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ONTOGENESIS OF HEMOPOIETIC AND CONNEKTIVE TISSUE CELLS

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✓ ***Resume***

Basing on the published data and the carried-out investigations of a human ontoenesis, the origination of the hemopoietic and connective tissue cells in the process of hemopoiesis in the corresponding extraembryonic and embryonic mesoderma have benn studied. The connective tissue cells originated from the embryonic mesenchymal elements and differentiated into the cells of fibroblastic, chondroblastic, osteoblastic, adipocytic, smooth muscular and vascular cells types. Combination of various elements provided by the mechanisms of transcription, creates very complex and flexible system for controlling the transcription processes. It helps the connective tissue cells to become differentiated and to provide definite types of function.

Key words: histogenesis, ontoenesis, connective tissue.

ОНТОГЕНЕЗ ГЕМОПОЭТИЧЕСКИХ И СОЕДИНИТЕЛЬНОТКАННЫХ КЛЕТОК

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✓ ***Резюме***

На основании данных литературы и изучения онтогенеза человека рассматривается происхождение в эмбриогенезе гемопоэтических и соединительнотканных клеток соответственно из внезародышевой и зародышевой мезодермы. Клетки соединительной ткани развиваются и дифференцируются из эмбриональных мезенхимальных элементов в клетки фибробластической, хондробластической, остеобластической, адипоцитарной, гладкомышечной, сосудистой линий. Комбинация различных элементов транскрипционных механизмов создает очень сложную и гибкую систему контроля транскрипции, что позволяет дифференцироваться и функционировать клеткам соединительной ткани определенного типа.

Ключевые слова: гистогенез, онтогенез, соединительная ткань.

ГЕМОПОЭТИК ВА БИРИКТИРУВЧИ ТЎҚИМА ХУЖАЙРАЛАРИНИНГ ОНТОГЕНЕЗИ

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✓ ***Резюме***

Адабиёт ва олинган муаллифларни натижаларига кўра одам организмнинг онтогенези асосида эмбриогенезда бириктирувчи тўқима ва гемопоэтик хужайраларини монанд равишда ҳомилани ва ундан ташқари жойлашган аъзолар мезодермасидан тараққий этиши аниқланган. Ҳомиланинг эмбрионал мезенхимасидан ихтисосланиб фибробластик, хондробластик, остеобластик, адипоцитар, силлиқ мушак ва қон томир хужайраларини тараққий этади. Транскриптцион механизмларини элементларининг турли комбинациялари транскрипцияни мураккаб ва эгулувчан тизимини яратади. Бу эса бириктирувчи тўқима хужайрасини маълум туринг ихтисослашишига ва фаолият оборишга имконият беради.

Калит сўзлар: гистогенез, онтогенез, бириктирувчи тўқима.

Relevance

The study of biology, histogenesis and cell differentiation significantly deepened the existing understanding of the structure and function of blood cells and connective tissue. However, despite this, our knowledge of connective tissue stem cells is insufficient, often contradictory, and requires systematization and understanding, and consideration in accordance with the theoretical provisions on histogenetic series, or cell differons, [1,3,5].

After fertilization of germ cells and the formation of a zygote in the lumen of the fallopian tubes, there is a splitting, blastula formation, and determination of 2 types of cells: trophoblast (trophoectodermal, or surface) and embryoblast (internal). From the cells of the trophoblast, cytotrophoblast and syncytiotrophoblast are differentiated, lining the surface of the villous and smooth chorion. Embryoblast cells at the stage of gastrulation (day 7, phase I - delamination; day 14-15, phase II - immigration) form 2 germ leaves:

epiblast (facing the trophoblast) and 2. hypoblast (facing the blastocyst cavity). At this stage, EPI - and hypoblast cells are not sufficiently determined.

Epiblast subsequently becomes a source of formation of extra-germ and germ ectoderm; hypoblast-extra-germ

and germ endoderm. With the participation of epiblast and hypoblast cells, extra-germ and germ mesoderm are formed

From the cells of the extra-germ endoderm develop: a) the epithelium of the yolk SAC and b) allantois. The cells of the germ endoderm form a) the integumentary and glandular epithelium of the stomach, b) the epithelium lining the villi and crypts of the intestine, C) the pancreas and d) the liver. From the composition of the hypoblast cells to the extra-germ mesoderm, 2 cell lines migrate under the epithelium of the forming yolk vesicle for subsequent differentiation into hemoblasts and gonadoblasts. The extra-germ mesoderm is differentiated into a mesenchyma located between the trophoblast and the epithelium of the amnion, yolk SAC and allantois, under the epithelium of the umbilical cord. The intrauterine mesoderm is also differentiated into the mesenchyma, which is involved in the formation of muscle, connective (own, skeletal, with special properties) tissues and vessels, epithelium of the kidneys, uterus, gonads and VAS deferens, mesothelium, adrenal cortex, organs of the cardiovascular, hematopoietic and immune systems [1].

Based on this, it should be concluded that the structures of both mesoderms are induced by the same regulatory factors of the maternal organism up to a certain time (it is possible and during the entire period of intrauterine development). Both in the developing embryo and in extra-fetal organs (placenta, yolk SAC), mesenchyma, cells of loose connective tissue (fibroblasts, endotheliocytes, reticular, etc.) synthesizing the main substance are differentiated asynchronously, but interconnected (by feedback type). Finally, non-deterministic cells of the extra-embryonic mesoderm, under the influence of factors of vascular formation and growth, hematopoiesis under the trophoblast of the villous and smooth chorion, under the epithelium of the amnion and yolk SAC, differentiate into mesenchymal cells, endothelium, stem and blast blood cells. Capillaries in the germ mesoderm appear 1-2 days later than in the mesenchyma of the extra-germ mesoderm. They are secondarily connected to the vessels of the extra-fetal mesoderm at the junction of the umbilical cord with the body of the embryo, in the area of accumulation of endodermal epithelial cells involved in the formation of liver lobes. After the connection between the capillaries outside and inside the germ mesoderm, the formation of microcirculatory vessels in them occurs both by budding previously formed, and primarily, from mesenchymal cells.

Hematopoiesis in the mesoderm under the epithelium of the yolk SAC, which begins at 4 weeks of embryonic development, stops at the end of the second month. Blood stem cells and inducing regulatory factors migrate from the extra-fetal mesoderm through the forming umbilical cord to the fetal mesoderm, in the area of the liver bookmark. By the 5th week of embryonic development, the embryonic mesenchyma with hemoblasts grows into the endodermal epithelium of the formed liver. As a result, from 6 weeks of embryonic development, single capillaries and foci of extra - and intravascular hematopoiesis are detected between the strands of epithelial cells of the forming liver lobes. By the end of week 6, fragments of formed capillaries and small foci of intra - and extravsacular hematopoiesis are detected in the mesenchyma between epithelial cells and other forming internal organs (kidneys, intestines, skin, etc.). This indicates a close relationship between the processes of determination, proliferation and differentiation, their regulation in the extra - and intra-germ mesoderm, in the mesenchyma of forming organs [1,3]. However, the most important, in our opinion, is the inductive interaction of the external and intrauterine endodermal epithelium with mesenchymal cells, blood stem cells. This is what determines the determination of mesenchymal cells in connective tissue, and hematopoietic stem cells - in blood cells. These processes are carried out under the influence of numerous factors of growth, determination and differentiation.

The processes of determination and differentiation of mesenchymal and hematopoietic cells that differ both in time (heterochrony) and spatially (extra-germ mesoderm under the epithelium of the villous and smooth chorion, yolk SAC and amnion) in the extra-germ and embryonic mesoderm (under the ectodermal and endodermal epithelium) should be considered as a measure of adaptation, increasing the reliability of histogenetic processes formed in evolution and manifested during individual development [1,2].

Thus, 1) nazaralieva mesoderm with 5 weeks of embryonic development interact with vnutrisosudistoi; 2) hematopoietic stem cells (CCM) of nazaralieva mesoderm move in vnutriserdecnuu; 3) nazaralieva capillary network in the mesenchyme beneath the epithelium of the yolk SAC, villous and smooth chorion, the amnion and umbilical cord interacts with vnutrisosudistoi and forms with it a single vascular network. Due to this, the interaction of afferent and efferent links of the functional system rises to a qualitatively higher level, and the feedback in the functional system is mother-extra-fetal organs-fetus;

4) trophic and regulatory humoral substrates from the mother to the fetus come through the extra-fetal mesenchyma first diffusely, as part of the interstitial fluid, and then through the intensively formed vascular system. The epithelium of the emerging liver and other internal organs becomes the area of interaction of the extra - and intra-fetal mesoderm, flows of trophic and regulatory factors of the mother and fetus.

In the area of the emerging liver, blood flows from the hepatic artery, portal and umbilical veins are combined at the earliest stage of its development. The umbilical artery departs just below the hepatic artery, from the same arterial trunk and is directed through the umbilical ring to the umbilical cord, where it forms a circulatory system in the mesenchyma of the forming villous and smooth chorion, yolk SAC and amnion. Thus, 2 arteries that depart from the abdominal and iliac arteries of the fetus form 2 separate capillary networks: one - in the extra-fetal organs, the other-between the epithelial cords of the emerging liver.

Already at the earliest stage of intrauterine development, first in the extra-fetal and then intra-fetal mesoderm, the close interaction of deterministic mesenchymal and hematopoietic cells leads to the formation of internal environments of the body. Mesenchymal cells in the hematopoietic organs and various internal organs, the body as a whole are differentiated into connective tissue (actually connective, bone and cartilage tissue), which performs not only support (mechanical), but also trophic, protective, formative, regulatory, and other functions. According to numerous studies, stem, colony-forming and semi - stem precursors are concentrated in the stroma of hematopoietic

organs; semi-stem-everywhere (for example, pericytes in the wall of blood capillaries), in the connective tissue of internal organs [1,3,5].

At the earliest stage of intrauterine development (5-6 weeks), endodermal epithelial strands, stem and differentiating mesenchymal (germ mesoderm) and hematopoietic cells interact in the liver (stem, blast cells that migrated from the extra-germ mesenchyma) with foci of extra-and intravascular hematopoiesis. Blood flows through the capillaries between the strands of differentiating hepatocytes, which on the periphery of the primitive lobes of the liver is formed by merging mixing in different proportions of blood of the hepatic artery, portal vein and umbilical vein. Consequently, at an early stage of embryonic development, a unique functional system is formed in the structural and functional unit of the liver-the lobule - where capillaries with foci of intra - and extravascular hematopoiesis, lined with endothelium and macrophages, where mixed arterial (hepatic artery) and venous (portal and umbilical veins) blood flows between the hepatocyte strands of the endodermal epithelium. Stem cells (SC) of connective tissue, which are localized in the stroma of the bone marrow and other hematopoietic organs, have a mesenchymal origin, and under certain conditions have the ability to differentiate along the fibroblastic, chondroblastic or osteoblastic pathway.

The structure of the bone marrow stroma, loose connective tissue of the vascular tubules of bone tissue includes reticular, undifferentiated connective tissue, endostal, fibroblast-like, endothelial cells, adipocytes [2,3,5,6,8]. These cells are also present in the spleen, lymph nodes, and thymus. They are included in the pool of recirculating hematopoietic and connective tissue cells in the processes of physiological and reparative regeneration, provide adaptation to various influences and regulate homeostasis. Morphologically, stromal connective tissue cells (SSCs) are fusiform, process-like, and are mobilized during physiological and reparative regeneration of bone tissue [2,6,7,8]. In the adult body, SSCs as descendants of mesenchymal cells are capable of differentiating bone, cartilage, smooth muscle cells, fibroblasts, adipocytes [3,6]. SSCs are part of the so-called hematopoietic microenvironment, elements of which, first of all, synthesize and secrete hematopoietic cytokines (colon-stimulating growth factor of granulocytes and macrophages; CSFR, etc.). CSFR in combination with IL-1 and IL-3 provides phenotypic manifestations of osteoclasts, cf synthesis, and expression of calcitonin and fibronectin receptors [3,4,5]. Data were obtained on the circulation of SSC and SCC in the peripheral blood of various laboratory animals under normal and experimental conditions (non-microbial and contaminated with indigenous and pathogenic intestinal microorganisms;limb elongation [7,8,9].

SSCs can differentiate into fibroblasts, chondroblasts, and osteoblasts at the next stage. Osteogenic cells that are partially committed, cambial in the osteoblastic line of differentiation [2,3,5,6], are the result of the expression of a certain group of genes. The key role in this process is played by the transcription factor CBFA: the transcription of genes encoding proteins that are involved in proliferation and adhesion is reduced, and the transcription of genes for osteoblast-specific proteins is increased. At the final stage of differentiation, osteoblasts synthesize mainly type I collagen, as well as non-collagenic proteins of the bone matrix-osteopectin, bone morphogenetic proteins, transforming growth factor β (Tfrβ), schf, etc. In experiments on cultures of osteogenic cells of mice and rats, it was shown that when Tfrβ2 is added, cells differentiate into osteoblasts, and under the action of Tfrβ1 - into chondroblasts [11]. Differentiation and proliferation of chondroblasts is stimulated by binding to the fibroblast growth factor receptor (FRF-2). The population of SSCs is heterogeneous: in natural conditions (reparative bone regeneration) or cultivation can give rise to two types of cells-differons - fibroblasts or osteoblasts. In the formation of osteoblastic differon, deterministic and inducible osteogenic progenitor cells are distinguished: the former do not need any induction to realize their osteogenic potencies: they need close contacts with microenvironment cells for osteoblastic differentiation. Inducible cells-prestestvenniki osteogenic properties show only after the action of certain inducers: they are enclosed in the wall of capillaries (perivasculocytes, or pericytes), the periosteum, extraskeletal organs. Deterministic progenitor cells of osteoblasts are determined in the bones of the skeleton [5,6,8,9].

In the adult body, the source of systemic regulation of the population of osteoblasts are SSCs (their share increases significantly after fractures, the formation of bone defects), which are part of the inner layer of the periosteum, endost, and basal membrane of capillaries (pericytes). In physiological conditions, Desmo -, chondro - and osteogenesis can be observed simultaneously after injury and the occurrence of a defect in the area of the diaphysis of tubular bones. Connective and cartilage tissues are phylogenetically older, with higher rates of growth and regeneration, compared to bone tissue. The recovery process of the bone defect may be accompanied by reparative (replacement) the chondrogenesis and dermagenesis [2,6].

Osteoblasts (OB) are the most active cells differon constitute a functional pool when osteohistogenesis. By their phenotype, THEY are typical intensely synthesizing and secreting cells with distinct polarization. The cytoplasm has a well-developed granular endoplasmic network, Golgi complex, numerous ribosomes and polysomes, and a moderate number of mitochondria [2]. The process of differentiation occurs in time and space, at each specific moment the cell is at a certain stage of differentiation, varying synthesis and secretion of intercellular substance. For highly differentiated OB, a gradual decrease in the activity of alkaline phosphatase and matrix proteins is typical. Some of them, covering the bone from the side of the bone marrow canal, become flat (lining cells) and are part of the endost. It is possible that they represent two populations of osteogenic differon cells: cambial (differentiating) and highly differentiated, which have completed their life cycle. They are characterized by close contacts both with each other and with osteons by means of processes that penetrate their tubular system [6].

Osteocytes (OC) represent the terminal stage of differentiation and blocking proliferation. Relatively few organelles are detected in their cytoplasm: the variability of their number depends on the stage of the life cycle and the impact of exogenous and endogenous factors [2,6]. OCS perform the function of ensuring the integrity of the bone matrix by participating in the formation of protein and polysaccharide components of the intercellular substance, in the regulation of bone mineralization,

osteocytic osteolysis and provide a response to mechanical stimuli. The lining cells and OCS are optimally positioned to perceive any changes in the elastic tension of the bone tissue and, by transforming mechanical stimuli and biochemical signals, initiate remodeling processes at a certain locus. OCS have long branching processes that contact each other on the surface of the bone plates, in the tubules. With the help of appendages, they contact the OB, lining cells, SSC, SCC, interstitial. Their combination with the structures that make up the bone as an organ should be regarded as FS, which provides homeostasis of the internal environment and has high metabolic properties.

Thus, the presented data allow us to conclude about a unitary model of cell types from SSCs originating from embryonic mesenchymal elements, their differentiation into cells of fibroblastic, chondroblastic, osteoblastic, adipocytic, muscular and vascular lines.The combination of various elements of transcription mechanisms creates avery complexand flexible system of transcription control, which allows cells of a certain type to differentiate and function.

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