A Call to Standardize the Nomenclature of Human Fetal Membrane at the Feto-Maternal Interface

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Abstract

Despite being one of the largest intrauterine tissues in surface area, the fetal membrane that lines the intrauterine cavity is often overlooked, forgotten, or misidentified in clinical and basic science research. The feto-maternal interface is comprised of the fetal membrane (fetal component) and decidua parietalis (maternal component), which lines the intrauterine cavity and provides essential mechanical, immune, hormonal, and transport support to maintain pregnancy. Fetal membrane plays an important role in triggering and regulating labor via complex signaling cascades. Whilst several researchers have investigated the membranes world-wide, nomenclature remains

inconsistent, leading to widespread ambiguity across inter-disciplinary disciplines involving science, bioengineering, and reproductive medicine. The ongoing confusion regarding its terminology, origins, structure, and function has resulted in several significant issues, including diagnostic errors and misrepresentation clinically, limitations and inaccuracies in scientific research, and regulatory and clinical miscommunication. Therefore, the Fetal Membrane Society (FMS) calls upon the field to standardize fetal membrane nomenclature, define its architecture, and summarize its region-specific differences to facilitate understanding of its biological role. Clear and consistent identification of the fetal membrane is essential in improving research accuracy, clinical outcomes, and effective communication within and between the medical and scientific communities.

Purpose – The need to standardize fetal membrane nomenclature

The majority of intrauterine tissues have been extensively studied for their role in implantation, embryogenesis, pregnancy, and parturition. Yet the fetal membrane remains comparatively understudied and forms the innermost lining adjacent to the uterine decidua and placenta[1]. Recognition of the human fetal membrane as a distinct anatomical structure, separate from the placenta, has evolved gradually through centuries of medical observation and scientific research. Furthermore, it was not until the 19th and 20th centuries, through advancements in modern embryology and obstetrics, that the amnion and chorion were clearly delineated as separate structures within the fetal membrane, each with unique origins and functions[2,3]. Throughout the period since its initial identification, the fetal membrane has had many names such as: placental membrane[4-6], embryonic membrane, amniochorionic (or chorioamniotic) membrane[7-9], gestational membrane[10-12], gestational sac[13], and feto-maternal interface[14-16], reflecting both the complexity of its structure and the diversity of scientific perspectives. This varied nomenclature spans multiple disciplines, including reproductive biology[17,18] and regenerative medicine[19,20], further underscoring the need for a unified understanding and terminology.

Although the fetal membrane has traditionally been considered an appendage of the placenta, modern embryological, histological, and imaging tools like OCT, MRI, and ultrasound

demonstrate that the membranes are structurally different from the placenta[21]. The fetal membranes consist of the amnion and chorion, which originate independently during early embryogenesis: the amnion arises from the epiblast, while the chorion develops from the trophoblast and extraembryonic mesoderm. The fusion of the amnion and chorion at the end of the first trimester (approximately 12-14 weeks gestation)[21-24] forms the fetal membranes which serve as a protective barrier, maintains the amniotic fluid environment, and plays a crucial role in immune modulation. In contrast, the placenta proper—specifically the placental disk—is composed of chorionic villi embedded in maternal decidua and is specialized for maternal-fetal exchange of gases, nutrients, and waste products. Unlike the placenta, the fetal membrane is avascular and lacks the villous architecture necessary for direct exchange between maternal and fetal blood. Therefore, while the fetal membrane is closely associated with the placenta and umbilical cord, it is an anatomically, developmentally, and functionally distinct structure and should not be considered an extension of the placenta (**Figure 1**).

In this white paper, the Fetal Membrane Society (FMS) calls upon the field to standardize fetal membrane nomenclature, define its architecture, and summarize its region-specific differences to facilitate understanding of its biological role. This call to standardization is essential to 1) avoid heterogeneity in discussing this tissue, 2) avoid ambiguity in interpretation, function, and clinical relevance, 3) encourage collaboration between researchers and 4) to coordinate and highlight the importance of the fetal membrane. Understanding the fetal membrane is incredibly important in the context of preterm birth and preterm premature rupture of membrane prevention but also in the normal physiology of amniotic fluid circulation and the timing of parturition.

Definitions

Though there are many names to describe the fetal membrane in the literature or even discrepancies in the field regarding which cell types should be included in this tissue definition, the FMS has reached a majority consensus as a Society and provides the following definitions for

158 future use (**Table 1-2**). The fetal membrane feto-maternal interface is comprised of two main
159 components: the fetal membrane itself and the decidua parietalis. The fetal membrane is the fetal
160 component of this interface and is formed by the fusion of the amnion membrane (AM) and the
161 chorion membrane (CM). The FMS proposes that post-fusion of the AM and CM, the fetal
162 membrane is a singular unit and should be referred to in the singular form ("it" rather than "their").
163 The fetal membrane contains distinct cell types; present in the AM are amnion epithelial cells
164 (AECs), which form the innermost lining facing the amniotic cavity, and amnion mesenchymal
165 cells (AMCs), which reside within the underlying mesenchymal layer. The CM contains chorion
166 mesenchymal cells (CMC) within the connective tissue matrix and chorion trophoblast cells
167 (CTC). The decidua parietalis, the maternal component of the fetal membrane feto-maternal
168 interface, lines the intrauterine cavity and provides essential mechanical, immune, hormonal, and
169 transport support necessary for maintaining pregnancy. Additionally, the fetal membrane and
170 decidua parietalis are the main drivers of labor signaling, both at term and preterm. Together, the
171 connection between the fetal membrane and the decidua parietalis constitutes one of the primary
172 feto-maternal interfaces during pregnancy. When referring to this structure as a whole, the FMS
173 proposes that it is most accurate to use the term "fetal membrane feto-maternal interface".
174
175 **Consequences of mixed nomenclature**
176 *Impacts in the field of obstetrics:* One of the ~~main~~ sources of ambiguity in the nomenclature
177 of the fetal membrane arises from obstetricians, neonatologists, epidemiologists, and basic
178 scientists misinterpreting placental pathologic evaluation of the placenta, fetal membrane, and
179 umbilical cord following adverse pregnancy outcomes, such as spontaneous preterm birth (sPTB)
180 or preterm premature rupture of the membrane (PPROM). Fetal membrane pathologies often
181 include complications arising from retromembranous hemorrhage, diffuse chorioamniotic
182 hemosiderosis, meconium-related changes, isolated amnion rupture, amniochorionic dehiscence,

and noninfectious chronic chorioamnionitis, clinical chorioamnionitis, or histologic chorioamnionitis. In these scenarios, pathological analysis typically includes assessment of the umbilical cord insertion site and identification of the placental infarcts. However, a critical focus of the evaluation is often the fetal membrane itself, particularly for the diagnosis of histological chorioamnionitis. Histologic chorioamnionitis is characterized by a maternal and or fetal inflammatory response[25], the presence of infiltration of > 3-5 polymorphonuclear (PMNs) leukocytes[26], monocytes and macrophages into the chorion or amnion layers. The ongoing debate is regarding the necessity of grading and staging[27] of inflammation in placental pathology reports[25]. This diagnosis is clinically important, as it is indicative of fetal exposure to intrauterine inflammation, and is associated with a fetal inflammatory response, and correlates with increased risks for neonatal morbidity[28-30] compared to a maternal inflammatory response. Pathologists will distinguish acute chorioamnionitis involving the fetal membrane, chorionic plate, and umbilical cord from other forms of placentitis (i.e., villitis, intervillous abscess formation, acute or chronic intervillositis, and isolated chronic deciduaitis). The use of '*maternal inflammatory response'* and *'fetal inflammatory response'* in pathological reports[25] needs to be defined better. Differences in reporting strategies and generalization of placental pathology report results in a dilemma among the obstetrical community about the pathological contributions of the fetal membranes vs. the placenta. As a result, it has been challenging to identify biomarkers or intervention targets to address the membrane pathology and rupture. Therefore, this manuscript underscores the importance of defining the fetal membrane and distinguishing it from the placenta.

Impacts in the field of regenerative medicine: The fetal membrane has become a valuable resource in regenerative medicine, with investigators increasingly isolating human cells, or extracellular vesicles for *in vitro* mechanobiology studies or preserved intact membranes (i.e., lyophilized, frozen, dehydrated) for a variety of clinical applications. This is due to the fetal

208 membrane's unique cellular composition, which includes pluripotent stem cells that produce a
209 variety of growth factors ideal for cell differentiation, tissue regeneration and wound healing.
210 Utilizing the fetal membrane after delivery for such purposes provides an innovative and
211 sustainable approach to treating wound-related or inflammatory conditions with a clinical sample
212 that is otherwise disposed of. Numerous companies market fetal membrane-derived products;
213 however, there is significant inconsistency in how these products are described. Common issues
214 include: 1) the use of non-standardized nomenclature, 2) lack of information on labor status of
215 samples, 3) unspecified anatomical region of where the samples are collected from, and 4)
216 unspecified distinction of whether the product is composed of the whole fetal membrane, AM, or
217 CM. These inconsistencies contribute to heterogeneity in both clinical and research settings,
218 complicating the interpretation and comparison of results. Additionally, many pre-clinical trials
219 employ fetal membrane derivatives without clear definitions or standardized terminology which
220 can: 1) confuse clinicians and patients regarding the origin of the biologic product they are using,
221 2) complicate FDA (or other health agency) approval of said products due to the ambiguous
222 nomenclature within the field, sample type, collection methods, and cellular composition, 3)
223 propagate biologically inaccurate information that “placentas” contain healing properties and
224 physiological factors that are not native to that tissue and 4), create a missed opportunity to
225 understand the true biological context or mechanism of these biologics for potential clinical
226 applications. Standardizing the nomenclature in both obstetrics and regenerative medicine fields,
227 will enable more effective communication across the fields, enhancing reproducibility,
228 synchronizing biological context, and enhancing clinical and scientific advancements in the field.
229 *Ethical and regulatory considerations:* The increasing use of fetal membrane-derived
230 products in regenerative medicine raises important ethical and regulatory considerations that
231 necessitate precise and transparent terminology. These tissues, often obtained after delivery, are
232 widely used for their anti-inflammatory, anti-scarring, and stem cell–like properties. However,

inconsistency in labeling, such as describing products as “placental” or “stem cell–based” without an apparent anatomical reference, can lead to public misunderstanding, regulatory ambiguity, and ethical concerns. Accurate nomenclature is critical to ensure informed consent, product traceability, and compliance with tissue handling and usage guidelines across jurisdictions. Furthermore, clear identification of the tissue source (e.g., amnion vs. chorion, region of membrane, labor status) is essential for institutional review boards, biobanks, and health regulatory agencies when evaluating the scientific validity, safety, and ethical appropriateness of fetal membrane-derived therapies. The FMS acknowledges the ongoing societal and legal discourse surrounding the use of human fetal tissues[31]. The fetal membranes are typically obtained postnatally and are genetically similar to the fetus but they are ethically distinct from embryonic or aborted fetal tissues. However, public perception and policy frameworks vary globally. Thus, harmonized nomenclature not only supports scientific rigor but also promotes ethical transparency and reinforces trust among patients, clinicians, regulators, and the general public.

To facilitate the adoption of standardized fetal membrane nomenclature, the FMS proposes several actionable strategies. First, academic journals can encourage consistent terminology by incorporating standardized nomenclature guidelines into author instructions and peer review checklists. Second, funding agencies and regulatory bodies such as NIH and FDA can require applicants to adhere to defined tissue terminology in grant submissions and product labeling. Third, the FMS plans to conduct targeted educational outreach through webinars, position statements, and guideline publications. Finally, integration of fetal membrane terminology into medical and graduate education curricula will ensure that trainees across disciplines adopt a shared language early in their careers. Together, these efforts aim to build a unified framework for fetal membrane research and clinical translation, reducing ambiguity and improving scientific communication across fields.

Below is a summary of the life cycle, collection documentation, anatomical regions, and cellularity of the fetal membrane that should be used going forward to define fetal membrane specimens.

Unique life cycle of fetal membrane

The formation of the fetal membrane begins in early embryogenesis. During the second week of development, the amniotic cavity arises within the inner cells mass of the blastocyst. Here, the epiblast layer of the embryonic disc separates from the overlying cytotrophoblasts, giving rise to the distinct layer called the amniotic ectoderm. This layer surrounds the amniotic cavity and as embryonic development progresses, it expands to surround the fetus and ultimately form the AM[32] (**Figure 1A**). Simultaneously, the maternal endometrium undergoes decidualization and the syncytiotrophoblasts layer invades into the decidua, facilitating nutrient and gas exchange. Further differentiation leads to the formation of cytotrophoblast and amnion cells (**Figure 1B**). At approximately 15 days gestation, the placental cytotrophoblasts differentiate into CTC forming a unique cellular layer that lines the outer surface of the developing embryo and the amniotic cavity (**Figure 1C**)[32]. The amnion is filled with amniotic fluid, providing protection and cushioning for the developing embryo and fetus throughout gestation. At approximately 12-14 weeks gestations[21-24], the basal chorion trophoblast layer fuses with the AM, forming the fetal membrane (**Figure 1D**). The fused fetal membrane undergoes rapid expansion and remodeling during the second trimester to accommodate the growing fetus and increasing volume of amniotic fluid, thereby maintaining a robust protective barrier (**Figure 1E**). Nutrient and hormonal support is partially derived from maternal blood vessels in the decidua, which is integrated into the chorion trophoblasts' basal side[33], as well as from constituents of the amniotic fluid. Throughout gestation, the fetal membrane is dynamically maintained; its cellular and collagen layers are constantly shed, replaced, and remodeled to maintain structural integrity[34]. Approaching term, a combination of fetal (i.e., placental hypoxia[35,36], fetal maturation markers[37,38], increased metabolic demands[39,40]) and maternal signals (i.e., suppression of antioxidants such as a lack of the oxidative stress

induced transcription factor Nrf2[41]) induce oxidative stress within the amniotic cavity. This oxidative stress drives the maturation (i.e., aging) of the fetal membrane through a process of cellular senescence[42-48], resulting in progressive weakening (**Figure 1F**). Additionally, oxidative stress also induces the transition of amnion epithelial cells to a more proinflammatory mesenchymal phenotype and impairs autophagic processes. The culmination of these changes – cellular senescence, inflammation and activation of signaling cascades contributes to the physiological weakening and eventual rupture of the fetal membrane, a key event in the initiation of labor (**Figure 1G**).

At the end of its life cycle, the fetal membrane is collected after delivery of the baby and the following information should be documented regarding its collection: 1) inclusion/exclusion criteria relevant to collection, 2) gestational age (i.e., term [≥37 weeks] or preterm [<37 weeks]), 3) delivery classification (i.e., scheduled cesarean section or vaginal delivery), 4) labor status (i.e., in labor or not in labor), and 5) anatomical region of collection. If the sex of the baby is available, this should be documented as well. This information should be included in every method section utilizing the fetal membrane or its biological components.

Macroscopic Anatomical Regions of the Fetal Membrane

The fetal membrane is divided into regions based on interaction(s) and proximity to maternal tissues and/or the placenta. In general, it is divided into the membrane overlying the placenta, termed the placental membrane (i.e., the region lining the fetal-facing side of the placenta - composed of just the AM) or the reflective membranes (i.e., the region lining the intrauterine cavity) (**Figure 2**). Although termed "placental" membrane, the region of the fetal membrane that lines the placenta is functionally and anatomically distinct from the placenta itself. While the placental and reflective membranes have similar AEC and stromal architecture, the placental membrane contains a condensed extracellular matrix and no chorion layer. The placental membrane only comprises a small portion (~17%)[49] of the overall surface area of the

fetal membrane. The reflective membrane can be further divided into the peri-placental zone (i.e., 2-3 inches from the placenta), mid-zone (i.e., middle and largest region), and cervical zone (i.e., overlapping the cervix); this nomenclature is dependent on its proximity to the placenta or the cervix (**Figure 2**). However, it is important to note that there is a wide variety of overlap between these areas based on individual and pregnancy-specific anatomy and gestational age. In preparation for parturition, a specific region of the fetal membrane within the cervical zone – known as the zone of altered morphology (ZAM) -undergoes significant structural and morphological changes[3,50-53]. Within the ZAM, swelling occurs in the spongy layer of the AM and thickening of collagen fibers within the underlying connective tissue. These changes are accompanied by thinning of the cellular layers, specifically the trophoblast layer of the CM. Collectively, these morphological changes result in a localized area of structural weakness in the fetal membrane, which is hypothesized to serve as the primary site for membrane rupture during labor or in cases of PPROM[54].

Fetal membrane histology

The fetal membrane is a composite tissue consisting of two epithelial layers, the amnion and the chorion, separated by collagen-rich layers that contain AMCs[44,55,56] (**Figure 3**). The fetal membrane can be manually separated at the spongy layer, resulting in two distinct components: the AM, which consists of AECs and the fibrous ECM layer with stromal cells; and the CM, which contains the reticular ECM layer connected to the CTC. If the maternal decidua remains attached to the CM, the structure is referred to as the choriodecidua membrane.

The fetal membrane plays a vital role in maintaining pregnancy. It acts as a barrier against infections due to its abundance of antimicrobial factors, facilitates nutrient exchange through transporter proteins[57-60] similar to those expressed in the placenta, and provides essential structural support resulting from its diverse collagen and elastin[61,62] content. The specialized, multi-layered architecture of the fetal membrane - including collagen-rich ECM and fetal-derived

cells adjacent to the maternal decidua – underpins its notable tensile strength and functional capacity throughout gestation. The fetal membrane forms the critical interface between the fetal and maternal environments, contributing to the overall function and integrity of the fetal membrane feto-maternal interface[63,64]. Defining the fetal membrane as part of the feto-maternal interface is insufficient to comprehensively characterize this tissue.

Fetal membrane 'cellular and collagen components

The amnion epithelial layer: AECs form the outermost layer of the fetal membrane. Like other epithelial cells, AECs derive their barrier function from their cuboidal shape, tight junctions with neighboring cells and strong adhesion to the underlying basement membrane (**Figure 3**)[65-67]. Furthermore, AECs possess microvilli that enable them to sense the *in utero* environment, a feature common to many epithelial monolayers. The apical surface of these cells are bathed in amniotic fluid[43], positioning the AECs ideally to facilitate communication between the fetus and the maternal uterus. This communication occurs through the secretion of cellular products into the amniotic fluid and the response to solutes present in the amniotic fluid. These signals can then be transmitted to maternal tissues via a 'chain reaction 'of signaling through the tissue[33] or through exosome trafficking[68-70].

AECs are dynamic, undergoing constant turnover, shedding[66,71] and gap formation[9,66,71-73] – processes that are repaired by cellular transitions such as epithelial-to-mesenchymal transition (EMT) or mesenchymal-to-epithelial transition (MET)[71,74-79]. These remodeling mechanisms are essential for the maintenance of the structural integrity of the fetal membrane as it expands and matures[71,76,80]. Although epithelial in nature, AECs are also considered pluripotent stem cells. They express stemness markers such as OCT4, SOX2, NANOG[81-84], in addition to unique cytoskeletal markers indicative of metastate[71,74-76], including co-expression of both epithelial and mesenchymal intermediate filaments (vimentin and cytokeratin). Furthermore, AECs have the ability to produce paracrine (i.e., progesterone and cytokines)[68,85] and endocrine signals (i.e.,

363 exosomes, prostaglandins), thereby regulating their microenvironment. Through their basal
364 surface, AECs secrete various types of collagen (Type I, III, IV, and VII) and glycoproteins,
365 contributing to the formation of a robust interface with the ECM via the basement membrane[85].
366
367 *The ECM-rich layers of the fetal membrane:* The amnion basement membrane is
368 predominantly composed of Type IV collagen, but it also contains small amounts of Type III and
369 V collagen, as well as laminin, fibronectin, and nidogen[63,85-87]. The expression of these
370 components is regulated by matrix metalloproteinases (MMPs), specifically MMP9 and MMP2,
371 which are produced by both AECs and AMCs. The basement membrane is anchored to the
372 underlying compact layer that contains Types I, III, V, and VI collagens, which connects to the
373 next ECM layer, the fibrous (i.e., fibroblast) layer. Within the fetal membrane, the three distinct
374 ECM layers, the fibrous, spongy, and reticular layers, each contain unique compositions of
375 collagen, elastin, and microfibrils (**Figure 3)**. These specialized structures contribute to the
376 viscoelastic properties of the fetal membrane, enabling it to withstand stresses associated with
377 fetal growth, movement, and uterine contractions prior to labor. Additional ECM components, such
378 as fibronectin, laminins, proteoglycans, and hyaluronan, also contribute significant structural and
379 functional roles in the development and remodeling of fetal membrane ECM.
380 AMCs secrete Type I, III, and VI collagen within the compact and fibroblast layers,
381 contributing to the elasticity and tensile strength of the AM. The fibrous layer of the stromal region
382 primarily contains AMCs[88] , in addition to a smaller number of immune cells such as macrophages
383 and, under certain conditions, neutrophils).[89-94] These cells play an important role in modulating
384 inflammation and tissue remodeling by secreting both pro-inflammatory mediators (including
385 cytokines such as IL-1β, IL-6, and TNFα) and MMPs as well as anti-inflammatory and
386 immunosuppressive mediators (such as IL-10, TGFβ, and prostaglandins). Through these
387 secretions, AMCs communicate with other cellular layers and actively participate in fetal
388 membrane remodeling[76,95,96].

AMCs, characterized by their elongated mesenchymal morphology and expression of vimentin, are the most prevalent cell type found in the fibroblast layer of the AM. (**Table 1-2**) (**Figure 3**). AMCs are well known to undergo MET to seal AEC gaps[9,97] in the mesenchymal network, thereby maintaining fetal membrane integrity throughout gestation[71]. Recent studies suggest that AMCs may not be a permanent population within the ECM, but rather are transient forms of AECs or CTCs that are recycled back to their parent cell type[71,76,98].

AMCs have been shown to be more susceptible to apoptosis towards the end of pregnancy, and their loss may compromise the AM's ability to maintain its ECM in the fibrous layer[99]. As previously described, the processes of cell recycling and remodeling are necessary for accommodating the rapid growth of the membrane during gestation and for repairing and remodeling areas affected by cell shedding and death. Furthermore, during intrauterine infection, AMCs become activated and express innate immune markers, highlighting their important role in host defense[100-103].

The fibrous layer of the AM is connected to an underlying spongy layer, which serves as an intermediate layer between the AM and CM. This layer is rich in glycosaminoglycans, proteoglycans (i.e., décorin, biglycan), glycoproteins (i.e., laminin, fibronectin), elastin, and Type I, III, and IV collagen[61-63,104,105]. This intermediary layer maintains distinct populations of cells in the AM (AMCs in the fibroblast layer) and CM (CMCs in the reticular layer) by preventing the movement of cells across the layers (**Figure 3**)[106,107].

The reticular layer of the CM consists of fibrillar bundles of Type I, III, IV, V and VI collagens. It is positioned between the apical spongy layer and the CM basement membrane that is anchored to the CTCs (**Figure 3**). The CM basement membrane is made up of Type VI collagen, fibronectin, and laminin and is degraded by MMPs produced by CMCs and CTCs. CMCs are derived from CTCs and, similar to AMCs, can undergo EMT and MET facilitating tissue remodeling[107,108]. CMCs exhibit the classic elongated, spindle-shaped morphology of mesenchymal cells and express cytoskeletal proteins such as vimentin and N-cadherin), much

like AMCs. However, CMCs also secrete hormones such as progesterone, at levels comparable to CTCs[109-112].

The chorion trophoblast layer: Though derived from the same origin, the CTCs of the fetal membrane are functionally distinct from the cytotrophoblasts, syncytiotrophoblasts, and extravillous trophoblasts found in the placenta[113,114]. The CM, often referred to as the "great wall" of the fetal membrane, forms a critical barrier at the feto-maternal interface, providing essential protection against external stressors and pro-inflammatory mediators[115,116]. Multiple layers of CTCs are anchored to the basement membrane of the CM. These CTCs exhibit a cuboidal epithelial morphology similar to that of AECs. However, recent studies suggest that, unlike AECs, CTCs are notably resistant to stress-induced EMT mediated by p38 mitogen-activated kinases[117]. This resistance is likely crucial for maintaining the barrier function of the CM, as EMT within this layer could otherwise lead to localized inflammation and compromise the CM's ability to shield the more vulnerable AM[117,118]. Whilst the predominant cell type within the CM are CTCs, there are a small number of laeve cells around the basement membrane[119] (**Figure 3**). Laeve cells, derived from the placental trophoblasts, are distinguished from CTCs by their large vacuoles.

CTCs are not only structurally important but also immunologically active. CTCs produce a range of immunomodulatory molecules, including progesterone, non-classical major histocompatibility complex (MHC) class I antigens (HLA-E, HLA-F, and HLA-G)[120] and pro- and anti-inflammatory cytokines such as IL-10[109-112,121,122]. These mediators enable the CM to directly modulate the decidual immune microenvironment. This immunological interface is crucial in preventing excessive inflammation, which could trigger premature labor in response to maternal exposure to exogenous factors.

In addition to immunomodulatory molecules, CTCs secrete hormones (i.e., progesterone, estrogen), growth factors (i.e., phosphatidylinositol glycan anchor biosynthesis class F, insulin-like growth factor, epidermal growth factor, fibroblast growth factor), and a range of prostaglandins

(i.e., prostaglandin E2, prostaglandin F2alpha, prostaglandin E1, prostaglandin E3, prostaglandin I2) that support the maintenance and function of the fetal membrane. The CM's dual role in maintaining the structural integrity of the fetal membrane and modulating immune responses highlights its importance in protecting the developing fetus. Disruption to this barrier can lead to adverse pregnancy outcomes, such as intra-amniotic infections and inflammation.

Summary

The fetal membrane forms a crucial feto-maternal interface with the maternal decidua parietalis that is functionally and anatomically distinct from the placenta. Formed by the fusion of the AM and CM by 15 weeks of gestation, it provides a large surface area for communication between mother and fetus throughout the pregnancy. Enveloping the developing fetus, the fetal membrane lines both the intrauterine cavity (as the reflective membrane) and the placenta (as the placental membrane), giving rise to anatomically and structurally specialized regions. The reflective and placental membranes contain multiple fetal cell layers and collagen-rich extracellular matrices, together forming a dynamic barrier that separates the maternal circulation from the fetal amniotic environment. This barrier is actively maintained by coordinated cellular turnover, collagen remodeling, hormonal signaling, and immune regulation, processes that are not only essential for fetal protection but also play a role in the onset of labor.

A clear understanding of the origins, organization and regional differences of fetal membrane cells is critical for accurately modeling these tissues *in* vitro and advancing regenerative medicine.. Standardizing fetal membrane nomenclature and precisely defining tissue collection and anatomical regions will help unify research efforts, reduce clinical confusion and advance the scientific and therapeutic potential of this amazing tissue.

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Table 1: Fetal Membrane Nomenclature

Table 2: Fetal Membrane Feto-Maternal Interface Nomenclature

Figure 1: Life cycle of the fetal membrane during gestation

Graphic schematic of fetal membrane formation, maturation, and fetal delivery.

A) During implantation of the blastocyst into the endometrium, the differentiates into trophoblast cells (later forming the chorion) (purple), and the inner cell mass (orange) begins to form the amniotic cavity (grey). **B**) As implantation continues, the trophoblast layer differentiates into the syncytiotrophoblast (grey with dark grey dots) that connects to the maternal vasculature and the cytotrophoblast (purple) that connects to the amniotic cavity (grey). The amniotic cavity now contains amnion epithelial cells (blue) that line its border. **C**) Close to 15 days gestation, the formation of the chorion (yellow/orange) occurs as cytotrophoblast (purple) differentiates to create the chorion cavity lining the amniotic cavity (grey). **D**) These layers continue to differentiate to form the villous structure of the placenta (orange outlined in purple) and the chorion trophoblast (yellow) and amnion (blue) of the fetal membrane. Around 15 weeks of gestation, the amnion (blue) and chorion (yellow) layers fuse to form the fetal membranes. The membranes line the intrauterine cavity, providing structural, mechanical, and immune support during pregnancy. **E-F**)

The fetal membrane (black line) grows, expands, and matures alongside the fetus during the second trimester. **G**) During the third trimester, changes in the inflammatory status of the intrauterine cavity induce senescence (i.e., aging) that contributes to fetal membrane weakening (dashed lines). **H**) At approximately 40 weeks of gestation, a combination of both fetal and maternal-derived signaling initiates fetal membrane (black line) weakening and rupture, myometrial contractions, cervical ripening, and delivery of the fetus and intrauterine tissues. Created with Motifolio.com.

Figure 2: Classification of fetal membrane regions

The fetal membrane is divided into two sections (dashed line): the placental membrane and the reflective membrane. The placental membrane overlaps the basal side of the placenta and contains a layer of AM (blue), while the reflective membrane lines the intrauterine cavity, and thus, the CM (yellow) is in direct contact with the decidua. The reflective membrane is divided into three zones based on its proximity to the placenta or the cervix. These zones are termed peri-placental, mid, and cervical (outlined by black boxes). These reflective regions are used to clarify the location of sample collection when the fetal membrane is used for *ex vivo/in vitro* research. The zone of altered morphology over the cervix develops near term. Created with Motifolio.com.

Figure 3: Intrauterine and feto-maternal interface anatomy

Within the intrauterine cavity, there are a variety of maternal (i.e., myometrium and cervix) and fetal (i.e., placenta, umbilical cord, an amniotic cavity containing amniotic fluid, and the fetal membrane) derived organs that surround the fetus and contribute to pregnancy maintenance. The fetal membrane (white) lines the cavity and forms a protective barrier around the fetus throughout gestation. They are derived from multiple fetal and maternal cellular and collagen layers to form the feto-maternal interface. The AECs (orange) are connected to the basement membrane (blue) and compact layer (blue dashes) of the extracellular matrix (ECM), forming an amniotic fluid-tight barrier. Within the first layer of the ECM (i.e., the fibrous layer), AMCs (pink) migrate and interact with the collagen environment. Between the fibrous and reticular layers of the ECM is the spongy

595 layer that separates the AM and CM (purple) portions of the fetal membrane. The reticular layer
596 of the ECM contains CMCs (dark blue) that are connected to the basement membrane of the CM.
597 The multi-layer of CTCs (purple) forms the second epithelial layer of the fetal membrane and is
598 critical for immune homeostasis. The fetal chorion layer is directly connected to the maternal
599 decidua layer (light teal), forming the feto-maternal interface of the membranes. Resident immune
600 cells (yellow) predominantly reside in the decidual layer but can migrate into the CM and AM
601 layers if stimulated. Maternal blood vessels (green endothelial and red blood cells) are also
602 present in the maternal decidua, providing nutrients to the fetal membrane layers.
603

References

1. Richardson L, Menon R. Fetal membrane at the feto-maternal interface: An underappreciated and understudied intrauterine tissue. *Placenta Reprod Med*. Jul 6 2022;1doi:10.54844/prm.2022.0104
2. Bourne GL. The anatomy of the human amnion and chorion. *Proc R Soc Med*. Nov 1966;59(11 Part 1):1127-8.
3. McLaren J, Malak TM, Bell SC. Structural characteristics of term human fetal membranes prior to labour: identification of an area of altered morphology overlying the cervix. *Hum Reprod*. Jan 1999;14(1):237-41.
4. Menon R, Behnia F, Polettini J, Saade GR, Campisi J, Velarde M. Placental membrane aging and HMGB1 signaling associated with human parturition. *Aging (Albany NY)*. Feb 2016;8(2):216-30.
5. Roy A, Griffiths S. Intermediate layer contribution in placental membrane allografts. *J Tissue Eng Regen Med*. Aug 2020;14(8):1126-1135. doi:10.1002/term.3086
6. Bonvallet PP, Damaraju SM, Modi HN, et al. Biophysical Characterization of a Novel Tri-Layer Placental Allograft Membrane. *Adv Wound Care (New Rochelle)*. Feb 2022;11(2):43-55. doi:10.1089/wound.2020.1315
7. Fortunato SJ, Menon R, Swan KF, Lyden TW. Organ culture of amniochorionic membrane in vitro. *Am J Reprod Immunol*. Oct 1994;32(3):184-7.
8. Menon R, Swan KF, Lyden TW, Rote NS, Fortunato SJ. Expression of inflammatory cytokines (interleukin-1 beta and interleukin-6) in amniochorionic membranes. *Am J Obstet Gynecol*. Feb 1995;172(2 Pt 1):493-500. doi:10.1016/0002-9378(95)90562-6
9. Richardson LS, Vargas G, Brown T, et al. Discovery and Characterization of Human Amniochorionic Membrane Microfractures. *The American Journal of Pathology*. doi:https://doi.org/10.1016/j.ajpath.2017.08.019
10. Keelan JA, Khan S, Yosaatmadja F, Mitchell MD. Prevention of inflammatory activation of human gestational membranes in an ex vivo model using a pharmacological NF-kappaB inhibitor. *J Immunol*. Oct 15 2009;183(8):5270-8. doi:10.4049/jimmunol.0802660
11. Potts LC, Feng L, Seed PC, et al. Inflammatory Response of Human Gestational Membranes to Ureaplasma parvum Using a Novel Dual-Chamber Tissue Explant System. *Biol Reprod*. May 2016;94(5):119. doi:10.1095/biolreprod.115.137596
12. Sayres LC, Younge NE, Rikard B, Corcoran DL, Modliszewski JL, Hughes BL. The gestational membrane microbiome in the presence or absence of intraamniotic infection. *Am J Obstet Gynecol MFM*. Mar 2023;5(3):100837. doi:10.1016/j.ajogmf.2022.100837
13. Robinson HP. "Gestation sac" volumes as determined by sonar in the first trimester of pregnancy. *Br J Obstet Gynaecol*. Feb 1975;82(2):100-7. doi:10.1111/j.1471-0528.1975.tb02205.x
14. Huppertz B. The feto-maternal interface: setting the stage for potential immune interactions. *Semin Immunopathol*. Jun 2007;29(2):83-94. doi:10.1007/s00281-007-0070-7
15. Richardson L, Kim S, Menon R, Han A. Organ-On-Chip Technology: The Future of Feto-Maternal Interface Research? *Front Physiol*. 2020;11:715. doi:10.3389/fphys.2020.00715
16. Saji F, Samejima Y, Kamiura S, Koyama M. Dynamics of immunoglobulins at the feto-maternal interface. *Rev Reprod*. May 1999;4(2):81-9. doi:10.1530/ror.0.0040081
17. Moore RM, Mansour JM, Redline RW, Mercer BM, Moore JJ. The physiology of fetal membrane rupture: insight gained from the determination of physical properties. *Placenta*. Nov-Dec 2006;27(11-12):1037-51. doi:10.1016/j.placenta.2006.01.002

18. Radnaa E, Urrabaz-Garza R, Elrod ND, et al. Generation and characterization of human Fetal membrane and Decidual cell lines for reproductive biology experiments†. *Biol Reprod*. Dec 22 2021;doi:10.1093/biolre/ioab231
19. Lim R. Concise Review: Fetal Membranes in Regenerative Medicine: New Tricks from an Old Dog? *Stem Cells Transl Med*. Sep 2017;6(9):1767-1776. doi:10.1002/sctm.16-0447
20. Ilancheran S, Moodley Y, Manuelpillai U. Human fetal membranes: a source of stem cells for tissue regeneration and repair? *Placenta*. Jan 2009;30(1):2-10. doi:10.1016/j.placenta.2008.09.009
21. Wu D, Cao J, Xu M, et al. Fetal membrane imaging: current and future perspectives-a review. *Front Physiol*. 2024;15:1330702. doi:10.3389/fphys.2024.1330702
22. Kim YN, Jeong DH, Jeong SJ, Sung MS, Kang MS, Kim KT. Complete chorioamniotic membrane separation with fetal restrictive dermopathy in two consecutive pregnancies. *Prenat Diagn*. Apr 2007;27(4):352-5. doi:10.1002/pd.1673
23. Bromley B, Shipp TD, Benacerraf BR. Amnion-chorion separation after 17 weeks' gestation. *Obstet Gynecol*. Dec 1999;94(6):1024-6. doi:10.1016/s0029-7844(99)00457-3
24. Bibbo C, Little SE, Bsat J, Botka KA, Benson CB, Robinson JN. Chorioamniotic Separation Found on Obstetric Ultrasound and Perinatal Outcome. *AJP Rep*. Jul 2016;6(3):e337-43. doi:10.1055/s-0036-1593407
25. Khong TY, Mooney EE, Ariel I, et al. Sampling and Definitions of Placental Lesions: Amsterdam Placental Workshop Group Consensus Statement. *Arch Pathol Lab Med*. Jul 2016;140(7):698-713. doi:10.5858/arpa.2015-0225-CC
26. Matsubara S, Yamada T, Minakami H, Watanabe T, Takizawa T, Sato I. Polymorphonuclear leukocytes in the fetal membranes are activated in patients with preterm delivery: ultrastructural and enzyme-histochemical evidence. *Placenta*. Mar-Apr 1999;20(2-3):185-8. doi:10.1053/plac.1998.0366
27. Redline RW, Faye-Petersen O, Heller D, Qureshi F, Savell V, Vogler C. Amniotic infection syndrome: nosology and reproducibility of placental reaction patterns. *Pediatr Dev Pathol*. Sep-Oct 2003;6(5):435-48. doi:10.1007/s10024-003-7070-y
28. Been JV, Lievense S, Zimmermann LJ, Kramer BW, Wolfs TG. Chorioamnionitis as a risk factor for necrotizing enterocolitis: a systematic review and meta-analysis. *J Pediatr*. Feb 2013;162(2):236-42.e2. doi:10.1016/j.jpeds.2012.07.012
29. Wu YW, Colford JM, Jr. Chorioamnionitis as a risk factor for cerebral palsy: A meta-analysis. *Jama*. Sep 20 2000;284(11):1417-24. doi:10.1001/jama.284.11.1417
30. Jones MH, Corso AL, Tepper RS, et al. Chorioamnionitis and subsequent lung function in preterm infants. *PLoS One*. 2013;8(12):e81193. doi:10.1371/journal.pone.0081193
31. Lee TS, Feeney MB, Schmainda KM, Sherley JL, Prentice DA. Human Fetal Tissue from Elective Abortions in Research and Medicine: Science, Ethics, and the Law. *Issues Law Med*. Spring 2020;35(1):3-61.
32. Horii M, Touma O, Bui T, Parast MM. Modeling human trophoblast, the placental epithelium at the maternal fetal interface. *Reproduction*. Jul 2020;160(1):R1-r11. doi:10.1530/rep-19-0428
33. Genbačev O, Vićovac L, Larocque N. The role of chorionic cytotrophoblasts in the smooth chorion fusion with parietal decidua. *Placenta*. Jul 2015;36(7):716-22. doi:10.1016/j.placenta.2015.05.002
34. Shi JW, Lai ZZ, Yang HL, et al. Collagen at the maternal-fetal interface in human pregnancy. *Int J Biol Sci*. 2020;16(12):2220-2234. doi:10.7150/ijbs.45586

35. Soares MJ, Iqbal K, Kozai K. Hypoxia and Placental Development. *Birth Defects Res*. Oct 16 2017;109(17):1309-1329. doi:10.1002/bdr2.1135
36. Zhao H, Wong RJ, Stevenson DK. The Impact of Hypoxia in Early Pregnancy on Placental Cells. *Int J Mol Sci*. Sep 7 2021;22(18)doi:10.3390/ijms22189675
37. Myatt L, Sun K. Role of fetal membranes in signaling of fetal maturation and parturition. *Int J Dev Biol*. 2010;54(2-3):545-53. doi:10.1387/ijdb.082771lm
38. Hoyer D, Żebrowski J, Cysarz D, et al. Monitoring fetal maturation-objectives, techniques and indices of autonomic function. *Physiol Meas*. May 2017;38(5):R61-r88. doi:10.1088/1361-6579/aa5fca
39. King JC. Physiology of pregnancy and nutrient metabolism. *Am J Clin Nutr*. May 2000;71(5 Suppl):1218s-25s. doi:10.1093/ajcn/71.5.1218s
40. Lain KY, Catalano PM. Metabolic changes in pregnancy. *Clin Obstet Gynecol*. Dec 2007;50(4):938-48. doi:10.1097/GRF.0b013e31815a5494
41. Dutta EH, Behnia F, Boldogh I, et al. Oxidative stress damage-associated molecular signaling pathways differentiate spontaneous preterm birth and preterm premature rupture of the membranes. *Mol Hum Reprod*. Feb 2016;22(2):143-57. doi:10.1093/molehr/gav074
42. Menon R. Oxidative stress damage as a detrimental factor in preterm birth pathology. Review. *Frontiers in Immunology*. 2014;5:567.
43. Bredeson S, Papaconstantinou J, Deford JH, et al. HMGB1 promotes a p38MAPK associated non-infectious inflammatory response pathway in human fetal membranes. Research Support, Non-U.S. Gov't. *PLoS ONE [Electronic Resource]*. 2014;9(12):e113799.
44. Menon R, Boldogh I, Hawkins HK, et al. Histological evidence of oxidative stress and premature senescence in preterm premature rupture of the human fetal membranes recapitulated in vitro. Research Support, Non-U.S. Gov't. *American Journal of Pathology*. 2014;184(6):1740-51.
45. Polettini J, Behnia F, Taylor BD, Saade GR, Taylor RN, Menon R. Telomere Fragment Induced Amnion Cell Senescence: A Contributor to Parturition? *PLoS ONE [Electronic Resource]*. 2015;10(9):e0137188.
46. Behnia F, Taylor BD, Woodson M, et al. Chorioamniotic membrane senescence: a signal for parturition? *Am J Obstet Gynecol*. Sep 2015;213(3):359.e1-16. doi:10.1016/j.ajog.2015.05.041
47. Dutta EH, Behnia F, Boldogh I, et al. Oxidative stress damage-associated molecular signaling pathways differentiate spontaneous preterm birth and preterm premature rupture of the membranes. *Mol Hum Reprod*. Feb 2016;22(2):143-57. doi:10.1093/molehr/gav074
48. Menon R, Bonney EA, Condon J, Mesiano S, Taylor RN. Novel concepts on pregnancy clocks and alarms: redundancy and synergy in human parturition. *Hum Reprod Update*. Sep 2016;22(5):535-60. doi:10.1093/humupd/dmw022
49. Joyce EM, Diaz P, Tamarkin S, et al. In-vivo stretch of term human fetal membranes. *Placenta*. Feb 2016;38:57-66. doi:10.1016/j.placenta.2015.12.011
50. Song D, Shi Y. Immune system modifications and feto-maternal immune tolerance. *Chin Med J (Engl)*. 2014;127(17):3171-80.
51. El Khwad M, Stetzer B, Moore RM, et al. Term human fetal membranes have a weak zone overlying the lower uterine pole and cervix before onset of labor. *Biol Reprod*. Mar 2005;72(3):720-6. doi:10.1095/biolreprod.104.033647

52. El Khwad M, Pandey V, Stetzer B, et al. Fetal membranes from term vaginal deliveries have a zone of weakness exhibiting characteristics of apoptosis and remodeling. *J Soc Gynecol Investig*. Apr 2006;13(3):191-5. doi:10.1016/j.jsgi.2005.12.010
53. Malak TM, Bell SC. Structural characteristics of term human fetal membranes: a novel zone of extreme morphological alteration within the rupture site. *Br J Obstet Gynaecol*. May 1994;101(5):375-86.
54. Marcellin L, Schmitz T, Messaoudene M, et al. Immune Modifications in Fetal Membranes Overlying the Cervix Precede Parturition in Humans. *J Immunol*. Feb 1 2017;198(3):1345-1356. doi:10.4049/jimmunol.1601482
55. Richardson LS, Severino ME, Chauhan R, et al. Spatial transcriptomics of fetal membrane-Decidual interface reveals unique contributions by cell types in term and preterm births. *PLoS One*. 2024;19(8):e0309063. doi:10.1371/journal.pone.0309063
56. Truong N, Menon R, Richardson L. The Role of Fetal Membranes during Gestation, at Term, and Preterm Labor. *Placenta Reprod Med*. Jan 31 2023;2doi:10.54844/prm.2022.0296
57. Ganguly E, Kammala AK, Benson M, Richardson LS, Han A, Menon R. Organic Anion Transporting Polypeptide 2B1 in Human Fetal Membranes: A Novel Gatekeeper for Drug Transport During Pregnancy? *Front Pharmacol*. 2021;12:771818. doi:10.3389/fphar.2021.771818
58. Kammala AK, Lintao RCV, Vora N, et al. Expression of CYP450 enzymes in human fetal membranes and its implications in xenobiotic metabolism during pregnancy. *Life Sci*. Oct 15 2022;307:120867. doi:10.1016/j.lfs.2022.120867
59. Kammala A, Benson M, Ganguly E, et al. Fetal Membranes Contribute to Drug Transport across the Feto-Maternal Interface Utilizing the Breast Cancer Resistance Protein (BCRP). *Life (Basel)*. Jan 23 2022;12(2)doi:10.3390/life12020166
60. Kammala A, Benson M, Ganguly E, Richardson L, Menon R. Functional role and regulation of permeability-glycoprotein (P-gp) in the fetal membrane during drug transportation. *Am J Reprod Immunol*. Feb 2022;87(2):e13515. doi:10.1111/aji.13515
61. Bircher K, Ehret AE, Spiess D, et al. On the defect tolerance of fetal membranes. *Interface Focus*. Oct 6 2019;9(5):20190010. doi:10.1098/rsfs.2019.0010
62. Verbruggen SW, Oyen ML, Phillips AT, Nowlan NC. Function and failure of the fetal membrane: Modelling the mechanics of the chorion and amnion. *PLoS One*. 2017;12(3):e0171588. doi:10.1371/journal.pone.0171588
63. Malak TM, Ockleford CD, Bell SC, Dalgleish R, Bright N, Macvicar J. Confocal immunofluorescence localization of collagen types I, III, IV, V and VI and their ultrastructural organization in term human fetal membranes. *Placenta*. Jul-Aug 1993;14(4):385-406.
64. Kumar D, Moore RM, Mercer BM, Mansour JM, Redline RW, Moore JJ. The physiology of fetal membrane weakening and rupture: Insights gained from the determination of physical properties revisited. *Placenta*. Jun 2016;42:59-73. doi:10.1016/j.placenta.2016.03.015
65. Avila-González D, García-López G, Díaz-Martínez NE, et al. In Vitro Culture of Epithelial Cells from Different Anatomical Regions of the Human Amniotic Membrane. *J Vis Exp*. Nov 28 2019;(153)doi:10.3791/60551
66. Richardson, Lauren, Vargas, et al. Redefining 3Dimensional placental membrane microarchitecture using multiphoton microscopy and optical clearing. 2017;53(66-75)
67. Champliaud MF, Lunstrum GP, Rousselle P, Nishiyama T, Keene DR, Burgeson RE. Human amnion contains a novel laminin variant, laminin 7, which like laminin 6, covalently

associates with laminin 5 to promote stable epithelial-stromal attachment. *J Cell Biol*. Mar 1996;132(6):1189-98. doi:10.1083/jcb.132.6.1189
68. Sheller S, Papaconstantinou J, Urrabaz-Garza R, et al. Amnion-Epithelial-Cell-Derived Exosomes Demonstrate Physiologic State of Cell under Oxidative Stress. *PLoS One*. 2016;11(6):e0157614. doi:10.1371/journal.pone.0157614
69. Sheller-Miller S, Urrabaz-Garza R, Saade G, Menon R. Damage-Associated molecular pattern markers HMGB1 and cell-Free fetal telomere fragments in oxidative-Stressed amnion epithelial cell-Derived exosomes. *J Reprod Immunol*. Sep 2017;123:3-11. doi:10.1016/j.jri.2017.08.003
70. Radnaa E, Richardson LS, Sheller-Miller S, et al. Extracellular vesicle mediated feto-maternal HMGB1 signaling induces preterm birth. *Lab Chip*. May 18 2021;21(10):1956-1973. doi:10.1039/d0lc01323d
71. Richardson L, Menon R. Proliferative, Migratory, and Transition Properties Reveal Metastate of Human Amnion Cells. *Am J Pathol*. Jul 6 2018;doi:10.1016/j.ajpath.2018.05.019
72. Richardson LS, Radnaa E, Urrabaz-Garza R, Lavu N, Menon R. Stretch, scratch, and stress: Suppressors and supporters of senescence in human fetal membranes. *Placenta*. Jul 25 2020;99:27-34. doi:10.1016/j.placenta.2020.07.013
73. Gratacos E, Sanin-Blair J, Lewi L, et al. A histological study of fetoscopic membrane defects to document membrane healing. *Placenta*. Apr-May 2006;27(4-5):452-6. doi:10.1016/j.placenta.2005.03.008
74. Richardson L, Dixon CL, Aguilera-Aguirre L, Menon R. Oxidative Stress-Induced TGF-beta/TAB1-mediated p38MAPK activation in human amnion epithelial cells. *Biol Reprod*. Jun 11 2018;doi:10.1093/biolre/ioy135
75. Richardson L, Jeong S, Kim S, Han A, Menon R. Amnion membrane organ-on-chip: an innovative approach to study cellular interactions. *Faseb j*. Apr 30 2019:fj201900020RR. doi:10.1096/fj.201900020RR
76. Richardson LS, Taylor RN, Menon R. Reversible EMT and MET mediate amnion remodeling during pregnancy and labor. *Sci Signal*. Feb 11 2020;13(618)doi:10.1126/scisignal.aay1486
77. Alcaraz A, Mrowiec A, Insausti CL, et al. Autocrine TGF-beta induces epithelial to mesenchymal transition in human amniotic epithelial cells. *Cell Transplant*. 2013;22(8):1351-67. doi:10.3727/096368912x657387
78. Roy R, Kukucka M, Messroghli D, et al. Epithelial-to-Mesenchymal Transition Enhances the Cardioprotective Capacity of Human Amniotic Epithelial Cells. *Cell Transplant*. 2015;24(6):985-1002. doi:10.3727/096368913x675151
79. Janzen. Carla Chaudhuri G. The Role of Epithelial to Mesenchymal Transition in Human Amniotic Membrane Rupture. *The Journal of Clinical Endocrinology and Metabolism*. 2016;
80. Menon R, Richardson LS. Preterm prelabor rupture of the membranes: A disease of the fetal membranes. *Semin Perinatol*. Nov 2017;41(7):409-419. doi:10.1053/j.semperi.2017.07.012
81. Miki T, Lehmann T, Cai H, Stolz DB, Strom SC. Stem cell characteristics of amniotic epithelial cells. *Stem Cells*. Nov-Dec 2005;23(10):1549-59. doi:10.1634/stemcells.2004-0357
82. Marongiu F, Gramignoli R, Dorko K, et al. Hepatic differentiation of amniotic epithelial cells. *Hepatology*. May 2011;53(5):1719-29. doi:10.1002/hep.24255
83. Miki T. Stem cell characteristics and the therapeutic potential of amniotic epithelial cells. *Am J Reprod Immunol*. Oct 2018;80(4):e13003. doi:10.1111/aji.13003

84. Weidinger A, Poženel L, Wolbank S, Banerjee A. Sub-Regional Differences of the Human Amniotic Membrane and Their Potential Impact on Tissue Regeneration Application. *Front Bioeng Biotechnol*. 2020;8:613804. doi:10.3389/fbioe.2020.613804
85. Whittle WL, Gibb W, Challis JR. The characterization of human amnion epithelial and mesenchymal cells: the cellular expression, activity and glucocorticoid regulation of prostaglandin output. *Placenta*. May 2000;21(4):394-401. doi:10.1053/plac.1999.0482
86. Miosge N, Holzhausen S, Zelent C, Sprysch P, Herken R. Nidogen-1 and nidogen-2 are found in basement membranes during human embryonic development. *Histochem J*. Sep-Oct 2001;33(9-10):523-30. doi:10.1023/a:1014995523521
87. Tamiolakis D, Papadopoulos N, Anastasiadis P, et al. Expression of laminin, type IV collagen and fibronectin molecules is related to embryonal skin and epidermal appendage morphogenesis. *Clin Exp Obstet Gynecol*. 2001;28(3):179-82.
88. Menon R, Richardson LS, Lappas M. Fetal membrane architecture, aging and inflammation in pregnancy and parturition. *Placenta*. Nov 10 2018;doi:10.1016/j.placenta.2018.11.003
89. Jacobs SO, Sheller-Miller S, Richardson LS, Urrabaz-Garza R, Radnaa E, Menon R. Characterizing the immune cell population in the human fetal membrane. *Am J Reprod Immunol*. May 2021;85(5):e13368. doi:10.1111/aji.13368
90. Gomez-Lopez N, Garcia-Flores V, Chin PY, et al. Macrophages exert homeostatic actions in pregnancy to protect against preterm birth and fetal inflammatory injury. *JCI Insight*. Oct 8 2021;6(19)doi:10.1172/jci.insight.146089
91. Hamilton S, Oomomian Y, Stephen G, et al. Macrophages infiltrate the human and rat decidua during term and preterm labor: evidence that decidual inflammation precedes labor. *Biol Reprod*. Feb 2012;86(2):39. doi:10.1095/biolreprod.111.095505
92. Tong M, Smith AH, Abrahams VM. Activated Neutrophils Propagate Fetal Membrane Inflammation and Weakening through ERK and Neutrophil Extracellular Trap-Induced TLR-9 Signaling. *J Immunol*. Mar 1 2021;206(5):1039-1045. doi:10.4049/jimmunol.2001268
93. Zhang C, Cao J, Xu M, Wu D, Li W, Chang Y. The role of neutrophils in chorioamnionitis. *Front Immunol*. 2023;14:1198831. doi:10.3389/fimmu.2023.1198831
94. McParland PC, Taylor DJ, Bell SC. Myofibroblast differentiation in the connective tissues of the amnion and chorion of term human fetal membranes-implications for fetal membrane rupture and labour. *Placenta*. Jan 2000;21(1):44-53. doi:10.1053/plac.1999.0439
95. Farhadihosseinabadi B, Farahani M, Tayebi T, et al. Amniotic membrane and its epithelial and mesenchymal stem cells as an appropriate source for skin tissue engineering and regenerative medicine. *Artif Cells Nanomed Biotechnol*. 2018;46(sup2):431-440. doi:10.1080/21691401.2018.1458730
96. Tago Y, Kobayashi C, Ogura M, et al. Human amnion-derived mesenchymal stem cells attenuate xenogeneic graft-versus-host disease by preventing T cell activation and proliferation. *Sci Rep*. Jan 28 2021;11(1):2406. doi:10.1038/s41598-021-81916-y
97. Mogami H, Hari Kishore A, Akgul Y, Word RA. Healing of Preterm Ruptured Fetal Membranes. *Sci Rep*. Oct 13 2017;7(1):13139. doi:10.1038/s41598-017-13296-1
98. Menon R. Epithelial to mesenchymal transition (EMT) of feto-maternal reproductive tissues generates inflammation: a detrimental factor for preterm birth. *BMB Rep*. 2022:370-379. vol. 8.

874 99. Moore RM, Silver RJ, Moore JJ. Physiological apoptotic agents have different effects
875 upon human amnion epithelial and mesenchymal cells. *Placenta*. Feb-Mar 2003;24(2-3):173-80.
876 doi:10.1053/plac.2002.0886
877 100. Presicce P, Cappelletti M, Morselli M, et al. Amnion responses to intrauterine
878 inflammation and effects of inhibition of TNF signaling in preterm Rhesus macaque. *iScience*.
879 Nov 17 2023;26(11):108118. doi:10.1016/j.isci.2023.108118
880 101. Suvakov S, Richards C, Nikolic V, et al. Emerging Therapeutic Potential of
881 Mesenchymal Stem/Stromal Cells in Preeclampsia. *Curr Hypertens Rep*. Apr 14 2020;22(5):37.
882 doi:10.1007/s11906-020-1034-8
883 102. Aneman I, Pienaar D, Suvakov S, Simic TP, Garovic VD, McClements L. Mechanisms
884 of Key Innate Immune Cells in Early- and Late-Onset Preeclampsia. *Front Immunol*.
885 2020;11:1864. doi:10.3389/fimmu.2020.01864
886 103. Magatti M, Vertua E, Cargnoni A, Silini A, Parolini O. The Immunomodulatory
887 Properties of Amniotic Cells: The Two Sides of the Coin. *Cell Transplant*. Jan 2018;27(1):31-44.
888 doi:10.1177/0963689717742819
889 104. Méhats C, Schmitz T, Marcellin L, Breuiller-Fouché M. [Biochemistry of fetal
890 membranes rupture]. *Gynecol Obstet Fertil*. Jun 2011;39(6):365-9. Biochimie de la rupture des
891 membranes fœtales. doi:10.1016/j.gyobfe.2011.04.006
892 105. Strauss JF, 3rd. Extracellular matrix dynamics and fetal membrane rupture. *Reprod Sci*.
893 Feb 2013;20(2):140-53. doi:10.1177/1933719111424454
894 106. Joyce EM, Moore JJ, Sacks MS. Biomechanics of the fetal membrane prior to mechanical
895 failure: review and implications. *Eur J Obstet Gynecol Reprod Biol*. May 2009;144 Suppl
896 1:S121-7. doi:10.1016/j.ejogrb.2009.02.014
897 107. Menon R, Radnaa E, Behnia F, Urrabaz-Garza R. Isolation and characterization human
898 chorion membrane trophoblast and mesenchymal cells. *Placenta*. Nov 2020;101:139-146.
899 doi:10.1016/j.placenta.2020.09.017
900 108. Bush B, Richardson LS, Radnaa E, et al. Do progesterone receptor membrane
901 components (PGRMC)s play a role in the chorions refractoriness to epithelial-to-mesenchymal
902 transition (EMT)? *J Reprod Immunol*. Feb 21 2025;169:104463. doi:10.1016/j.jri.2025.104463
903 109. Fariha MM, Chua KH, Tan GC, Tan AE, Hayati AR. Human chorion-derived stem cells:
904 changes in stem cell properties during serial passage. *Cytotherapy*. May 2011;13(5):582-93.
905 doi:10.3109/14653249.2010.549121
906 110. Apps R, Murphy SP, Fernando R, Gardner L, Ahad T, Moffett A. Human leucocyte
907 antigen (HLA) expression of primary trophoblast cells and placental cell lines, determined using
908 single antigen beads to characterize allotype specificities of anti-HLA antibodies. *Immunology*.
909 May 2009;127(1):26-39. doi:10.1111/j.1365-2567.2008.03019.x
910 111. Le Bouteiller P. HLA-G in human early pregnancy: control of uterine immune cell
911 activation and likely vascular remodeling. *Biomed J*. Jan-Feb 2015;38(1):32-8.
912 doi:10.4103/2319-4170.131376
913 112. Hiden U, Wadsack C, Prutsch N, et al. The first trimester human trophoblast cell line
914 ACH-3P: a novel tool to study autocrine/paracrine regulatory loops of human trophoblast
915 subpopulations--TNF-alpha stimulates MMP15 expression. *BMC Dev Biol*. Dec 19 2007;7:137.
916 doi:10.1186/1471-213x-7-137
917 113. Vidal MS, Jr., Radnaa E, Vora N, et al. Establishment and comparison of human term
918 placenta-derived trophoblast cells†. *Biol Reprod*. May 9 2024;110(5):950-970.
919 doi:10.1093/biolre/ioae026

114. Choudhury J, Richardson LS, Urrabaz-Garza R, Jacob J, Kammala AK, Menon R. Chorionic trophoblast cells demonstrate functionally different phenotypes from placental trophoblasts†. *Biol Reprod*. Mar 16 2025;112(3):530-539. doi:10.1093/biolre/ioaf003
115. Ryan C. V. Lintao LR, Leslie Michelle M. Dalmacio, Arum Han, Ramkumar Menon. Modeling Infection-Induced Compromise to Choriodecidual Interface Leading to Immune Cell Infiltration Using a Microphysiological System. *Society of Reproductive Investigation Abstract Book*. 2023;
116. Lintao RCV, Richardson LS, Kammala AK, et al. PGRMC2 and HLA-G regulate immune homeostasis in a microphysiological model of human maternal-fetal membrane interface. *Commun Biol*. Aug 23 2024;7(1):1041. doi:10.1038/s42003-024-06740-2
117. Goldman B, Radnaa E, Kechichian T, Menon R. Silencing P38 MAPK reduces cellular senescence in human fetal chorion trophoblast cells. *Am J Reprod Immunol*. Jan 2023;89(1):e13648. doi:10.1111/aji.13648
118. Yang L, Semmes EC, Ovies C, et al. Innate immune signaling in trophoblast and decidua organoids defines differential antiviral defenses at the maternal-fetal interface. *Elife*. Aug 17 2022;11doi:10.7554/eLife.79794
119. Yeh IT, O'Connor DM, Kurman RJ. Vacuolated cytotrophoblast: a subpopulation of trophoblast in the chorion laeve. *Placenta*. Sep-Oct 1989;10(5):429-38. doi:10.1016/0143-4004(89)90053-2
120. Hackmon R, Pinnaduwage L, Zhang J, Lye SJ, Geraghty DE, Dunk CE. Definitive class I human leukocyte antigen expression in gestational placentation: HLA-F, HLA-E, HLA-C, and HLA-G in extravillous trophoblast invasion on placentation, pregnancy, and parturition. *Am J Reprod Immunol*. Jun 2017;77(6)doi:10.1111/aji.12643
121. Zaga-Clavellina V, Flores-Espinosa P, Pineda-Torres M, et al. Tissue-specific IL-10 secretion profile from term human fetal membranes stimulated with pathogenic microorganisms associated with preterm labor in a two-compartment tissue culture system. *J Matern Fetal Neonatal Med*. Sep 2014;27(13):1320-7. doi:10.3109/14767058.2013.857397
122. Zaga-Clavellina V, Garcia-Lopez G, Flores-Herrera H, et al. In vitro secretion profiles of interleukin (IL)-1beta, IL-6, IL-8, IL-10, and TNF alpha after selective infection with Escherichia coli in human fetal membranes. *Reprod Biol Endocrinol*. Dec 13 2007;5:46. doi:10.1186/1477-7827-5-46

953 Table 1
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Term	Definition		
Fetal membrane	The fetal membrane, comprised of the amnion and chorion membranes, is the fetal component of the feto-maternal interface (i.e., fetal membrane-decidua parietalis) that has no vascular connection to the fetus.		
Cellular components	**Membrane**	**Cell type**	**Abbreviations**
	Amnion membrane	Amnion epithelial cells	AEC
		Amnion mesenchymal cells	AMC
	Chorion membrane	Chorion mesenchymal cells	CMC
		Chorion trophoblast cells	CTC

955 Table 2

Term	Definition		
Fetal membrane feto-maternal interface	The fetal membrane feto-maternal interface is comprised of the fetal membrane (fetal component) and decidua parietalis (maternal component) that lines the intrauterine cavity and provides essential mechanical, immune, hormonal, and transport support to maintain pregnancy, while additionally being the main driver of labor signaling at term or preterm.		
Cellular components	**Membrane**	**Cell type**	**Abbreviations**
	Amnion membrane	Amnion epithelial cells	AEC
		Amnion mesenchymal cells	AMC
Choriodecidua membrane	Chorion membrane	Chorion mesenchymal cells	CMC
		Chorion trophoblast cells	CTC
	Decidua	Decidua parietalis	DECP
		Decidual vasculature	
		Decidual immune cells	

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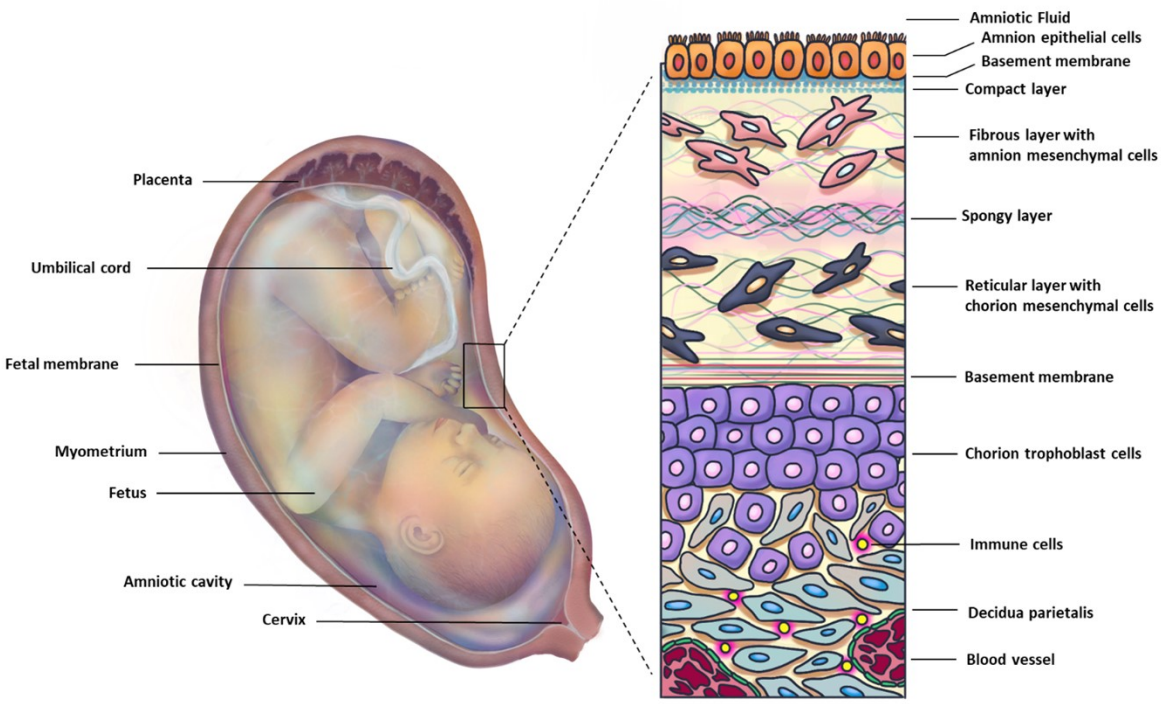

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959 Figure 3

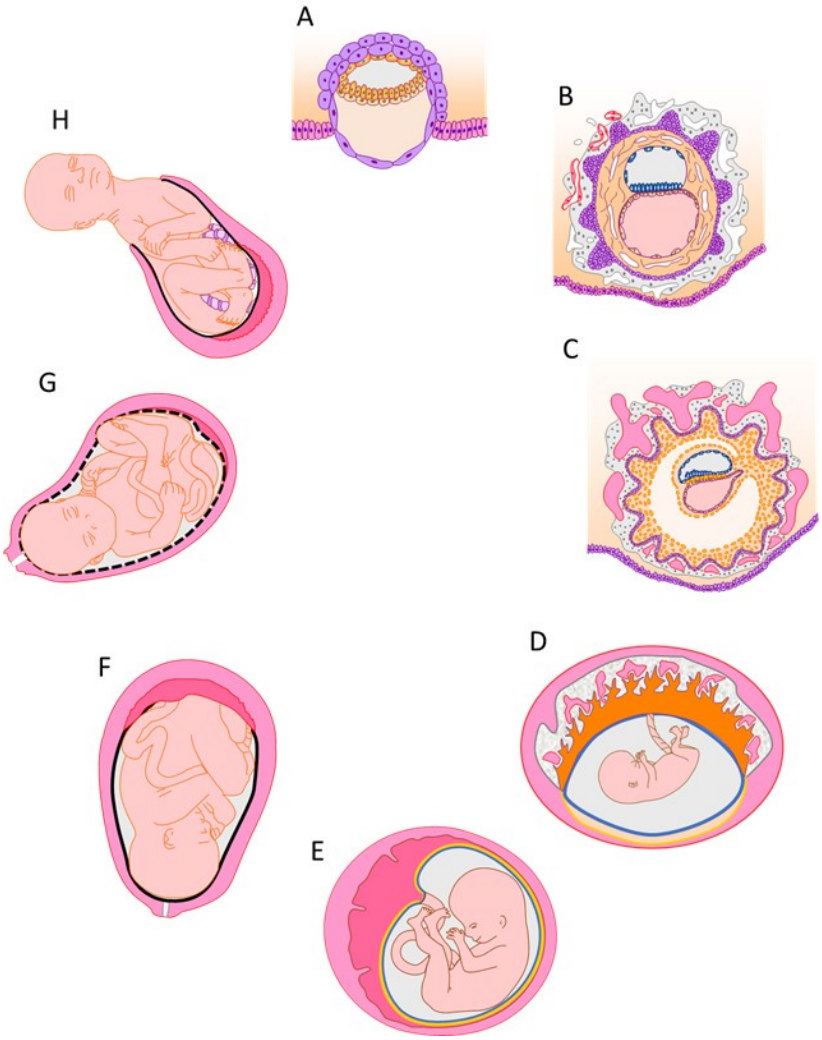
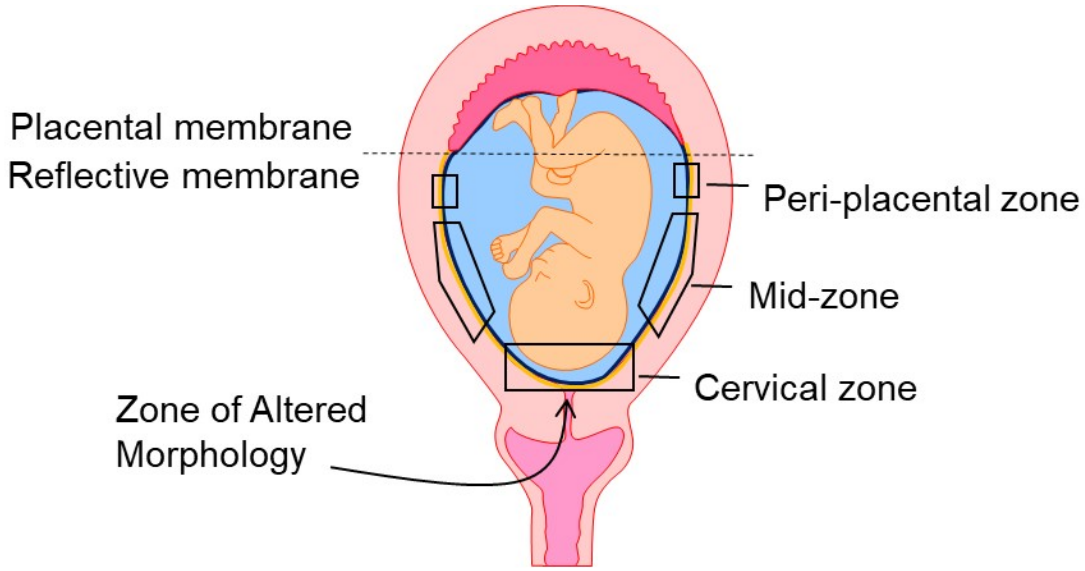


Figure 2



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967 Figure 1