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EDITORIAL

Recent progress in human embryology

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1. (Pre)history of embryology

Human embryology has developed through several major periods, each marked by different philosophical approaches, technological advances, and scientific breakthroughs.

Hippocrates (460–370 BC) wrote the first recorded embryological research on obstetrics and gynecology, proposing that embryos developed by extracting moisture and breath from the mother. Aristotle (384–322 BC) advanced the field through observational science, opening bird eggs at different developmental stages and dissecting mammalian embryos. He proposed epigenesis—the theory that organisms develop progressively from undifferentiated material.

During the Renaissance, Leonardo da Vinci (1452-1519) made quantitative measurements and was the first to demonstrate that embryos undergo changes in weight, size, and shape over time. William Harvey (1578–1657) examined deer and chicken embryos with low-powered lenses, identifying the blastoderm as the origin of the embryonic body.

Until the 18th century, preformationism dominated. It was the belief that organisms developed from pre-existing miniature versions of themselves, including the idea of a tiny "homunculus" hidden in the sperm head. This view was challenged by Caspar Friedrich Wolff (1733–1794), who argued for epigenesis in his landmark 1759 work, "Theory of Generation."[1] Only Karl Ernst von Baer's (1792-1876) observations of the mammalian ovum, dated to the year 1827, marked the birth of modern embryology. Next, von Baer and Heinz Christian Pander (1794-1865) developed the germ layer theory, explaining how embryos develop in progressive steps.

2. Real human embryology

Wilhelm His (1880–1904), a Swiss anatomist considered the founder of human embryology, published detailed side views of human embryos from 15 days to 8.5 weeks. Franklin Mall (1862-1917) began collecting human embryos at Johns Hopkins University in 1887, creating the Carnegie Collection, which now holds over 10,000 specimens. The Carnegie Institution of Washington established the first research institution devoted specifically to embryology at Johns Hopkins in 1914. This period saw the first descriptions of human embryos from the first 2 weeks after fertilization and elucidation of ovulation timing.

After World War II, human embryology declined as developmental biology shifted its focus to model organisms, such as flies, frogs, sea urchins, and mice, where experimental manipulation was easier. Embryologists believed that by describing the embryonic development of mice, rats, sheep, and cows, they could obtain information that could easily be extrapolated to human development. This was a highly convenient way of thinking, as it allowed them to study human development *per procura*, thereby circumventing the religious taboo against interfering with the dignity of a human being, which lasted from natural conception to natural death. However, this was false thinking, as it quickly became clear that, despite striking similarities, each mammalian embryo also has its own unique characteristics, requirements, and cellular and molecular mechanisms. Full extrapolation turned out to be an illusion.

3. The *in vitro* fertilization (IVF) breakthrough

The birth of the first IVF baby in 1978, thanks to Robert Edwards, Patrick Steptoe, and Jean Purdy, revolutionized access to early human embryos. The 1990 United Kingdom Human Fertilisation and Embryology Act permitted research on donated embryos up to 14 days. Biobanks, such as the Human Developmental Biology Resource in Newcastle and London provided ethical supplies of post-implantation embryos from pregnancy terminations. Embryology returned to the era of Leonardo da Vinci, but this time the objects of research were real human embryos.

The discovery of DNA structure in the 1950s launched molecular developmental biology, and the establishment of human embryonic stem cell lines in 1998 revolutionized regenerative medicine research. Recent advances, including synthetic embryo models, optogenetic control of development, and Clustered Regularly Interspaced Short Palindromic Repeats gene editing in human embryos, have brought us to the cutting-edge achievements of recent years.

Human embryology has thus evolved from philosophical speculation to detailed molecular understanding over approximately 2,400 years of inquiry. From this perspective, let us look at the major recent achievements in human embryology.

4. First complete visualization of human embryo implantation and advanced synthetic embryo models

Researchers achieved the first real-time observation of the entire sequence of human implantation using artificial uterine tissue in microfluidic chips.[2-5] This breakthrough allowed scientists to observe embryos burrow into lab-recreated womb tissue, revealing previously hidden details about this critical early pregnancy stage. Researchers utilized synthetic embryo models (blastoids) derived from human embryonic stem cells to study implantation without using actual embryos. Multiple teams created increasingly sophisticated stem cell-based embryo models that replicate early human development without fertilization, improving both reproducibility and accuracy. These synthetic embryology models allow researchers to study developmental stages that were previously inaccessible due to ethical and technical restrictions, addressing a significant cause of infertility and miscarriage.

5. Optogenetic control of embryonic development

Scientists have developed light-controlled embryo models that revealed the fundamental interplay between mechanical forces and chemical signals during gastrulation.[6] Using engineered human embryonic stem cells that respond to specific light wavelengths, researchers discovered that chemical cues alone, such as bone morphogenetic protein 4 (BMP4), are insufficient; proper mechanical conditions are also essential for cells to organize into the body's basic structure. This work from Rockefeller University demonstrated that gastrulation requires both chemical signals (like BMP4) and mechanical forces, using light-activated synthetic embryo models.

6. Artificial intelligence (AI)-powered embryo selection

New AI algorithms can select embryos with the best developmental potential using only a single time-lapse image, surpassing the capabilities of contemporary embryologists. The two 2025 reviews show continued improvements with newer algorithms achieving 77–92% accuracy in clinical pregnancy prediction.[7,8] This technology promises to give couples undergoing IVF a much better chance of success.

7. Pre-implantation genetic testing success

Studies have demonstrated the successful use of pre-implantation genetic testing for monogenic disorders to prevent the transmission of inherited kidney diseases, including autosomal dominant polycystic kidney disease, Alport syndrome, and other monogenic kidney disorders, with live births of healthy children reported.[9,10] This highlights the growing potential to eliminate hereditary diseases before pregnancy. Such achievements collectively represent a transformative year for understanding early human development, with major implications for treating infertility, preventing miscarriages, and developing regenerative therapies.

While writing this editorial, I learned that the US National Institutes of Health (NIH) will stop funding research involving human fetal tissues.[11,12] This announcement represents a significant hindrance to the development of human embryology, stem cell research, regenerative medicine, and the treatment of infectious, chronic, and neurodegenerative diseases and conditions. This marks another negative turn in the history of human embryology and developmental biology, at least in the USA.

Conflict of interest

Jacek Z. Kubiak is the Editor-in-Chief of this journal, but was not in any way involved in the editorial and peer-review process conducted for this paper, directly or indirectly. The author declared that he has no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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