COMPARATIVE MORPHOGENESIS OF THE URINARY SYSTEM IN HUMANS AND LABORATORY MICE

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ABSTRACT

Background. The organs and structures of the urinary system in humans and mammals undergo similar stages of ontogeny. However, the laboratory mouse, as a model for morphological research, does not always accurately replicate changes in the human body; therefore, improving the methodology of comparative studies remains highly relevant.

Aim. To conduct a comparative analysis of the developmental origins and chronological sequence of topographic-anatomical transformations within the structures and organs of the urinary system in humans and laboratory mice.

Materials and Methods. Serial histological sections of 18 human embryos and 20 laboratory mouse embryos were examined microscopically. The developmental stages of both species were determined using the Carnegie Staging (CS) system. Statistical analysis was not performed because the study was descriptive. The study was conducted within the framework of the research with state registration No.0126U003125.

Research Ethics. The study was conducted in compliance with the General Ethical Principles of Animal Experiments (Ukraine, 2001) and the World Medical Association Declaration of Helsinki (1964–2024). The Biomedical Ethics Committee of Bukovinian State Medical University (Protocol No.7 of May 19, 2026) found no violations of bioethical norms during the study.

Results. At stage CS13, the cranial border of the mesonephros in both human and laboratory mouse embryos is located at the T1/T2 level; due to mesonephric regression by stage CS19 it is visualized at the L4/L5 level. The caudal border of the mesonephros in human embryos was located at the S1–S3 level throughout its development, whereas in laboratory mouse embryos at stages CS9–CS19 it showed a tendency toward caudal growth until it reached the S1–S3 level. In humans, at stages CS12–CS19, well-developed glomeruli are visualized in the middle portion of the mesonephros, and the tubules penetrating from the mesonephric duct exhibit a more complex, branched structure than those in the laboratory mouse.

Conclusions. The mesonephroi of humans and laboratory mice displayed similar patterns regarding the initiation and development of the cranial portion of the mesonephros. However, while the caudal portion in human embryos had stable initiation boundaries, in mouse embryos at stages CS9–CS10 this boundary was located more cranially, and due to progressive growth by stage CS19, the topography of the caudal border reached the S1–S3 level.

Keywords: *theoretical medicine, anatomy, embryology, mesonephros, metanephros, embryogenesis.*

Introduction

To date, the laboratory mouse is the most common mammalian species used in biomedical research due to its accessibility and the extensive body of knowledge accumulated regarding its morphology [1; 2]. Clinical and experimental studies utilizing the laboratory mouse as a model are of significant importance for investigating morphological changes in human diseases and evaluating the effects of pharmaceuticals [3; 4]. However, this biological model does not always precisely replicate changes occurring within the human body; thus, improving the methodology of comparative studies remains a highly relevant direction in morphological science [5–7].

The organs and structures of the urinary system in humans and mammals undergo similar stages of ontogeny [8–10]. They share common origins, developing from the mesoderm, and pass through

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identical successive stages of the pronephros, mesonephros, and metanephros during embryogenesis. Pronephric and mesonephric (primary kidney) structures regress during embryogenesis, whereas the metanephros (secondary kidney) develops into the final, definitive organ. The gestational age at which urinary system structures are initiated varies by species; therefore, for the purposes of comparative embryology, staging according to the Carnegie system is used [8; 9; 11]. For instance, in human embryos, the metanephros begins its development during the 5th week of intrauterine development, whereas in the laboratory mouse, it initiates on the 11th day of prenatal ontogeny. This stage of development shares common morphological features: an outgrowth of the mesonephric duct is surrounded at its distal ramifications by condensed mesenchyme located caudal to the mesonephros [12]. Subsequent stages in mammals are characterized by the radial integration of numerous outgrowths from the distal end of the ureteric bud into the metanephric blastema, giving rise to the renal collecting ducts. The proximal portions of the mesonephric ducts develop into the cranial part of the ureter and the renal pelvis [12; 13].

Researchers report variations in the timing of definitive kidney completion among different mammalian species. It has been established that in humans, nephrogenesis is completed before birth, whereas in the laboratory mouse and the domestic pig, nephrogenesis continues postnatally [12–15].

Using the Carnegie staging system for the embryonic period of mammalian development provides a solid foundation for expanding knowledge of the comparative morphology and chronology of ontogenetic development in humans and laboratory mice [7–11]. Aggregating the results of these studies enhances insights within advanced, multidisciplinary fields such as bioengineering, regenerative medicine, and xenotransplantation [16–18].

The **aim** of the study was to conduct a comparative analysis of the developmental origins and chronological sequence of topographic-anatomical transformations within the structures and organs of the urinary system in humans and laboratory mice.

Materials and Methods

The study examined specimens from 18 human embryos and 20 laboratory mouse embryos. The research material was obtained from the collection of the Department of Histology, Cytology, and Embryology at Bukovinian State Medical University.

Staging of ontogenetic transformations in humans and laboratory mice was assessed using the Carnegie Stage (CS) system [8; 9; 11]. The table presents standardized morphometric parameters for comparing the developmental stages of human and laboratory mouse embryos based on embryological data [5; 7–9; 11; 12]. Gestational age and crown-rump length (CRL, in mm) of human and laboratory mouse embryos were used to determine the developmental stage (*Table*).

Morphological research methods were applied.

Table. Correlation of embryonic development between humans and laboratory mice according to Carnegie stages

Carnegie Stage	Human		Laboratory Mouse	
	Days	CRL (mm)	Days	CRL (mm)
CS11	29	3.2	10	3.5
CS12	30	3.9	10.5	4.2
CS13	32	4.9	11	5.5
CS14	34	6.5	11.5	6.5
CS15	36	7.8	12	8.0
CS16	39	9.6	12.5	9.0
CS17	41	12.2	13	10.0
CS18	44	14.9	13.5	11.0
CS19	46	18.2	14	11.5
CS20	49	20.7	14.5	12.5
CS21	51	22.9	15	13.0
CS22	54	25.5	15.5	14.5
CS23	56	28.8	16	15.5

Notes: CS – Carnegie Stage; CRL – crown-rump length.

Embryos were investigated by preparing and microscopically examining serial histological sections. Tissue dehydration was performed by passing the specimens through a graded series of ascending ethanol concentrations. The specimens were then embedded in paraffin. Microtome sections 7–10 μm thick were cut and stained with hematoxylin and eosin. The morphological study was descriptive and did not involve quantitative and statistical analyses.

Research Ethics

The studies were conducted in compliance with the core provisions of the General Ethical Principles of Animal Experiments, adopted by the Resolution of the First National Congress on Bioethics (Ukraine, September 2001), the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Harmonised Tripartite Guideline for Good Clinical Practice (1996), the Council of Europe Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Biomedicine (Oviedo, 1997), the World Medical Association Declaration of Helsinki (1964–2024), Directive 2010/63/EU of the European Parliament and of the Council (2010), and Orders of the Ministry of Health of Ukraine No.690 of September 23, 2009, and No.944 of December 14, 2009.

The Biomedical Ethics Committee of Bukovinian State Medical University (Protocol No.7 of May 19, 2026) found no violations of bioethical norms in the research.

Results

According to our data, the processes of initiation, histogenesis, and topographic transformations of the organs and structures of the urinary system are generally identical in humans and laboratory mice. The structures of the urogenital system originate from the intermediate mesoderm, which is localized along the dorsal part of the embryos. It serves as the site for the initial formation of the nephrogenic cord – the mesonephric (Wolffian) duct. In contrast, the ventral part of the intermediate mesoderm is the source of the paramesonephric (Müllerian) duct. Between stages CS8 and CS12, the latter undergoes significant syntopic changes in laboratory mouse embryos: at stage CS8, the structures of the Wolffian duct are identified in the cranial part of the embryo; at stage CS9, intensive growth in the caudal direction and the onset of regression of its cranial part are noted; at stages CS10–11, apoptosis of the cranial part of the Wolffian duct and its interaction with the mesonephros are observed; at stage CS12, further development of the Wolffian duct and its connection with the cavitary structures of the mesonephros and metanephros are noted.

A comparison of the syntopic transformations of the mesonephros in human and laboratory mouse embryos demonstrates that at CS13, the cranial border of the mesonephros is located at the T1/T2 level. Due to mesonephric regression, by stage CS19, the cranial portion is visualized at the L4/L5 level in both human and laboratory mouse embryos. The caudal border of the mesonephros in human embryos remains at the S1–S3 level throughout its development. However, in laboratory mouse embryos, the caudal border of the mesonephros at stages CS9–19 showed a tendency to grow caudally until it reached the S1–S3 level.

Consequently, the mesonephroi of humans and laboratory mice shared similar origins, initiation timelines, and developmental characteristics regarding the cranial portion of the organ. However, while the caudal part of the human mesonephros possessed stable syntopic boundaries, in laboratory mouse embryos at stages CS9–10, this boundary was located more cranially. Due to intensive growth by stage CS19, the topography of the caudal border in mice ultimately became similar to that observed in human embryos.

The chronology of nephron glomeruli initiation in the mesonephros of the laboratory mouse differs from that in humans. Up to stage CS21, the mesonephric anlage in the laboratory mouse contains only tubules, which are outgrowths of the mesonephric duct. The formation of nephron glomeruli in the laboratory mouse mesonephros is identified only at stages CS21–22. In contrast, in humans at stages CS12–19, well-developed vascular glomeruli are visualized in the middle portion of the mesonephros, and the tubules exhibit a more complex, branched structure than in the laboratory mouse.

The initiation of the metanephros in human and laboratory mouse embryos occurs at stage CS12. Its source is the ureteric bud from the caudal section of the mesonephric duct, which is surrounded by condensed mesenchyme – the metanephric blastema. This outgrowth toward the metanephric blastema is the anlage of the ureter and the cavitary system of the metanephros. Shortly thereafter, a tree-like branching of the ureteric bud is observed, forming the renal pelvis and calyces of the metanephros. During the organogenesis of the definitive kidney, the ramifications of the distal end of the ureteric bud divide down to the level of

the renal collecting ducts, around which nephron glomeruli form from the condensed metanephric mesenchyme. At stages CS15–22, intensive division and branching of the cavitary structures of the metanephros occur *(Fig. 1, 2)*; according to our observations, these processes are asynchronous and do not fully conform to the criteria for fractal division (which follows a self-similar, self-repetitive branching pattern). The formation of metanephric nephrons during stages CS12–20 constitutes a critical period during which renal developmental anomalies, such as polycystic and multicystic kidney diseases, can arise.

At stage CS22 in laboratory mouse embryos, the metanephros clearly differentiates into the renal cortex and medulla, with a well-developed cavitary system that continues into the ureter. The division of the metanephroi into two layers (an outer layer – the cortex, and an inner layer – the medulla) is characteristic of both species *(Fig. 3)*. Microscopically, nephron glomeruli as well as proximal and distal convoluted tubules are visualized within the renal cortex. The renal medulla contains loops of Henle and medullary collecting ducts arranged in parallel.

Discussion

The comparative study of urinary tract morphogenesis is attracting increasing attention from researchers in cutting-edge fields, such as regenerative medicine, bioengineering, and xenotransplantation [16–18]. Investigating the early developmental stages of the Wolffian and Müllerian ducts at stages CS10–11 provides insight into the morphogenesis of the renal cavitary system, while studying the interaction between the Wolffian duct and the metanephros at stage CS12 deepens the understanding of definitive kidney microanatomy formation [19; 20]. In both human and laboratory mouse embryos, the initiation of metanephric structures occurs at stage CS12 and arises at the level of the caudal section of the nephrogenic cord. This period is of particular interest for morphological research aimed at expanding knowledge in regenerative medicine and transplantology. It can be hypothesized that the fractal division of the Wolffian duct structures, which extends to the level of the renal collecting ducts, regulates nephron morphogenesis and quantitative parameters in the definitive kidney [21].

The prenatal ontogeny of the parenchymal structures of the metanephros follows similar developmental patterns in both humans and laboratory mice. In both species, microscopic changes in the renal medulla occur at later stages of development compared to the renal cortex. In humans, the kid-

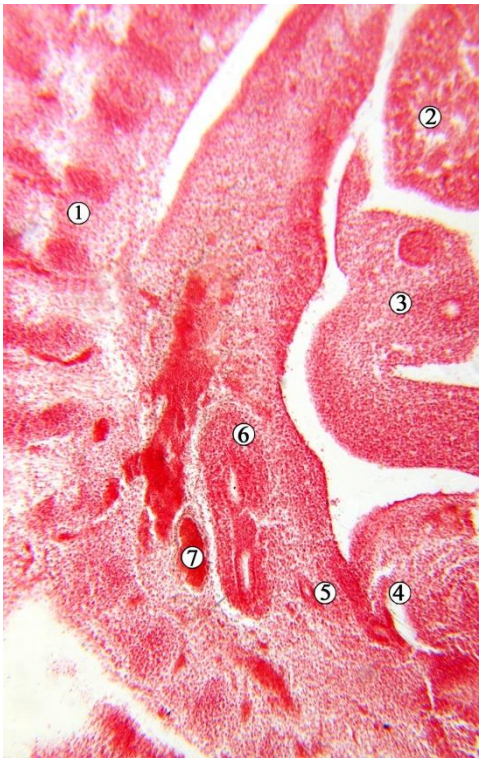
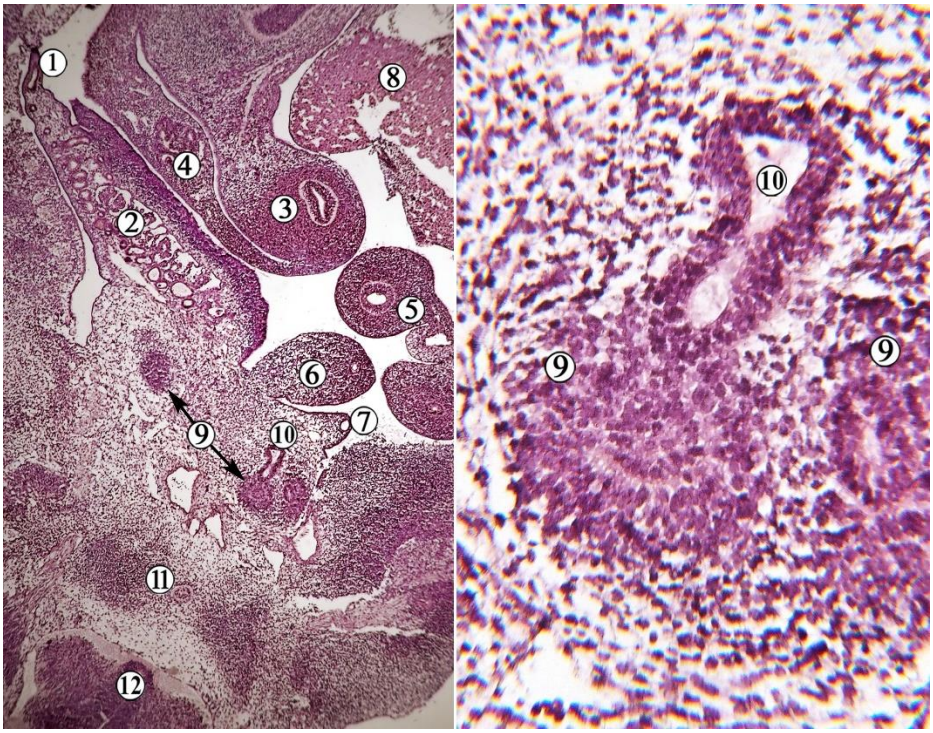
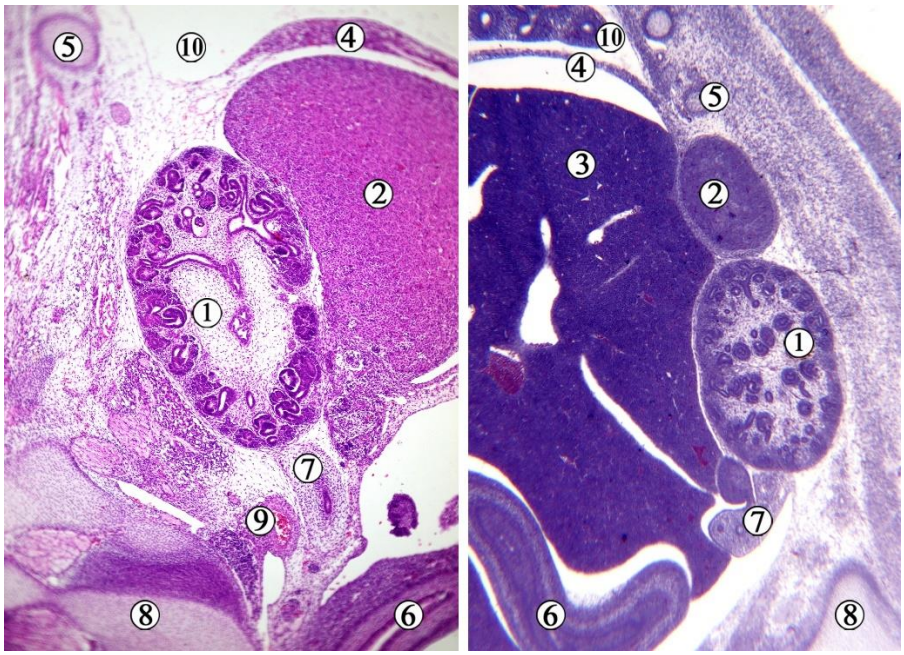


Fig. 1. Sagittal section of a laboratory mouse embryo, crown-rump length 7.5 mm (Carnegie stage 15). Hematoxylin and eosin staining. Photomicrograph. Magnification ×70: 1 – vertebral column primordium; 2 – liver; 3 – midgut; 4 – rectal primordium; 5 – ureteric bud; 6 – metanephrogenic blastema; 7 – dorsal aorta



A B

Fig. 2. Frontal section of a human embryo, crown-rump length 8.0 mm (Carnegie stage 15). Hematoxylin and eosin staining. Photomicrograph. Magnification ×70 (A); ×180 (B): 1 – Wolffian duct; 2 – mesonephros; 3 – gastric primordium; 4 – pancreatic primordium; 5 – midgut; 6 – rectal primordium; 7 – ureteric bud; 8 – liver; 9 – metanephrogenic blastema; 10 – renal pelvis primordium; 11 – notochord; 12 – spinal cord



A B

Fig. 3. Oblique-sagittal sections of embryos at Carnegie stage 22 (A – human, crown-rump length 25.0 mm; B – laboratory mouse, crown-rump length 14.5 mm). Hematoxylin and eosin staining. Photomicrographs. Magnification ×70: 1 – metanephros; 2 – adrenal gland; 3 – liver; 4 – diaphragm; 5 – 12th rib; 6 – hindgut; 7 – ureter; 8 – sacrum; 9 – internal iliac artery; 10 – thoracic cavity

ney structures are fully formed by the postnatal period, while the functional capacity of the medulla to concentrate urine matures by 18 months of age. In the laboratory mouse, the maturation of renal medullary structures continues postnatally for 3 days, and the full capacity to concentrate urine is reached at 6 weeks of age [15; 19]. In both humans and laboratory mice, the morphogenesis of the Wolffian duct influences nephron endowment, constitutes a critical period regarding the likelihood of developmental anomalies, and shapes the system that subsequently controls the kidneys' ability to concentrate urine. In recent years, the number of publications regarding the processes of kidney initiation and development has increased, reflecting growing research interest in this topic [13; 19–22].

Analyzing the temporal clusters of structural changes within the mesonephros of human and laboratory mouse embryos allows for the introduction of the term "morphogenetic wave" – the process of histo- and organogenesis in this structure proceeds like a wave in a craniocaudal direction.

The development of the definitive kidney is a complex, multi-stage process during which undifferentiated mesenchyme transforms into an organ with a highly organized architecture. Despite significant progress, the underlying patterns of these ontogenetic transformations remain the subject of ongoing research and are not yet fully elucidated. In experimental studies, the laboratory mouse metanephros is utilized as the primary model; however, studying the mouse pronephros and mesonephros holds greater promise for expanding and integrating these data into xenotransplantation and regenerative medicine [16–18]. Many stages of definitive kidney morphogenesis are evolutionarily conserved and proceed identically in mammals. The results of this study demonstrate that the architectural framework of urinary system ontogeny in humans and mice is highly similar when analyzed comparatively using the Carnegie staging system.

Conclusions

1. Temporal clusters of structural transformations within the nephrogenic cord in human and laboratory mouse embryos can be characterized by the term "morphogenetic wave" – the process of histo- and organogenesis in this structure proceeds like a wave in a craniocaudal direction.

2. The mesonephroi of humans and laboratory mice share similar developmental origins and patterns regarding their cranial portions. However, while the caudal portion in human embryos maintains stable anatomical boundaries throughout development, in laboratory mouse embryos at stages CS9–10, this boundary is located more cranially; owing to progressive growth by stage CS19, the topography of the caudal border ultimately reaches the S1–S3 level.

3. At stages CS15–22, intensive division and branching occur within the metanephric structures of both humans and laboratory mice. According to our observations, these processes are asynchronous and do not fully conform to the criteria for fractal division.

Prospects for Further Research

A promising direction for future research is to elucidate the specific features of the comparative embryology of the lower urinary tract in humans and laboratory mice.

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Declarations

Conflict of interest is absent.

The author has agreed to the publication of the article under the terms of the Creative Commons BY-NC-SA 4.0 license and the public agreement with Kharkiv National Medical University, the founder and publisher of the journal, and to the processing and publication of their personal data.

The author of the manuscript declares that in the process of conducting research, preparing, and editing this manuscript, they did not use any generative artificial intelligence tools or services to perform any of the tasks listed in the Generative Artificial Intelligence Delegation Taxonomy (GAIDeT, 2025). All stages of the work (from the development of the research concept to the final editing) were performed exclusively by the author, without the involvement of generative artificial intelligence.

References

1. Ten Tusscher K. Of mice and plants: Comparative developmental systems biology. Dev Biol. 2020;460(1):32-9. DOI: 10.1016/j.ydbio.2018.10.024. PMID: 30395805.

2. Oldak B, Aguilera-Castrejon A, Hanna JH. Recent insights into mammalian natural and synthetic ex utero embryogenesis. Curr Opin Genet Dev. 2022;77:101988. DOI: 10.1016/j.gde.2022.101988. PMID: 36179582.

3. Aceves M, Tucker A, Chen J, Vo K, Moses J, Amar Kumar P, et al. Developmental stage of transplanted neural progenitor cells influences anatomical and functional outcomes after spinal cord injury in mice. Commun Biol. 2023;6(1):544. DOI: 10.1038/s42003-023-04893-0. Erratum in: Commun Biol. 2023;6(1):635. DOI: 10.1038/s42003-023-05018-3. PMID: 37208439.

4. Lindström NO, Guo J, Kim AD, Tran T, Guo Q, De Sena Brandine G, et al. Conserved and Divergent Features of Mesenchymal Progenitor Cell Types within the Cortical Nephrogenic Niche of the Human and Mouse Kidney. J Am Soc Nephrol. 2018;29(3):806-24. DOI: 10.1681/ASN.2017080890. PMID: 29449449.

5. Schlindwein X, Werneburg I. Comparative embryogenesis in ungulate domesticated species. J Exp Zool B Mol Dev Evol. 2022;338(8):495-504. DOI: 10.1002/jez.b.23172. PMID: 35915572.

6. Saizonou MA, Kitazawa H, Kanahashi T, Yamada S, Takakuwa T. Epithelial development of the urinary collecting system in the human embryo. PLoS One. 2024;19(4):e0301778. DOI: 10.1371/journal.pone.0301778. PMID: 38598450.

7. Cooper TK, Meyerholz DK, Beck AP, Delaney MA, Piersigilli A, Southard TL, Brayton CF. Research-Relevant Conditions and Pathology of Laboratory Mice, Rats, Gerbils, Guinea Pigs, Hamsters, Naked Mole Rats, and Rabbits. ILAR J. 2021;62(1-2):77-132. DOI: 10.1093/ilar/ilab022. PMID: 34979559.

8. O'Rahilly R, Müller F. Developmental stages in human embryos: revised and new measurements. Cells Tissues Organs. 2010;192(2):73-84. DOI: 10.1159/000289817. PMID: 20185898.

9. O'Rahilly R, Müller F. Prenatal ages and stages-measures and errors. Teratology. 2000;61(5):382-4. DOI: 10.1002/(SICI)1096-9926(200005)61:5<382::AID-TERA10>3.0.CO;2-5. PMID: 10777834.

10. Richardson MK. Theories, laws, and models in evo-devo. J Exp Zool B Mol Dev Evol. 2022;338(1-2):36-61. DOI: 10.1002/jez.b.23096. PMID: 34570438.

11. Flierman S, Tijsterman M, Rousian M, de Bakker BS. Discrepancies in Embryonic Staging: Towards a Gold Standard. Life (Basel). 2023;13(5):1084. DOI: 10.3390/life13051084. PMID: 37240729.

12. Butler H, Juurlink BHJ. An Atlas for Staging Mammalian and Chick Embryos. Boca Raton: CRC Press; 2018. 218 p. DOI: 10.1201/9781351069939.

13. Piras M, Gerosa C, Congiu T, Cau F, Fanni D, Pichiri G, et al. Toward the renal vesicle: Ultrastructural investigation of the cap mesenchyme splitting process in the developing kidney. J Public Health Res. 2022;11(4):22799036221124076. DOI: 10.1177/22799036221124076. PMID: 36310827.

14. Qiu C, Martin BK, Welsh IC, Daza RM, Le TM, Huang X, et al. A single-cell time-lapse of mouse prenatal development from gastrula to birth. Nature. 2024;626(8001):1084-93. DOI: 10.1038/s41586-024-07069-w. PMID: 38355799.

15. Chang CH, Davies JA. In developing mouse kidneys, orientation of loop of Henle growth is adaptive and guided by long-range cues from medullary collecting ducts. J Anat. 2019;235(2):262-70. DOI: 10.1111/joa.13012. PMID: 31099428.

16. Davies JA, Elhendawi M, Palakkan AA, Sallam M. Renal engineering: strategies to address the problem of the ureter. Curr Opin Biomed Eng. 2021;20:100334. DOI: 10.1016/j.cobme.2021.100334. PMID: 36644495.

17. Saito Y, Matsumoto N, Yamanaka S, Yokoo T, Kobayashi E. Beneficial Impact of Interspecies Chimeric Renal Organoids Against a Xenogeneic Immune Response. Front Immunol. 2022;13:848433. DOI: 10.3389/fimmu.2022.848433. PMID: 35242145.

18. Matsumoto N, Matsui K, Saitou Y, Takamura T, Yamanaka S, Yokoo T, Kobayashi E. Techniques of fragile renal organoids transplantation in mice. Acta Cir Bras. 2021;36(11):e361102. DOI: 10.1590/ACB361102. PMID: 34932670.

19. Parvez RK, Csipán RL, Liu J, Gevorgyan A, Rutledge EA, Guo J, et al. Developmental and Cell Fate Analyses Support a Postnatal Origin for the Cortical Collecting System in the Mouse Kidney. J Am Soc Nephrol. 2025;36(5):812-24. DOI: 10.1681/ASN.0000000579. PMID: 39665296.

20. Davidson AJ, Lewis P, Przepiorski A, Sander V. Turning mesoderm into kidney. Semin Cell Dev Biol. 2019;91:86-93. DOI: 10.1016/j.semcdb.2018.08.016. PMID: 30172050.

21. Short KM, Smyth IM. Branching morphogenesis as a driver of renal development. Anat Rec (Hoboken). 2020;303(10):2578-87. DOI: 10.1002/ar.24486. PMID: 32790143.

22. Kim S, Koppitch K, Parvez RK, Guo J, Achieng M, Schnell J, et al. Comparative single-cell analyses identify shared and divergent features of human and mouse kidney development. Dev Cell. 2024;59(21):2912-30.e7. DOI: 10.1016/j.devcel.2024.07.013. PMID: 39121855.

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