



BDF Bioethics Briefing: July 2021

The Origin of Human Life at Sperm-Egg Fusion: Quotes Compiled from Medical Textbooks and Peer-Reviewed Scientific Literature

By Maureen L. Condic, Ph.D.

For Policy Consultation, contact:

Bioethics Defense Fund, bdfund.org, (602) 751-7234

© Bioethics Defense Fund, July 2021. Permission to print or repost this document is granted if it remains in its entirety and with attribution to the author. Requests for permission to reproduce portions of this document with attribution to the author may be directed to (602) 751-7234.

BDF Bioethics Briefing: July 2021

The Origin of Human Life at Sperm-Egg Fusion: Quotes Compiled from Medical Textbooks and Peer-Reviewed Scientific Literature



Dr. Maureen L. Condic

- BDF Policy Overview

This resource is comprised solely of short and direct quotations from medical textbooks and peer-reviewed journals as compiled from a review of the published literature by neuroscientist Maureen L. Condic, Ph.D.

These quotes are significant, not because the papers necessarily provide evidence for the conclusion that life begins at sperm-egg fusion (although some do provide such evidence), but rather because they have been published in peer-reviewed journals without citation or explanation. This supports the conclusion, based on my experience as the author or co-author of over 100 published papers, that the quoted statements are seen as uncontroversial matters of accepted fact by the scientific community. Had any of the authors, reviewers or editors objected, the statements would not have been retained in the published article.

The public debates surrounding bioethics issues are perceived as thorny and confusing because of the widespread misperception that we do not or cannot know when human life begins. This line of flawed reasoning commonly claims that the question is a matter of faith or religion. But if our nation is committed to restoring science to its rightful place, we must accept the reality that the question of when human life begins is simply a matter of science – in particular, the inconvenient science known as human embryology.

Once we have the intellectual integrity to squarely acknowledge the objective scientific facts of human embryology, only then can we have an honest debate in the democratic process and in the courts regarding unsettled moral questions of paramount concern, including

abortion, destructive human embryo research, human cloning, and the healthcare rights of conscience that surround these practices. While science establishes when human life begins, the societal question remains of whether we have an obligation to respect and legally protect human beings at their earliest and most vulnerable states of being.

To request contact with the author on science matters, or to request *pro bono* consultation of matters of law and public policy, contact:

BIOETHICS DEFENSE FUND

www.BDFund.org

(602) 751-7234

OTHER BDF POLICY GUIDES

www.BDFund.org

- 3 Parent Embryos as Reproductive Cloning
- Surrogacy as Reproductive Trafficking
- Human Embryo Trafficking Ban
- Prohibiting Abortion Providers in Schools
- Signs of Hope – Abortion Clinic Signage
- Abortion Clinics as Points of Rescue for Sex Trafficking Victims
- POLST: Keeping Control Over Your End of Life Decision Making
- Custom consultation



The Origin of Human Life at Sperm-Egg Fusion: Quotes Compiled from Medical Textbooks and Peer-Reviewed Scientific Literature

by Maureen L. Condic, Ph.D.¹
Last Compiled: July 2021

Executive Summary:

The following quotes are significant, not because the papers necessarily provide evidence for the conclusion that life begins at sperm-egg fusion (although some do provide such evidence), but rather because they have been published in peer-reviewed journals without citation or explanation. This indicates that they are seen as uncontroversial matters of accepted fact by the scientific community.

Note on the meaning of scientific terminology regarding human development:

"Organism" is the scientific name for a *living human being*. Only organisms undergo development.

"Zygote" is the one-cell human organism produced by sperm-egg fusion.

"Embryo" is a human organism during the first eight weeks of development.

I. Medical Textbooks

1. Keith L. Moore, *The Developing Human: Clinically Oriented Embryology*, 10th edition. Philadelphia, PA: Saunders, 2016. p. 11

"Human development begins at fertilization, when a sperm fuses with an oocyte to form a single cell, the zygote. This highly specialized, *totipotent cell* (capable of giving rise to any cell type) marks the beginning of each of us as a unique individual."

2. Schoenwolf, G. C. *Larsen's Human Embryology*, 5th edition. Philadelphia, PA: Elsevier, Saunders, 2015. p. 2, 14.

¹ Associate Professor of Neurobiology and Anatomy, University of Utah School of Medicine, 20 South 2030 East, Room 320 BPRB, Salt Lake City, UT 84112-9458 (academic institution listed for identification purposes only.) Requests to communicate with Dr. Condic may be directed to Bioethics Defense Fund at (602) 751-7234. © Bioethics Defense Fund 2021. Permission is granted to republish or repost this document with attribution to the author.

"All of us were once human embryos, so the study of human embryology is the study of our own prenatal origins and experiences." (p. 2)

"Fertilization, the uniting of egg and sperm, takes place in the oviduct. After the oocyte finishes meiosis, the paternal and maternal chromosomes come together, resulting in the formation of a zygote containing a single diploid nucleus. Embryonic development is considered to begin at this point." (p.14)

3. Jones, R. E. ***Human Reproductive Biology***, 4th edition. Waltham, MA. Elsevier, Academic Press, 2014, p. 169.

"the fertilized egg (zygote) is the beginning of a new diploid individual."

4. Keith L. Moore, ***Before We Are Born: Essentials of Embryology***, 7th edition. Philadelphia, PA: Saunders, 2008. p. 2:

"[The zygote], formed by the union of an oocyte and a sperm, is the beginning of a new human being."

5. Keith L. Moore, ***Before We Are Born: Essentials of Embryology***, 9th edition. Philadelphia, PA: Saunders, 2016. p. 1.

"Human development begins at fertilization when an oocyte (ovum) from a female is fertilized by a sperm (spermatozoon) from a male...Embryology is concerned with the origin and development of a human being from a zygote to birth."

6. Sadler, T. W. ***Langman's Medical Embryology***, 10th edition. Philadelphia, PA: Lippincott Williams & Wilkins, 2006. p. 11:

"Development begins with fertilization, the process by which the male gamete, the sperm, and the female gamete, the oocyte, unite to give rise to a zygote."

7. Sadler, T. W. ***Langman's Medical Embryology***, 13th edition. Philadelphia, PA: Lippincott Williams & Wilkins, 2015. p. 42 (*emphasis added*).

"The main results of fertilization are as follows: Restoration of the diploid number of chromosomes, half from the father half from the mother. Hence, the zygote contains a new combination of chromosomes different from both parents. Determination of the sex of the new individual. An X-carrying sperm produces a female (XX) embryo and a Y-carrying sperm produces a male (XY) embryo. Therefore, the chromosomal sex of the embryo is determined at fertilization."

8. Dudek, R. W. ***Embryology***, 4th edition. Philadelphia, PA. Lippincott Williams and Wilkins, 2008, p. 1.

“Sexual reproduction occurs when female and male gametes (oocyte and spermatozoon, respectively) unite at fertilization.”

9. Ronan O’Rahilly and Fabiola Miller, ***Human Embryology and Teratology***, 3rd edition. New York: Wiley-Liss, 2001. p. 8.

“Although life is a continuous process, fertilization... is a critical landmark because, under ordinary circumstances, a new genetically distinct human organism is formed when the chromosomes of the male and female pronuclei blend in the oocyte.”

10. Carlson, B. M. ***Human Embryology and Developmental Biology***, 5th edition. Philadelphia, PA. Elsevier, Saunders, 2014, p. 2.

“Human pregnancy begins with the fusion of an egg and a sperm within the female reproductive tract”

II. Peer-reviewed scientific literature; 2001-present (chronological order)

1. A profile of fertilization in mammals. Wassarman PM, Jovine L, Litscher ES. Nat Cell Biol. 2001.3(2):E59-64.

“When mammalian eggs and sperm come into contact in the female oviduct, a series of steps is set in motion that can lead to fertilization and ultimately to development of new individuals.”

2. Penetration, adhesion, and fusion in mammalian sperm-egg interaction. Primakoff P, Myles DG. Science. 2002. 296(5576):2183-5.

“Fertilization is the sum of the cellular mechanisms that pass the genome from one generation to the next and initiate development of a new organism.”

3. Egg activation at fertilization: where it all begins. Runft LL, Jaffe LA, Mehlmann LM. Dev Biol. 2002. 245(2):237-54.

4. In the beginning: lessons from fertilization in mice and worms. Jungnickel MK, Sutton KA, Florman HM. Cell. 2003 Aug 22;114(4):401-4.

"Sexual reproduction proceeds *by fertilization; formation of new individuals by the union of haploid gametes.*"

5. The cell cycle: a new entry in the field of Ca²⁺ signaling. Santella L, Ercolano E, Nusco GA. Cell Mol Life Sci. 2005. 62(21):2405-13.

"Ca²⁺ signaling plays a crucial role in virtually all cellular processes, from the *origin of new life at fertilization* to the end of life when cells die."

6. The immunoglobulin superfamily protein Izumo is required for sperm to fuse with eggs. Inoue N, Ikawa M, Isotani A, Okabe M. Nature. 2005. 434(7030):234-8.

"Representing the 60 trillion cells that build a human body, a sperm and an egg meet, recognize each other, and *fuse to form a new generation of life.*"

7. Signal transduction pathways leading to Ca²⁺ release in a vertebrate model system: lessons from Xenopus eggs. Sato K, Fukami Y, Stith BJ. Semin Cell Dev Biol. 2006. 17(2):285-92.

"At fertilization, eggs unite with sperm to initiate developmental programs that give rise to development of the embryo. Defining the molecular mechanism of this fundamental process at *the beginning of life* has been a key question in cell and developmental biology"

8. Cell fusion during development. Oren-Suissa M, Podbilewicz B. Trends Cell Biol. 2007. 17(11):537-46.

"Most readers of this review originated from a sperm-egg fusion event."

9. Ca²⁺ signaling differentiation during oocyte maturation. Machaca K. J Cell Physiol. 2007. 213(2):331-40.

"Oocyte maturation is an essential cellular differentiation pathway that prepares the egg for activation at fertilization leading to the *initiation of embryogenesis.*"

10. A comparative analysis of molecular mechanisms for blocking polyspermy: identification of a lectin-ligand binding reaction in mammalian eggs. Hedrick JL. Soc Reprod Fertil Suppl. 2007;63:409-19.

"Fertilization is a critically important event to the creation of a new individual organism and to the propagation of a species."

11. Sperm-egg fusion assay in mammals. Inoue N, Okabe M. Methods Mol Biol. 2008. 475:335-45.

"As representatives of the 60 trillion cells that make a human body, a sperm and an egg meet, recognize each other, and fuse to create a new generation."

12. Sperm chromatin: fertile grounds for proteomic discovery of clinical tools. Wu TF, Chu DS. Mol Cell Proteomics. 2008. 7(10):1876-86.

"Sperm are remarkably complex cells with a singularly important mission: to deliver paternal DNA and its associated factors to the oocyte to start a new life."

13. [Description of biological elements involved in new organism beginning. Review of contemporary investigations about early embryony development]. Huerta Zepeda A, Torres Padilla ME, Guerra López R. Ginecol Obstet Mex. 2008 Jan;76(1):52-64.

"The development of the mammalian embryo begins with the fertilization of the mature oocyte by the sperm."

14. Gene expression during the oocyte-to-embryo transition in mammals. Evsikov AV, Marín de Evsikova C. Mol Reprod Dev. 2009. 76(9):805-18.

"The seminal question in modern developmental biology is the origins of new life arising from the unification of sperm and egg."

15. A role for the elongator complex in zygotic paternal genome demethylation. Okada Y, Yamagata K, Hong K, Wakayama T, Zhang Y. Nature. 2010. 463(7280):554-8.

"The life cycle of mammals begins when a sperm enters an egg."

16. Fertilization and the oocyte-to-embryo transition in C. elegans. Marcello MR, Singson A. BMB Rep. 2010. 43(6):389-99.

"Fertilization is a complex process comprised of numerous steps. During fertilization, two highly specialized and differentiated cells (sperm and egg) fuse and subsequently trigger the development of an embryo from a quiescent, arrested oocyte."

17. The mammalian zona pellucida: a matrix that mediates both gamete binding and immune recognition? Clark GF. Syst Biol Reprod Med. 2010 Oct;56(5):349-64.

"Bound gametes then undergo a signal transduction cascade known as acrosomal exocytosis that enables them to penetrate this matrix and fuse with the oocyte to create a new individual."

18. Model systems for membrane fusion. Marsden HR, Tomatsu I, Kros A. Chem Soc Rev. 2011. 40(3):1572-85.

"The fusion of sperm and egg membranes *initiates the life* of a sexually reproducing organism."

19. Calcium channels in the development, maturation, and function of spermatozoa. Darszon A, Nishigaki T, Beltran C, Treviño CL. *Physiol Rev.* 2011. 91(4):1305-55.

"A proper dialogue between spermatozoa and the egg is essential for conception of a new individual in sexually reproducing animals. Ca(2+) is crucial in orchestrating this unique event *leading to a new life*."

20. Acrosome reaction in the cumulus oophorus revisited: involvement of a novel sperm-released factor NYD-SP8. Sun TT, Chung CM, Chan HC. *Protein Cell.* 2011. 2(2):92-8.

"Fertilization is a process involving multiple steps that lead to the final fusion of one sperm and oocyte to *form the zygote*."

21. *Starting a new life*: sperm PLC-zeta mobilizes the Ca²⁺ signal that induces egg activation and embryo development: an essential phospholipase C with implications for male infertility. Nomikos M, Swann K, Lai FA. *Bioessays.* 2012. 34(2):126-34.

22. Kinases, phosphatases and proteases during sperm capacitation. Signorelli J, Diaz ES, Morales P. *Cell Tissue Res.* 2012. 349(3):765-82.

"Fertilization is the process by which male and female haploid gametes (sperm and egg) unite to *produce a genetically distinct individual*."

23. Roles of the oviduct in mammalian fertilization. Coy P, Garcia-Vázquez FA, Visconti PE, Avilés M. *Reproduction.* 2012. 144(6):649-60.

"The oviduct or Fallopian tube *is the anatomical region where every new life begins* in mammalian species. After a long journey, the spermatozoa meet the oocyte in the specific site of the oviduct named ampulla, and fertilization takes place."

24. Oviductal, endometrial and embryonic gene expression patterns as molecular clues for pregnancy establishment. Salilew-Wondim D, Schellander K, Hoelker M, Tesfaye D. *Anim Reprod Sci.* 2012. 134(1-2):9-18.

"In higher animals, the *beginning of new life* and transfer of genetic material to the next generation occurs in the oviduct when two distinct gametes cells unite resulting in the formation of a zygote."

25. Sperm-egg interaction. Evans JP. *Annu Rev Physiol.* 2012. 74:477-502.

"A crucial step of fertilization is the sperm-egg interaction that allows the *two gametes to fuse and create the zygote.*"

26. Regulation of inositol 1,4,5-trisphosphate receptor function during mouse oocyte maturation. Wakai T, Vanderheyden V, Yoon SY, Cheon B, Zhang N, Parys JB, Fissore RA. J Cell Physiol. 2012. 227(2):705-17.

"At the time of fertilization, an increase in the intracellular Ca(2+) concentration ([Ca(2+)](i)) underlies egg activation and *initiation of development* in all species studied to date."

27. Fertilization. Marcello MR, Singaravelu G, Singson A. Adv Exp Med Biol. 2013. 757:321-50.

"Fertilization-the fusion of gametes to *produce a new organism*-is the culmination of a multitude of intricately regulated cellular processes."

28. The oocyte-to-embryo transition. Robertson S, Lin R. Adv Exp Med Biol. 2013. 757:351-72.

"The oocyte-to-embryo transition refers to the process whereby a fully grown, relatively quiescent oocyte undergoes maturation, fertilization, and is *converted into a developmentally active, mitotically dividing embryo*, arguably one of the most dramatic transitions in biology."

29. How to make a good egg!: The need for remodeling of oocyte Ca(2+) signaling to mediate the egg-to-embryo transition. Nader N, Kulkarni RP, Dib M, Machaca K. Cell Calcium. 2013. 53(1):41-54.

"The egg-to-embryo transition marks *the initiation of multicellular organismal development* and is mediated by a specialized Ca(2+) transient at fertilization."

30. Membrane rafts regulate phospholipase B activation in murine sperm. Asano A, Nelson-Harrington JL, Travis AJ. Commun Integr Biol. 2013. 6(6):e27362.

"It is intuitive that *fertilization-the start of life*-involves communication between a sperm cell and an egg."

31. Juno is the egg Izumo receptor and is essential for mammalian fertilization. Bianchi E, Doe B, Goulding D, Wright GJ. Nature. 2014. 508(7497):483-7.

"Fertilization occurs when *sperm and egg recognize each other and fuse to form a new, genetically distinct organism.*"

32. A transgenic insertion on mouse chromosome 17 inactivates a novel immunoglobulin superfamily gene potentially involved in sperm-egg fusion. Lorenzetti D, Poirier C, Zhao M, Overbeek PA, Harrison W, Bishop CE. *Mamm Genome*. 2014. 25(3-4):141-8.

“Fertilization is the process that leads to the formation of a diploid zygote from two haploid gametes.”

33. MicroRNA-34 family expression in bovine gametes and preimplantation embryos. Tscherner A, Gilchrist G, Smith N, Blondin P, Gillis D, LaMarre J. *Reprod Biol Endocrinol*. 2014. 12:85.

“In sexually reproducing organisms, embryogenesis begins with the fusion of two haploid gametes”

34. Chromatin dynamics during spermiogenesis. Rathke C, Baarends WM, Awe S, Renkawitz-Pohl R. *Biochim Biophys Acta*. 2014 Mar;1839(3):155-68.

“The function of sperm is to safely transport the haploid paternal genome to the egg containing the maternal genome. The subsequent fertilization leads to transmission of a new unique diploid genome to the next generation.”

35. Transmembrane signal transduction in oocyte maturation and fertilization: focusing on *Xenopus laevis* as a model animal. Sato K. *Int J Mol Sci*. 2014 Dec 23;16(1):114-34.

“Fertilization is a cell biological phenomenon of crucial importance for the birth of new life in a variety of multicellular and sexual reproduction species”

36. Erase-Maintain-Establish: Natural Reprogramming of the Mammalian Epigenome. Leseva M, Knowles BB, Messerschmidt DM, Solter D. *Cold Spring Harb Symp Quant Biol*. 2015;80:155-63.

“Upon union of these gametes, reprogramming of the new organism's epigenome is initiated, which eventually leads, through pluripotent cells, to the cell lineages required for proper embryonic development to a sexually mature adult.”

37. Cross-species fertilization: the hamster egg receptor, Juno, binds the human sperm ligand, Izumo1. Bianchi E, Wright GJ. *Philos Trans R Soc Lond B Biol Sci*. 2015. 370(1661):20140101.

“Fertilization is the culminating event in sexual reproduction and requires the recognition and fusion of the haploid sperm and egg to form a new diploid organism.”

38. Maternal non-Mendelian inheritance of a reduced lifespan? A hypothesis. Wilding M, Coppola G, De Icco F, Arenare L, Di Matteo L, Dale B. *J Assist Reprod Genet*. 2014. 31(6):637-43.

“Since a new individual is derived from the fusion of a single sperm and egg, we tested...”

39. An update on post-ejaculatory remodeling of the sperm surface before mammalian fertilization. Gadella BM, Boerke A. *Theriogenology*. 2015. 85(1):113-24.

“The fusion of a sperm with an oocyte to form new life is a highly regulated event.”

40. PLC ζ or PAWP: revisiting the putative mammalian sperm factor that triggers egg activation and embryogenesis. Kashir J, Nomikos M, Swann K, Lai FA. *Mol Hum Reprod*. 2015. 21(5):383-8.

“In mammals, egg activation is initiated by multiple cytosolic Ca(2+) transients (Ca(2+) oscillations) that are triggered following delivery of a putative sperm factor from the fertilizing sperm. The identity of this 'sperm factor' thus holds much significance, not only as a vital component in creating a new life, but also for its potential therapeutic and diagnostic value in human infertility.”

41. 2015 RANZCOG Arthur Wilson Memorial Oration 'From little things, big things grow: The importance of periconception medicine'. Norman RJ. *Aust N Z J Obstet Gynaecol*. 2015. 55(6):535-40.

“The time of our conception is when we are most vulnerable to survival and growing as a healthy human being.”

42. State of the art in cell-cell fusion. Willkomm L, Bloch W. *Methods Mol Biol*. 2015. 1313:1-

“Mammalian life begins with a cell-cell fusion event, i.e. the fusion of the spermatozoid with the oocyte”

43. Mapping the journey from totipotency to lineage specification in the mouse embryo. Leung CY, Zernicka-Goetz M. *Curr Opin Genet Dev*. 2015. 34:71-6.

“Mammalian life, with all its complexity comes from a humble beginning of a single fertilized egg cell.”

44. In vitro fertilization (IVF) in mammals: epigenetic and developmental alterations. Scientific and bioethical implications for IVF in humans. Ventura-Juncá P, Irarrázaval I, Rolle AJ, Gutiérrez JI, Moreno RD, Santos MJ. *Biol Res*. 2015 Dec 18;48:68.

“The advent of in vitro fertilization (IVF) in animals and humans implies an extraordinary change in the environment where the beginning of a new organism takes place.”

45. Broad histone H3K4me3 domains in mouse oocytes modulate maternal-to-zygotic transition. Dahl JA, Jung I, Aanes H, Greggains GD, Manaf A, Lerdrup M, Li G, Kuan S, Li B, Lee AY, Preissl S, Jermstad I, Haugen MH, Suganthan R, Bjørås M, Hansen K, Dalen KT, Fedorcsak P, Ren B, Klungland A. *Nature*. 2016 Sep 22;537(7621):548-552.

“Maternal-to-zygotic transition (MZT) is essential for the formation of a new individual”
[MZT begins at fertilization]

46. Dicalcin, a zona pellucida protein that regulates fertilization competence of the egg coat in *Xenopus laevis*. Miwa N. *J Physiol Sci*. 2015 Nov;65(6):507-14.

“Fertilization triggers the resumption of the cell cycle of the egg, ultimately leading to generation of a new organism”

47. The molecular basis of fertilization. Georgadaki K, Khoury N, Spandidos DA, Zoumpourlis V. *Int J Mol Med*. 2016 Oct;38(4):979-86.

“The process involves the fusion of an oocyte with a sperm, creating a single diploid cell, the zygote, from which a new individual organism will develop.”

48. Molecular architecture of the human sperm IZUMO1 and egg JUNO fertilization complex. Aydin H, Sultana A, Li S, Thavalingam A, Lee JE. *Nature*. 2016 Jun 23;534(7608):562-5.

“The fusion of the haploid spermatozoon and oocyte is the culminating event in mammalian fertilization, enabling the creation of a new, genetically distinct diploid organism.”

49. Structure of IZUMO1-JUNO reveals sperm-oocyte recognition during mammalian fertilization. Ohto U, Ishida H, Krayukhina E, Uchiyama S, Inoue N, Shimizu T. *Nature*. 2016 Jun 23;534(7608):566-9.

“Fertilization is a fundamental process in sexual reproduction, creating a new individual through the combination of male and female gametes”

50. Sperm Meets Egg: The Genetics of Mammalian Fertilization. Bianchi E, Wright GJ. *Annu Rev Genet*. 2016 Nov 23;50:93-111.

“Fertilization is the culminating event of sexual reproduction, which involves the union of the sperm and egg to form a single, genetically distinct organism.”

51. The anaphase-promoting complex initiates zygote division in Arabidopsis through degradation of cyclin B1. Guo L, Jiang L, Zhang Y, Lu XL, Xie Q, Weijers D, Liu CM. *Plant J*. 2016. 86(2):161-74.

“As the start of a new life cycle, activation of the first division of the zygote is a critical event in both plants and animals.”

52. The role of syncytins in human reproduction and reproductive organ cancers. Soygur B, Sati L. *Reproduction*. 2016. 152(5):R167-78.

“Human life begins with sperm and oocyte fusion.”

53. Parental Control Begins at the Beginning. Chu D. *Genetics*. 2016. 204(4):1377-1378.

“New parents anticipate their job begins at birth. Little do they know *they have been exerting control within the baby’s first cell since fertilization.*”

54. Oocyte activation and latent HIV-1 reactivation: AMPK as a common mechanism of action linking *the beginnings of life* and the potential eradication of HIV-1. Finley J. *Med Hypotheses*. 2016 Aug;93:34-47.

[A study linking events that happen at sperm-egg fusion (i.e., egg activation) and the mechanism of HIV reactivation.]

55. Gamete activation: basic knowledge and clinical applications. Tosti E, Ménézo Y. *Hum Reprod Update*. 2016 Jun;22(4):420-39.

“Here we describe in detail the reciprocal induction of the two activation processes, the molecules involved and the mechanisms of cell interaction and signal transduction that *ultimately result in successful embryo development and creation of a new individual.*” [at gamete fusion]

56. The challenges involved in elucidating the molecular basis of sperm-egg recognition in mammals and approaches to overcome them. Wright GJ, Bianchi E. *Cell Tissue Res*. 2016 Jan;363(1):227-235.

“Sexual reproduction is used by many different organisms *to create a new generation of genetically distinct progeny.* Cells originating from separate sexes or mating types segregate their genetic material into haploid gametes which must then recognize and fuse with each other in a process known as *fertilization to form a diploid zygote.*”

57. Epigenetics in preimplantation mammalian development. Canovas S, Ross PJ. *Theriogenology*. 2016 Jul 1;86(1):69-79.

“As a result of finely tuned interactions between numerous mechanisms, *the goal of fertilization is to form a full healthy new individual.*”

58. Epigenetic Control of Early Mouse Development. Lim CY, Knowles BB, Solter D, Messerschmidt DM. *Curr Top Dev Biol.* 2016;120:311-60.

“The genomes of the sperm and egg are hypermethylated, hence transcriptionally silent. Their union, in the prepared environment of the egg, initiates their epigenetic genomic reprogramming into a totipotent zygote...Herein, we describe the factors, DNA and histone modifications, activation and repression of retrotransposons, and cytoplasmic localizations, known to influence the activation of the mammalian genome at the initiation of new life.”

59. Meiotic Divisions: No Place for Gender Equality. El Yakoubi W, Wassmann K. *Adv Exp Med Biol.* 2017. 1002:1-17.

“In multicellular organisms the fusion of two gametes with a haploid set of chromosomes leads to the formation of the zygote, the first cell of the embryo.”

60. Signal transduction in mammalian oocytes during fertilization. Machaty Z. *Cell Tissue Res.* 2016. 363(1):169-83.

“Mammalian embryo development begins when the fertilizing sperm triggers a series of elevations in the oocyte's intracellular free Ca(2+) concentration.”

61. ZYGOTE-ARREST 3 that encodes the tRNA ligase is essential for zygote division in Arabidopsis. Yang KJ, Guo L, Hou XL, Gong HQ, Liu CM. *J Integr Plant Biol.* 2017. 59(9):680-692.

“In sexual organisms, division of the zygote initiates a new life cycle.”

62. *When sperm meets egg: the spark of new life.* Wozniak KL, Luque GM, Ahn SH. *Mol Reprod Dev.* 2017. doi: 10.1002/mrd.22857. [Epub ahead of print]

63. Histone 3 lysine 9 acetylation is a biomarker of the effects of culture on zygotes. Rollo C, Li Y, Jin XL, O'Neill C. *Reproduction.* 2017. 154(4):375-385.

“Fertilisation triggers a round of chromatin remodelling that prepares the genome for the first round of transcription from the new embryonic genome.”

64. Hutchinson-Gilford Progeria Syndrome: A Premature Aging Disease. Ahmed MS, Ikram S, Bibi N, Mir A. *Mol Neurobiol.* 2017. doi: 10.1007/s12035-017-0610-7. [Epub ahead of print]

“Aging is a developmental process that begins with fertilization and ends up with death involving a lot of environmental and genetic factors.”

65. Egg Activation at Fertilization. Machaty Z, Miller AR, Zhang L. Adv Exp Med Biol. 2017. 953:1-47.

“Fertilization is the union of gametes to initiate development of a new individual.”

66. LINE-1 activation after fertilization regulates global chromatin accessibility in the early mouse embryo. Jachowicz JW, Bing X, Pontabry J, Bošković A, Rando OJ, Torres-Padilla ME. Nat Genet. 2017. 49(10):1502-1510.

[referring to events in the zygote] “Our data suggest that activation of LINE-1 regulates global chromatin accessibility at the beginning of development and indicate that retrotransposon activation is integral to the developmental program.”

67. “This is where it all started” - the pivotal role of PLCζ within the sophisticated process of mammalian reproduction: a systemic review. Gat I, Orvieto R. Basic Clin Androl. 2017. 21;27:9.

“At the end of oogenesis and spermatogenesis, both haploid gametes contain a single set of chromosomes ready to form the zygote, the first cell of the newly developing individual.”

68. Epigenetic modifications and reprogramming in paternal pronucleus: sperm, preimplantation embryo, and beyond. Okada Y, Yamaguchi K. Cell Mol Life Sci. 2017. 74(11):1957-1967.

“Pronuclear/zygotic stage is the very first stage of life.”

69. PLCζ is the physiological trigger of the Ca²⁺ oscillations that induce embryogenesis in mammals but conception can occur in its absence. Hachem A, Godwin J, Ruas M, Lee HC, Ferrer Buitrago M, Ardestani G, Bassett A, Fox S, Navarrete F, de Sutter P, Heindryckx B, Fissore R, Parrington J. Development. 2017. 144(16):2914-2924.

“Activation of the egg by the sperm is the first, vital stage of embryogenesis.”

70. Structural Basis of Egg Coat-Sperm Recognition at Fertilization. Raj I, Sadat Al Hosseini H, Dioguardi E, Nishimura K, Han L, Villa A, de Sanctis D, Jovine L. Cell. 2017. 169(7):1315-1326.e17.

“Recognition between sperm and the egg surface marks the beginning of life in all sexually reproducing organisms.”

71. Human imprinting disorders: Principles, practice, problems and progress. Mackay DJG, Temple IK. Eur J Med Genet. 2017 Nov;60(11):618-626.

“Every generation, these epigenetic marks are re-set twice: in the germline, to enable differentiation of sperm and eggs, and at fertilisation, to create the totipotent zygote that then begins growth and differentiation into a new human.”

72. Parthenogenesis in Insects: The Centriole Renaissance. Riparbelli MG, Gottardo M, Callaini G. Results Probl Cell Differ. 2017;63:435-479.

“Building a new organism usually requires the contribution of two differently shaped haploid cells, the male and female gametes, each providing its genetic material to restore diploidy of the new born zygote.”

73. Single-nucleus Hi-C reveals unique chromatin reorganization at oocyte-to-zygote transition. Flyamer IM, Gassler J, Imakaev M, Brandão HB, Ulianov SV, Abdennur N, Razin SV, Mirny LA, Tachibana-Konwalski K. Nature. 2017 Apr 6;544(7648):110-114. doi: 10.1038/nature21711. Epub 2017 Mar 29. PMID: 28355183 Free PMC article.

“Chromatin is reprogrammed after fertilization to produce a totipotent zygote with the potential to generate a new organism.”

74. Mammalian zygotic genome activation. Svoboda P. Semin Cell Dev Biol. 2018 Dec;84:118-126. doi: 10.1016/j.semcdb.2017.12.006.

“Zygotic genome activation (ZGA) denotes the initiation of gene expression after fertilization. It is part of the complex oocyte-to-embryo transition (OET) in which a highly specialized cell - the oocyte - is fertilized and transformed into a zygote that gives rise to an embryo that will develop into a newborn.”

75. Protecting and Diversifying the Germline. Gleason RJ, Anand A, Kai T, Chen X. Genetics. 2018 Feb;208(2):435-471.

“restarting a new life cycle upon fertilization is a unique challenge faced by gametes”

76. Molecular organization and mechanical properties of the hyaluronan matrix surrounding the mammalian oocyte. Salustri A, Campagnolo L, Klinger FG, Camaioni A. Matrix Biol. 2018 Feb 9. pii: S0945-053X(18)30025-8.

“Successful ovulation and oocyte fertilization are essential prerequisites for the beginning of life in sexually reproducing animals.”

77. The oviduct: from sperm selection to the epigenetic landscape of the embryo. Pérez-Cerezales S, Ramos-Ibeas P, Acuña OS, Avilés M, Coy P, Rizo D, Gutiérrez-Adán A. Biol Reprod. 2018 Mar 1;98(3):262-276.

“The mammalian oviduct is the place where life begins as it is the site of fertilization and preimplantation embryo development”

78. CHD1 Controls Cell Lineage Specification Through Zygotic Genome Activation. Suzuki S, Minami N. *Adv Anat Embryol Cell Biol.* 2018;229:15-30.

“Life begins with the encounter of eggs and spermatozoa”

79. The *Caenorhabditis elegans* spe-49 gene is required for fertilization and encodes a sperm-specific transmembrane protein homologous to SPE-42. Wilson LD, Obakpolor OA, Jones AM, Richie AL, Mieczkowski BD, Fall GT, Hall RW, Rumbley JN, Kroft TL. *Mol Reprod Dev.* 2018 Jul;85(7):563-578.

“Fertilization, the fusion of sperm and oocyte to form a zygote, is the first and arguably the most important cell-cell interaction event in an organism's life.”

80. The role of Ca²⁺ in oocyte activation during In Vitro fertilization: Insights into potential therapies for rescuing failed fertilization. Swann K. *Biochim Biophys Acta Mol Cell Res.* 2018 May 8. pii: S0167-4889(18)30086-7.

“At fertilization the mature mammalian oocyte is activated to begin development by a sperm-induced series of increases in the cytosolic free Ca²⁺ concentration.”

81. Sex Steroid-Mediated Control of Oviductal Function in Cattle. Binelli M, Gonella-Diaza AM, Mesquita FS, Membrive CMB. *Biology (Basel).* 2018 Feb 2;7(1). pii: E15.

“The oviduct lumen [where fertilization occurs] stages a dynamic set of cellular and molecular interactions to fulfill the noble role of generating a new individual.”

82. Double trouble at the beginning of life. Zielinska AP, Schuh M. *Science.* 2018 Jul 13;361(6398):128-129.

“Every human life begins with the fertilization of an egg.”

83. The dualistic origin of human tumors. Liu J. *Semin Cancer Biol.* 2018 Dec;53:1-16.

“Life starts with a zygote, which is formed by the fusion of a haploid sperm and egg.”

84. Dual-spindle formation in zygotes keeps parental genomes apart in early mammalian embryos. Reichmann J, Nijmeijer B, Hossain MJ, Eguren M, Schneider I, Politi AZ, Roberti MJ, Hufnagel L, Hiiragi T, Ellenberg J. *Science.* 2018 Jul 13;361(6398):189-193.

“At the beginning of mammalian life, the genetic material from each parent meets when the fertilized egg divides.”

85. History, origin, and function of transzonal projections: the bridges of communication between the oocyte and its environment. Clarke HJ. *Anim Reprod*. 2018 Aug 16;15(3):215-223.

“Development and differentiation of a functional oocyte that following fertilization is able to give rise to a new individual”

86. Molecular organization and mechanical properties of the hyaluronan matrix surrounding the mammalian oocyte. Salustri A, Campagnolo L, Klinger FG, Camaioni A. *Matrix Biol*. 2019 May;78-79:11-23.

“Successful ovulation and oocyte fertilization are essential prerequisites for the beginning of life in sexually reproducing animals.”

87. The eggstraordinary story of how life begins. Parrington J, Arnoult C, Fissore RA. *Mol Reprod Dev*. 2019 Jan;86(1):4-19.

[This paper reviews the sperm-supplied factor, phospholipase C ζ 1 (PLC ζ), that initiates development of mammalian embryos at sperm-egg fusion.]

88. The "life code": a theory that unifies the human life cycle and the origin of human tumors. Jinsong L. *Semin Cancer Biol*. 2019 Sep 12. pii: S1044-579X(19)30053-7.

“Human life starts with fertilization of an egg to form a zygote.”

89. Totipotency continuity from zygote to early blastomeres: a model under revision. Boiani M, Casser E, Fuellen G, Christians ES. *Reproduction*. 2019 Aug;158(2):R49-R65.

“The mammalian zygote is a totipotent cell that generates all the cells of a new organism through embryonic development.”

90. Mechanisms regulating zygotic genome activation. Schulz KN, Harrison MM. *Nat Rev Genet*. 2019 Apr;20(4):221-234.

“Following fertilization, the two specified gametes must unite to create an entirely new organism.”

91. Find and fuse: Unsolved mysteries in sperm-egg recognition. Bianchi E, Wright GJ. *PLoS Biol*. 2020 Nov 13;18(11):e3000953.

“The interaction of sperm and egg culminates with the fusion of their cell membranes, triggering the molecular events that result in the formation of a new genetically distinct organism.”

92. The landscape of RNA Pol II binding reveals a stepwise transition during ZGA. Liu B, Xu Q, Wang Q, Feng S, Lai F, Wang P, Zheng F, Xiang Y, Wu J, Nie J, Qiu C, Xia W, Li L, Yu G, Lin Z, Xu K, Xiong Z, Kong F, Liu L, Huang C, Yu Y, Na J, Xie W. Nature. 2020 Nov;587(7832):139-144.

“Zygotic genome activation (ZGA) [this event occurs at the one-cell stage] is the first transcription event in life.”

93. Methylation: An Ineluctable Biochemical and Physiological Process Essential to the Transmission of Life. Menezo Y, Clement P, Clement A, Elder K. Int J Mol Sci. 2020 Dec 7;21(23):9311.

“During reproduction, the two genomes that unite to create a new individual [at fertilization] are complementary”

94. Heterochromatin establishment during early mammalian development is regulated by pericentromeric RNA and characterized by non-repressive H3K9me3. Burton A, Brochard V, Galan C, Ruiz-Morales ER, Rovira Q, Rodriguez-Terrones D, Kruse K, Le Gras S, Udayakumar VS, Chin HG, Eid A, Liu X, Wang C, Gao S, Pradhan S, Vaquerizas JM, Beaujean N, Jenuwein T, Torres-Padilla ME. Nat Cell Biol. 2020 Jul;22(7):767-778.

“Following fertilization in mammals, the gametes are reprogrammed to create a totipotent zygote”

95. Gamete quality in a multistressor environment. Gallo A, Boni R, Tosti E. Environ Int. 2020 May;138:105627.

“Sexual reproduction is the process that allows the formation of a new individual and is underpinned by gamete quality defined as the ability of spermatozoa and oocytes to interact during fertilization leading to the creation and development of a normal embryo.”

96. Unscrambling the oocyte and the egg: clarifying terminology of the female gamete in mammals. Duncan FE, Schindler K, Schultz RM, Blengini CS, Stein P, Stricker SA, Wessel GM, Williams CJ. Mol Hum Reprod. 2020 Nov 1;26(11):797-800.

“Eggs are most impressive cells, capable of supporting development of an entirely new organism following fertilization”

97. Physiological polyspermy: Selection of a sperm nucleus for the development of diploid genomes in amphibians. Iwao Y, Kimoto C, Fujimoto A, Suda A, Hara Y. Mol Reprod Dev. 2020 Mar;87(3):358-369.

“The union between a sperm and an egg nucleus in egg fertilization is necessary to mix genetic materials to create a new diploid genome for the next generation.”

98. Rebooting the Epigenomes during Mammalian Early Embryogenesis. Xia W, Xie W. Stem Cell Reports. 2020 Dec 8;15(6):1158-1175.

“Upon fertilization, terminally differentiated gametes are transformed to a totipotent zygote, which gives rise to an embryo.”

99. PRC2 and EHMT1 regulate H3K27me2 and H3K27me3 establishment across the zygote genome. Meng TG, Zhou Q, Ma XS, Liu XY, Meng QR, Huang XJ, Liu HL, Lei WL, Zhao ZH, Ouyang YC, Hou Y, Schatten H, Ou XH, Wang ZB, Gao SR, Sun QY. Nat Commun. 2020 Dec 11;11(1):6354.

“The formation of zygote is the beginning of mammalian life”

100. PLK-1 promotes the merger of the parental genome into a single nucleus by triggering lamina disassembly. Velez-Aguilera G, Nkombo Nkoula S, Ossareh-Nazari B, Link J, Paouneskou D, Van Hove L, Joly N, Tavernier N, Verbavatz JM, Jantsch V, Pintard L. Elife. 2020 Oct 8;9:e59510.

“Life of sexually reproducing organisms starts with the fusion of the haploid egg and sperm gametes to form the genome of a new diploid organism.”

101. Shadow enhancers can suppress input transcription factor noise through distinct regulatory logic. Waymack R, Fletcher A, Enciso G, Wunderlich Z. Elife. 2020 Aug 17;9:e59351. doi: 10.7554/eLife.59351.

“In all higher organisms, life begins with a single cell.”

102. Initiation of Parental Genome Reprogramming in Fertilized Oocyte by Splicing Kinase SRPK1-Catalyzed Protamine Phosphorylation. Gou LT, Lim DH, Ma W, Aubol BE, Hao Y, Wang X, Zhao J, Liang Z, Shao C, Zhang X, Meng F, Li H, Zhang X, Xu R, Li D, Rosenfeld MG, Mellon PL, Adams JA, Liu MF, Fu XD. Cell. 2020 Mar 19;180(6):1212-1227.e14.

“Upon fertilization...the previously characterized splicing kinase SRPK1 initiates this life-beginning event by catalyzing site-specific phosphorylation of protamine, thereby triggering protamine-to-histone exchange in the fertilized oocyte.”

103. Two mechanisms drive pronuclear migration in mouse zygotes. Scheffler K, Uraji J, Jentoft I, Cavazza T, Mönnich E, Mogessie B, Schuh M. Nat Commun. 2021 Feb 5;12(1):841.

“A new life begins with the unification of the maternal and paternal chromosomes upon fertilization.”

104. Insights into epigenetic patterns in mammalian early embryos. Xu R, Li C, Liu X, Gao S. Protein Cell. 2021 Jan;12(1):7-28.

“Mammalian fertilization begins with the fusion of two specialized gametes, followed by major epigenetic remodeling leading to the formation of a totipotent embryo.”

105. Totipotency of mouse zygotes extends to single blastomeres of embryos at the four-cell stage. Maemura M, Taketsuru H, Nakajima Y, Shao R, Kakiyama A, Nogami J, Ohkawa Y, Tsukada YI. Sci Rep. 2021 May 27;11(1):11167.

“In multicellular organisms, oocytes and sperm undergo fusion during fertilization and the resulting zygote gives rise to a new individual.”

106. Oolemma Receptors in Mammalian Molecular Fertilization: Function and New Methods of Study. Jiménez-Movilla M, Hamze JG, Romar R. Front Cell Dev Biol. 2021 May 19;9:662032.

“Fertilization is a key process in biology to the extent that a new individual will be born from the fusion of two cells.”

107. The Fertilization Enigma: How Sperm and Egg Fuse. Deneke VE, Pauli A. Annu Rev Cell Dev Biol. 2021 Jul 21. doi: 10.1146/annurev-cellbio-120219-021751. Online ahead of print.

“Fertilization is a multistep process that culminates in the fusion of sperm and egg, thus marking the beginning of a new organism in sexually reproducing species.”

108. Cellular and molecular modification of egg envelope hardening in fertilization. Wang Y, Chen F, He J, Xue G, Chen J, Xie P. Biochimie. 2021 Feb;181:134-144.

“An egg changes dramatically after fertilization mediating the beginning of life”

109. Epithelial Cell Transformation and Senescence as Indicators of Genome Aging: Current Advances and Unanswered Questions. Kitakaze M, Chijimatsu R, Vecchione A, Kitagawa T, Doki Y, Eguchi H, Ishii H. Int J Mol Sci. 2021 Jul 14;22(14):7544.

“The age of the genome is defined by the sum of individual (inherited) and acquired genomic traits, based on internal and external factors that impact ontogenesis from the moment of egg fertilization and embryonic development.”