Leo Loeb (1869-1959) [1]


Leo Loeb [6] developed an experimental approach to studying cancer and pioneered techniques for tissue culture and in vitro [7] tissue transplantation which impacted early-to-mid twentieth century experimental embryology [8]. Loeb received his medical degree from the University of Zurich [9] in 1897. As part of his doctorate, he completed a thesis on the outcomes of tissue transplantation in guinea pigs. Loeb's thesis inspired a life-long interest in tissue transplantation. His research culminated in greater than 400 publications, including a book called The Biological Basis of Individuality [10], in which he demonstrated the potential immortality of certain mammalian tissues.

Loeb was born in Mayen, Prussia, on 21 September 1869 to Barbara and Benedict Loeb. Loeb's mother died when he was three and his father when he was six, leaving Loeb and his older brother Jacques Loeb [11] orphaned. After their parents died, the brothers lived with their maternal grandfather in Trier, Prussia. When Loeb was ten, they moved to Berlin, Prussia to live with a maternal aunt and uncle.

Beginning in 1889, Loeb briefly attended several universities in order to study natural sciences with a variety of professors. Loeb's universities included the University of Freiburg [12], in Freiburg, Prussia, where he studied under August Weismann [13], and the University of Basel [14] in Basel, Switzerland, where he studied with Gustav von Bunge [15] and Johannes Friedrich Miescher [16]. Eventually, Loeb moved to Zurich, Switzerland, where he studied medicine at the University of Zurich [9] from 1890 until 1892. He completed his clinical work at the University of Edinburgh [17], in Edinburgh, Scotland, and the medical school of London Hospital [18], in London, England. Loeb returned to the University of Zurich [9] in 1895 to complete his medical studies and the thesis required to earn his MD. He studied and completed his thesis in 1897 under the tutelage of pathologist Hugo Ribbert [19]. For his thesis, Ribbert assigned Loeb the task of determining the outcome of transplanting the skin of a white guinea pig [20] onto a black guinea pig [20], and vice versa. Loeb's thesis, titled Über Transplantation von weisser Haut auf einen Defekt in schwarzer Haut und umgekehrt am Ohr des Meerschweinchens [21]? (On the Transplantation of a Defect in Black Skin onto White Skin and vice versa on the Ear of a Guinea pig [22]) was published in1897.

After completing his MD, Loeb moved to Chicago, Illinois where his brother, Jacques, was a professor of physiology at the University of Chicago [23]. In 1897, Loeb rented a room behind a drug store where he briefly tried to establish his own medical practice before becoming a physician in John Dewey's experimental school [24] and adjunct professor of pathology at the Rush Medical College [25].

Loeb used the rented room to perform experimental research on skin transplantation and healing in guinea pigs. He further developed his research as a visiting scholar in the department of pathology at Johns Hopkins University School of Medicine [26], in Baltimore,
Maryland, where he met Georgiana Sands, whom he married on 3 January 1922. During the summers, Loeb worked at the Marine Biological Laboratory (MBL) in Woods Hole, Massachusetts. He spent a year as a research fellow at McGill University, in Montreal, Canada, and became an assistant professor of experimental pathology at the University of Pennsylvania, in Philadelphia, Pennsylvania, in 1904. In 1910, Loeb moved to St. Louis, Missouri, in order to become the director of research at Barnard Skin and Cancer Hospital. He held this post until 1915, when he accepted the position of professor of comparative pathology at Washington University School of Medicine, in the same city. Loeb performed research in the department until he retired from the university in 1941, and he maintained his summer research at the MBL until 1950.

One focus of Loeb's research was the outcome of transplanting normal and cancerous tissue, and the body's reactions and healing processes after those transplantations. Loeb addressed these interests in his 1901 article, "On the Growth of Epithelium". This research focused on the wound healing process in guinea pigs, specifically how epithelium grows in the coagulated blood of healing wounds. Epithelium is a type of animal cell that lines glands, hollow organs, and the surface of the body. One side of epithelial tissue is unbound while the other side attaches to a thin layer of connective tissue, a type of animal tissue that protects and supports other organs and tissues.

Loeb's experiments also focused on transplanting tumorous tissues. In 1901, Loeb published "On Transplantation of Tumors", where he hypothesized that tumor cells developed under certain conditions might be immortal like germ cells, the cells that are involved in reproduction. In this set of experiments, Loeb transplanted the same tumorous tissue throughout many consecutive generations of white rats. He observed that these somatic cells seemed to be able to outlast the life of the original organism because while the original source of the cells died, the tumorous cells could be reused for many different generations.

Through his experiments, Loeb explored the effects of separating epithelial tissue from connective tissue in order to study the reactions and growth of each. He investigated the relationship between epithelial and connective tissues in two ways. First, he observed the reactions of epithelial tissue in the presence of agar, a gelatinous substance used to make culture media, which he had placed in the guinea pigs' wounds. Second, he cut a piece of guinea pig skin and placed it in coagulated blood serum, then transplanted it into a live animal. From these experiments, Loeb concluded that individual epithelial cell masses continued to grow even when no connective tissue, in this case blood, was present. He proposed applying these methods to isolate other types of cells in order to study reactions of isolated tissue. This set of experiments helped to develop some of the earliest in vitro tissue transplantation techniques and demonstrate that tissue could be cultured.

In addition to tissue transplantation, Loeb also conducted research on the corpus luteum, a transient structure of the ovary. In 1906, Loeb published "The Formation of the Corpus Luteum in the Guinea Pig" in which he detailed his observations of guinea pig ovaries at consecutive time intervals after copulation. The purpose of his research was to determine what happened at each stage of corpus luteum formation, which he felt bore a strong resemblance to the processes seen in both wound healing and tumor growth. Loeb examined
sixty ovaries from thirty guinea pigs by creating serial sections and detailed his observations from each period leading up to the formation of the **corpus luteum** [35].

In 1945, Loeb published his book, *The Biological Basis of Individuality* [10], which detailed the organismal differences that define individuality of organisms. Loeb outlined two principle methods by which to study the differences between organisms: through transplantation and through studying blood serum and other bodily fluids. In this book, he asserted that there were properties that make each individual distinct. This distinctiveness resulted from bodies being composed of combinations of many tissues and organs each with their own unique functions and ways of metabolizing. Loeb also concluded that some properties were common to all parts of an organism. The common properties scientists could study by examining how the cells and tissues of one organism reacted to the cells and tissues of another organism.

Loeb received many awards throughout his lifetime for his research on cancer and healing. In 1935, he received the John Phillips Memorial Prize, a prize awarded annually by the American College of Physicians, for his research on the thyroid-stimulating hormone [37] in the pituitary gland [38]. In the same year, Loeb’s students at Washington University [39] in St. Louis established an annual lectureship in his name. In 1941, in recognition of his work on hormones [40] and the aging process, he delivered a lecture at the Harvey Society [41] at The Rockefeller University [42] in New York, New York. The Harvey Society [41] lecture series is a distinguished circuit in which each year seven of the nation’s most prestigious scientists are asked to give a presentation. Loeb also received an honorary doctorate from Washington University [39] in St. Louis in 1948. In 1950, a special issue of the American Medical Association’s *Archives of Pathology* containing a list of 400 of his writings was dedicated to him. Loeb also served as a leader and member in many professional organizations, including president of the Association for Cancer Research in 1911, president of the American Association of Pathologists and Bacteriologists in 1914, and an officeholder and member of the National Academy of Sciences [43] from 1937 until his death.

Loeb died on 28 December 1959 in St. Louis, Missouri. After his death, Ernest W. Goodpasture composed Loeb's memorial piece for the National Academy of Sciences [43]. According to Goodpasture, Loeb’s work on tissue transplantation conceptually made possible *in vitro* [7] culture of cells by developing techniques to grow cells without connective tissue.

**Sources**

Leo Loeb developed an experimental approach to studying cancer and pioneered techniques for tissue culture and in vitro tissue transplantation which impacted early-to-mid twentieth century experimental embryology. Loeb received his medical degree from the University of Zurich in 1897. As part of his doctorate, he completed a thesis on the outcomes of tissue transplantation in guinea pigs. Loeb's thesis inspired a life-long interest in tissue transplantation. His research culminated in greater than 400 publications, including a book called The Biological Basis of Individuality, in which he demonstrated the potential immortality of certain mammalian tissues.