, but can function only within the parental organs and their group. Modern cell technologies use cambial elements present in each organ. Stromal hemopoietic stem cell (SHC) of the bone marrow is not ESC [5], but it possesses greater potential compared to other non-mesenchymal organs. SHC are heterogeneous [5]. Some of them can integrate into the hemopoietic system, which often determined the positive therapeutic effect. However, other SHC (mesenchymal stem cells) can form only the connective tissue stroma or a niche for blood cells. Implantation of these cells can lead to negative therapeutic effect. These cells proliferate with the formation of a cicatrix tissue. Heterogeneity of HSC is determined by their mesenchymal histogenesis.

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MATERIALS AND METHODS

The interaction between allogeneic donor tissue with the recipient tissue can be studied by culturing epithelial tissue by the method of F. M. Lazarenko. This method does not require labeling of implanted tissues, because proliferation of epithelium in the implant is often clearly seen. This method was described previously [1,3]. In brief, a pea-sized implant consisting of thoroughly minced tissues of a

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donor epithelial organ mixed with small dense celloidin particles is placed into a small pocket in the subcutaneous fat of the recipient. Recipient organism respond by local aseptic inflammation, the exudate pulls out the implanted tissue fragments. Celloidin particles potentiate and prolong the inflammation to 20-30 days. Changes in the implanted tissues can be observed during this period. The implants were removed at different terms of the experiment and processed using routine histological methods.

RESULTS

It was found that tissue processes in the implant and adjacent tissue correspond to the stages of local inflammation in the recipient organism. During the first two days we observed activation of the loose connective tissue of the recipient and cambial cells of the implanted epithelium. The connective tissue with small blood vessels grows between the implanted tissue elements, which creates normal microenvironment for proliferation of the implanted epithelium. Epithelial cells divide by mitosis and spread along the newly formed connective tissue. After attenuation of the inflammatory reaction in the implantation zone, changes are observed in the implanted tissue.

On days 8-10, proliferation of the epithelium becomes less active giving way to differentiation of epithelial structures and organogenesis. Histogenetic characteristics of the implanted epithelium manifest at this stage. For instance, skin epithelium forms defense layers and glands, skin derivatives, around the celloidin particles (Fig. 1, *a*). The appearing structures are under the control of regulatory factors of the recipient. For instance, cords of mammary gland epithelium implanted to a lactating female form new lobules of the secretory epithelium (Fig. 1, *b*) lacking excretory ducts; some alveoli become extremely dilated and their epithelium looks thinned.

Experiments with implantation of rabbit epithelial tissues showed that the first two days, when the recipient organism responds to donor tissue by local aseptic inflammation, are a critical period in the implantation process. This inflammation leads to activation and growth of cambial elements of the implanted donor tissues. The implanted tissues adapt to the recipient organism; fine connective tissue, small blood vessels, and nerves grow into it. New layers of recipient tissue elements appear and implanted epithelium grows on these elements. On day 6-8 of the experiment, new organ structures retaining characteristics of a certain embryonic pri-

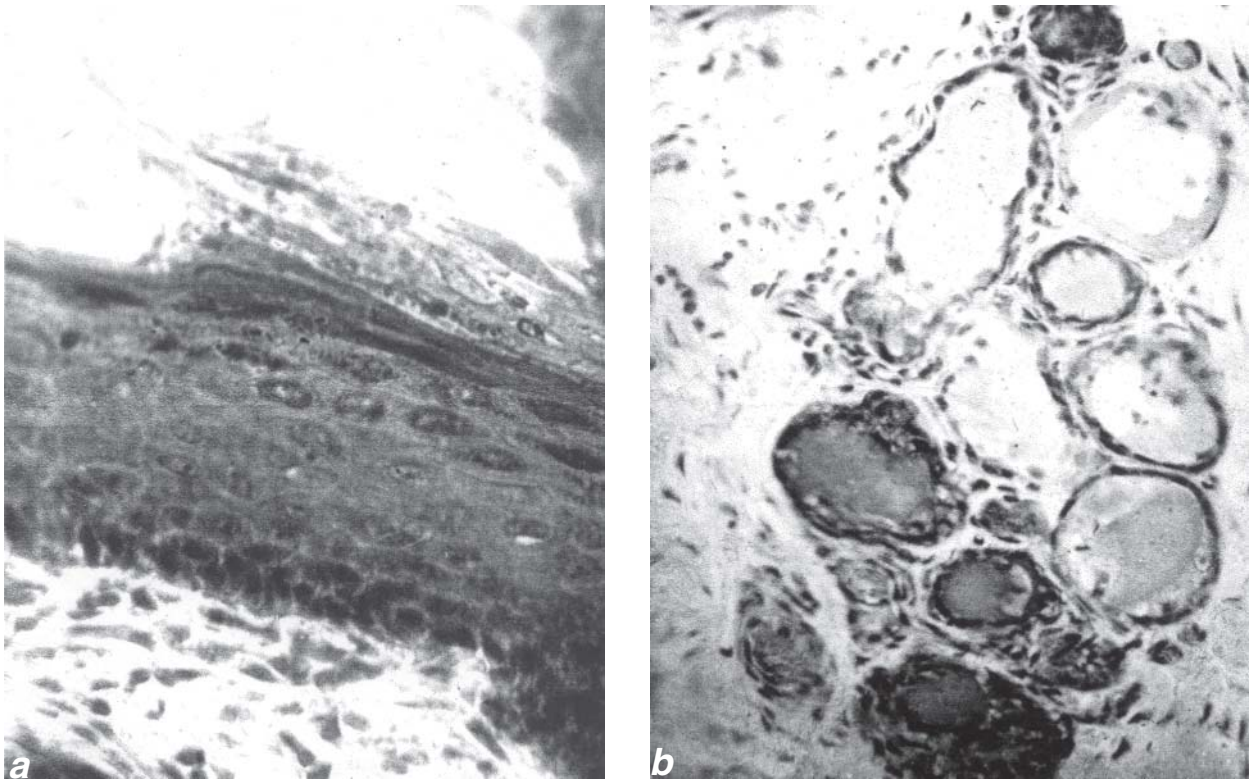

Fig. 1. Epithelium of organs (skin derivatives) cultured in the organism by the method of Lazarenko, *a*) skin epithelium, day 6; *b*) mammary gland epithelium, day 15. Fixation in Zenker fluid, hematoxylin and eosin staining, ×80 (*a*), ×280 (*b*).

mordium and unchanged morphogenetic nature are formed from the amorphous cell mass of the implant. The implanted epithelium grows within the inflammatory focus. The recipient organism plays a regulatory role during differentiation of the implanted structures. For instance, implantation of skin epithelium or mammary gland tissue under similar conditions leads to the formation of defense layers of skin epithelium surrounding solid foreign particles (celloidin) or mammary gland lobules corresponding to the structure of this organ in the recipient female, whose hormone background determines differentiation of the implanted epithelium.

After attenuation of the inflammation, new structures, defense layer and secreting alveoli grown from the allogeneic donor tissues, undergo reverse development due to immunological discordance between these tissues and the absence of recipient's need in these tissues. A dense connective tissue scar develops at the site of the implant.

Thus, after allogeneic implantation the formed epithelial structures after attenuation of aseptic inflammation undergo reverse development due to immunobiological discordance between these tissues and the absence of recipient's need in these tissues. Hence, the nature of donor cells and their proliferative potential should be taken into account during implantation to a recipient.

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