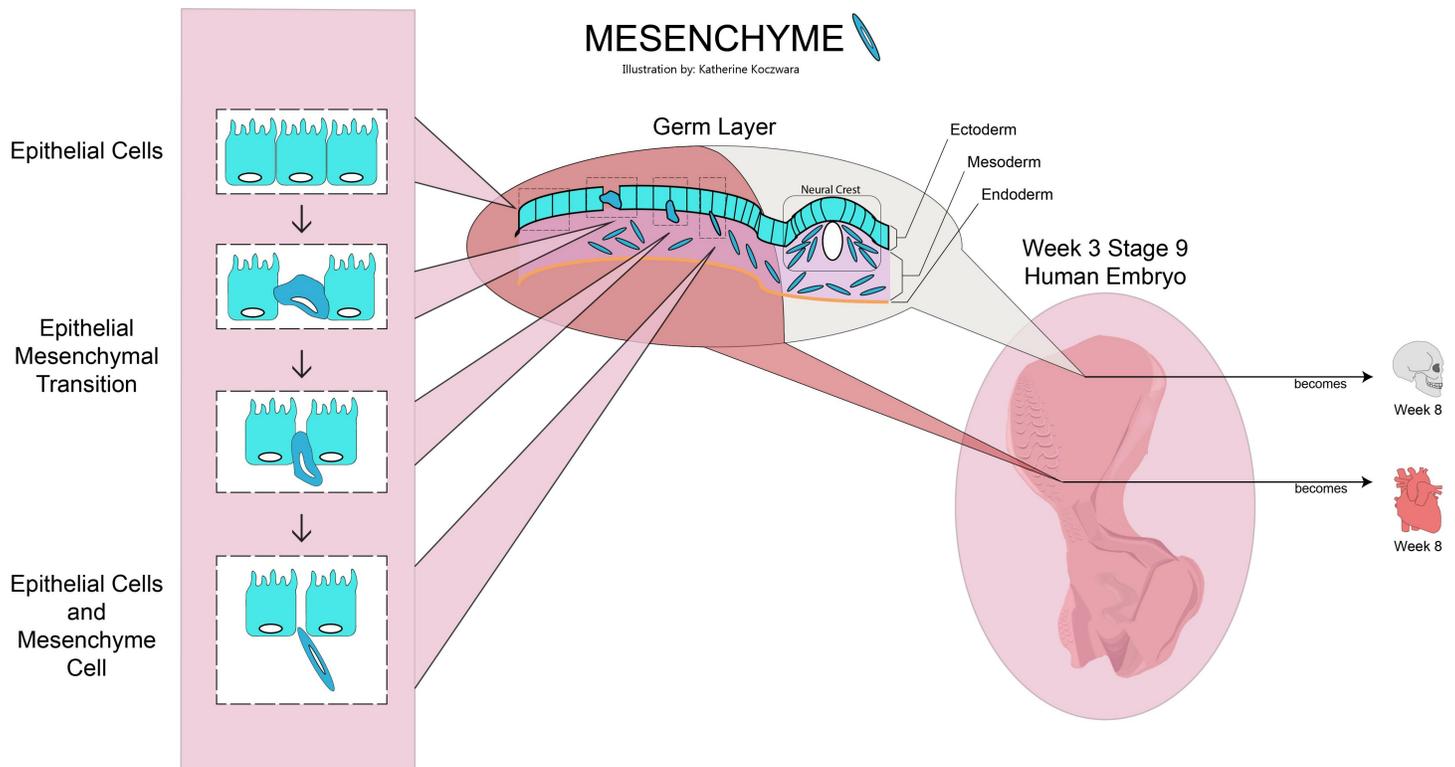


Mesenchyme ^[1]

By: MacCord, Kate Keywords: [Tissue](#) ^[2] [Developmental mechanics](#) ^[3]



Editor's note: Katherine Koczvara created the above image for this article. You can find the full image and all relevant information [here](#) ^[4].

Mesenchyme is a type of animal tissue comprised of loose cells embedded in a mesh of proteins and fluid, called the extracellular matrix. The loose, fluid nature of [mesenchyme](#) ^[5] allows its cells to migrate easily and play a crucial role in the origin and development of morphological structures during the embryonic and fetal stages of animal life. Mesenchyme directly gives rise to most of the body's connective tissues, from bones and cartilage to the lymphatic and circulatory systems. Furthermore, the interactions between [mesenchyme](#) ^[5] and another tissue type, [epithelium](#) ^[6], help to form nearly every organ in the body.

Although most [mesenchyme](#) ^[5] derives from the middle embryological germ layer, the [mesoderm](#) ^[7], the outer germ layer known as the [ectoderm](#) ^[8] also produces a small amount of [mesenchyme](#) ^[5] from a specialized structure called the [neural crest](#) ^[9]. Mesenchyme is generally a transitive tissue; while crucial to morphogenesis during development, little can be found in adult organisms. The exception is mesenchymal [stem cells](#) ^[10], which are found in small quantities in bone marrow, fat, muscles, and the dental pulp of baby teeth.

Mesenchyme forms early in embryonic life. As the primary [germ layers](#) ^[11] develop during [gastrulation](#) ^[12], cell populations lose their adhesive properties and detach from sheets of connected cells, called epithelia. This process, known as an epithelial-mesenchymal transition, gives rise to the mesodermal layer of the embryo, and occurs many times throughout development of higher vertebrates. Epithelial-mesenchymal transitions play key roles in cellular proliferation and tissue repair, and are indicated in many pathological processes, including the development of excess fibrous connective tissue (fibrosis) and the spread of disease between organs (metastasis). The reverse process, the mesenchymal-epithelial transition, occurs when the loose cells of [mesenchyme](#) ^[5] develop adhesive properties and arrange themselves into an organized sheet. This type of transition is also common during development, and is involved in kidney formation.

The concept of [mesenchyme](#) ^[5] has a long history, which has shaped our modern understanding of the tissue in many ways. In 1879, Charles Sedgwick Minot, an anatomist based out of [Harvard Medical School](#) ^[13] in Boston, Massachusetts, first described what he termed mesamoeboids, the cellular portion of what would soon come to be recognized as [mesenchyme](#) ^[5]. Minot found these cells in the context of histological studies of [mesoderm](#) ^[7]. He understood the loose, mobile cells of [mesenchyme](#) ^[5] as primitive representatives of the [mesoderm](#) ^[7], but did not consider these cells as a type of tissue. Two years after Minot's recognition of mesamoeboids, Oscar and Richard Hertwig, two brothers and doctoral students of [Ernst Haeckel](#) ^[14] at the [University of Jena](#) ^[15] in Jena, Germany, coined the term *mesenchyma* in their publication *Die Coelomtheorie. Versucheiner Erklärung des mittleren Keimblattes* (*Coelom Theory: An attempt to explain the middle germ layer*), and they used it to describe the type of tissue that was comprised of the amoeboid cells that Minot had

portrayed. The Hertwig brothers established that [mesenchyme](#)^[5] originates from [mesoderm](#)^[7], and they situated this relationship in the broader context of the development of the coelom, a fluid-filled body cavity. Their *Die Coelomtheorie* also advanced the idea that the three [germ layers](#)^[11] maintain separate identities and develop distinct tissues and organs, a concept known as germ-layer theory.

In 1888, N. Katschenko suggested that [mesenchyme](#)^[5] found in the region of the head originated from the [neural crest](#)^[9], an ectodermal derivative, effectively expanding the tissue's origins beyond that of a single germ layer. Five years later, [Harvard Medical School](#)^[13] doctoral student Julia Platt, in Cambridge, Massachusetts, provided evidence based on her studies of *Necturus maculosus* embryos, a type of [aquatic salamander](#)^[16], that the [mesenchyme](#)^[5] that developed into the skeletal elements of the branchial arches derived from [ectoderm](#)^[8]. Platt's 1893 publication, "Ectodermic Origin of the Cartilages of the Head," and her conclusions about the ectodermal origins of [mesenchyme](#)^[5] in the head region, and thus skeletal and cartilaginous tissues of the skull, went against the entrenched germ-layer theory and the mesodermal origins of [mesenchyme](#)^[5] advocated by the Hertwig brothers in their 1881 *Die Coelomtheorie*. Platt's findings were rejected by many established embryologists who upheld the theory of integrity of the [germ layers](#)^[11].

In the years following Platt's publication, several other embryologists identified ectodermal origins for [mesenchyme](#)^[5] and its derivative skeletal elements in the head region of [fish](#)^[17] and [birds](#)^[18]. It was not until nearly thirty years after Platt's initial publication that independent studies demonstrated a major ectodermal contribution to [mesenchyme](#)^[5]. In 1921, while investigating the limits of [neural crest](#)^[9] in the formation of cerebral ganglia in *Urodeles*, commonly known as [salamanders](#)^[19], Francis Landacre at the Ohio State University in Columbus, Ohio, showed the ectodermal origin of cranial [mesenchyme](#)^[5]. Landacre's work was followed by other studies which further concluded an ectodermal component of [mesenchyme](#)^[5]. The idea that [mesenchyme](#)^[5] in the cranial region derived from [neural crest](#)^[9] was finally abrogated in the 1940s by the independent research of embryologists Sven Hörstadius at Uppsala University in Uppsala, Sweden, and Gavin de Beer at the [University College](#)^[20] in London, England.

Soon after the debate over ectodermal [mesenchyme](#)^[5] ended, research on the role of [mesenchyme](#)^[5] during development erupted. By the 1960s, embryologists realized that [mesenchyme](#)^[5], in combination with [epithelium](#)^[6], played an essential role in the morphogenesis of many organs during embryonic and fetal development. Epithelio-mesenchymal interactions form nearly every organ of the body, from hair and sweat glands to the digestive tract, kidneys, and teeth.

In 1969, Edward Kollar and Grace Baird from the [University of Chicago](#)^[21] in Chicago, Illinois, designed a series of experiments to understand how [mesenchyme](#)^[5] and [epithelium](#)^[6] work together when cells differentiate, and how the two tissues combine to make embryonic structures. Their research drew on a long history of investigating tissue interactions during morphogenesis, and especially on the 1954 work of John Cairn at the University of Texas in Austin, Texas, and John Saunders, at [Marquette University](#)^[22] in Milwaukee, Wisconsin. Cairn and Saunders recognized that [mesoderm](#)^[7] holds the inductive stimulus within interactions between [mesoderm](#)^[7] and [epithelium](#)^[6]. Using tooth development as a model system, Kollar and Baird provided evidence that [mesenchyme](#)^[5] drives both [induction](#)^[23] and [differentiation](#)^[24] during epithelio-mesenchymal interactions, and is thus the tissue that confers structural specificity during these interactions, or determines what structure will form. Kollar and Baird published their findings in 1969 in "The Influence of the Dental Papilla on the Development of Tooth Shape in Embryonic Mouse Tooth Germs," and in 1970 in "Tissue Interactions in Embryonic Mouse Tooth Germs."

Shortly before Kollar and Baird published their account of epithelio-mesenchymal interactions, Alexander Friedenstein discovered mesenchymal [stem cells](#)^[10] in [mice](#)^[25] (*Mus musculus*). In publications from 1966 through 1987, Friedenstein, in conjunction with his peers at the University of Moscow in Moscow, Russia, provided evidence from transplantation experiments that [stem cells](#)^[10] taken from bone marrow can differentiate into mesenchymal tissues, such as fat, bone, and cartilage. These cells came to be known as mesenchymal [stem cells](#)^[10], and have subsequently been found in blood, cartilaginous, skeletal, and fatty tissues. Mesenchymal [stem cells](#)^[10] provide a reservoir of reserve cells that the body can use for normal or pathological tissue regeneration and repair. The abilities of mesenchymal [stem cells](#)^[10] to differentiate into different tissues, known as cell potency, has been a cause of debate in recent years, leading researchers to question whether these cells are truly multipotent, and can give rise to multiple cell types. The potential [multipotency](#)^[26] of mesenchymal [stem cells](#)^[10], in conjunction with their presence in adult organisms, has made them an attractive alternative to [embryonic stem cells](#)^[27] for research on tissue regeneration.

Current research on [mesenchyme](#)^[5] spreads across many biological fields. The focus of [mesenchyme](#)^[5] research, however, divides between two general interests: the role and expression of [mesenchyme](#)^[5]-specific [genes](#)^[28] during development, including pathological processes, and the locations and capabilities of mesenchymal [stem cells](#)^[10]. While some still investigate [mesenchyme](#)^[5] at the tissue level, the two current focuses reflect a trend towards the analysis and understanding of molecular-level mechanisms by which [mesenchyme](#)^[5] functions during development. Beginning with the definition by the Hertwig brothers, [mesenchyme](#)^[5] research has moved from anatomical investigations in developing embryos, to cellular contributions for organ formation and tissue level interactions, and now to the genetic mechanisms of development and tissue repair.

There is historical continuity within [mesenchyme](#)^[5] research, but there remain vestiges of the controversy that surrounded this tissue in the late nineteenth century. In her 1893 article in which she introduced the biological community to the ectodermal origins of [mesenchyme](#)^[5] in the head region, Julia Platt also suggested a change in terminology. Mesenchyme of ectodermal origins she specified by the term mesectoderm, while mesodermal [mesenchyme](#)^[5] she called mesendoderm. The medical community, especially pathologists, still employs this distinction between mesenchymal sources, only referring to a tissue as [mesenchyme](#)^[5] if it is derived from [mesoderm](#)^[7]. Pathologists maintain the distinction because the mesenchymal source determines the type and behavior of a disease. Meanwhile, developmental biologists tend to recognize [mesenchyme](#)^[5] by a single name, regardless of source.

The study of [mesenchyme](#)^[5] has a long history, from [mesenchyme](#)^[5]'s recognition within the framework of germ-layer theory, to controversy about [mesenchyme](#)^[5]'s origins, to uncovering [mesenchyme](#)^[5]'s roles in morphogenesis and its capacity to produce [stem](#)

cells^[10]. This history is in part due to the fact that [mesenchyme](#)^[5] is crucial for embryonic growth and development, as well as maintenance of connective tissues in adulthood. The loose nature of cells within [mesenchyme](#)^[5] allows the tissue to move and to be molded. During [embryogenesis](#)^[29], [mesenchyme](#)^[5] gives rise to the body's connective tissues, from cartilage and bone to fat, muscle, and the circulatory system. Meanwhile, nearly every organ forms through epithelio-mesenchymal interactions, in which [mesenchyme](#)^[5] provides both the inductive stimulus and determines the path of [differentiation](#)^[24]. Although little [mesenchyme](#)^[5] remains in the body during adulthood, the final remnants of this tissue, [mesenchymal stem cells](#)^[10], allow connective tissues to repair and regenerate.

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Subject

[Mesenchyme](#)^[35] [Gastrulation](#)^[36] [Minot, Charles Sedgwick, 1852-1914](#)^[37] [Haeckel, Ernst, 1834-1919](#)^[38] [Stem cells](#)^[39] [Mesenchymal stem cells](#)^[40] [Embryological development](#)^[41] [Embryos](#)^[42] [Cell differentiation](#)^[43] [Mesoderm](#)^[44]

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