

Introducing the Spemann-Mangold organizer: experiments and insights that generated a key concept in developmental biology

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"What has been achieved is but the first step; we still stand in the presence of riddles, but not without hope of solving them. And riddles with the hope of solution - what more can a man of science desire?"
(Hans Spemann, Croonian Lecture 1927)

The "organizer paper" by Hans Spemann and Hilde Mangold (1924) initiated a new epoch in developmental biology. It marked the climax of Spemann's life-long research, and the "organizer effect" received special mention by the committee that honoured him with the Nobel Prize for physiology and medicine in 1935. This introduction precedes a translation of that paper by Spemann's student, Viktor Hamburger. Its purpose is to retrace some of the steps by which Spemann arrived at the organizer concept, based on Spemann's publications, recollections of his students and collaborators (Baltzer 1942; Mangold 1953; Hamburger 1968, 1984, 1988, 1996; Holtfreter 1988, 1991; Waelsch 1992), historical essays (Oppenheimer 1970a, 1985; Saha 1991; Sander 1985, 1997) and detailed studies of original documents preserved at several places in Europe and the U.S.A. (Faessler 1994, 1996, 1997; Faessler and Sander 1996; Sander 1997). An additional document (of sorts), not strictly historical but nonetheless impressive, is a movie in which Richard M. Eakin renders the aged Spemann giving a fictitious lecture (Eakin 1975). Eakin in 1935/36

spent a year in Spemann's institute and helped him with the English version of his book (Spemann 1938). Two witnesses of that period who had seen the film felt that Eakin's performance gives a good impression of Spemann's gist for lecturing.

Hans Spemann (Fig. 1) gained early fame by his work on lens induction in frogs (Sander 1985, Saha 1991). Evocation of the "outer parts of the eye" by an outgrowth of the nerve tube (the optical vesicle) had been postulated early in the 19th century (von Baer 1828; Oppenheimer 1970b), but Spemann's experiments were the first to raise considerable interest; perhaps not so much by their results than by the long-lasting controversy these triggered. The struggle resulted, in a paradigmatic way, from Spemann's failure to consider a seemingly far-fetched possibility, namely that functional components of a developmental process might differ between closely related species. This contra-intuitive fact, although well documented meanwhile, tends to be overlooked even in our days of "Evo-Devo" research.

The controversy was resolved by Spemann's painstaking documentation of just such differences between *Rana fusca* and *R.*

Abbreviations used in this paper: UAF, Archives of Freiburg University; Um X, signifies "Urmund" which means "primitive mouth" (blastopore) followed by the serial number (X) of the relevant experiment; SAF, Spemann Archives in the Zoological Institute (Biologie I), Freiburg.

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esculenta (Spemann 1912). In the latter species, the lens formed despite experimental elimination of the optic vesicle, but in the former it failed to form - indicating that some kind of inducing signal from the optic vesicle was missing. Stringent experimental proof of lens induction, however, came not from Spemann but from Warren Harmon Lewis (of whom more below). Lewis (1904) demonstrated lens induction by displaced optic vesicles (which he had pushed caudally underneath the skin). He also achieved heteroplastic lens induction, by placing *Rana sylvatica* epidermis over the denuded optic vesicle of *R. palustris*, where it produced a lens. Subsequently, Lewis moved on to cell culture work where, among many other achievements, he discovered and named pinocytosis.

Induction in ontogenesis, incidentally, was not a new concept by that time. To mention just one proof, Curt Herbst - a lifelong friend of Hans Driesch and at one time hoping (in vain) to be Spemann's colleague at the Kaiser-Wilhelm-Institut - had published a book on the topic in 1901 (Oppenheimer 1970b). Therefore, it is not surprising that Spemann suspected induction to be implied in another of his early experimental results, too. The relevant experiment, performed while he was still with his great teacher and lifelong friend Theodor Boveri at Würzburg, was constricting cleavage stages of the newt (for Americans: salamander) incompletely, so that a bottle-neck remained between the two halves; the means



Fig. 1. Hans Spemann (1869-1941) at his laboratory desk, probably in the 1920's in a photograph owned by Otto Mangold (SAF) and to the right, Hans Spemann's Nobel title.

to achieve this were loops made from hairs of his baby daughter (Fig. 2A). Subsequent development frequently led to Siamese twins, with two anterior "individuals" being joined to a single trunc. The first malformations of this type (Fig. 3) were obtained in 1897, when Spemann noted in his files:

"The latter case has to be investigated more closely. How does the inner [= median] part arise from which the inner eyes derive? By a folding process? By regeneration?"

And a few lines on: "Cases 5 and 6 contradict the mosaic theory" (of embryogenesis). In the following years, his conceptual focus shifted. In a later analysis, Spemann (1901) concluded that the tip of the invaginating archenteron splits on encountering the internal bulge of the blastocoel wall (caused by the constriction), and this is followed by duplication of forehead and brain. Spemann shortly afterwards mused:

"It cannot be excluded that differentiation of the medullary plate is being induced by the archenteron; there are several facts that would well fit this assumption" (Spemann 1903).

Through many subsequent years, Spemann must have forgotten or subdued this assumption, as happened to him with Boveri's "centre of first differentiation" (Boveri, 1901) (see Spemann and Mangold 1924; Spemann 1931; Sander 1993). So both concepts may have influenced part of Spemann's way to the organizer concept only in the subconscious realm.

However, another result obtained by ligaturing newt eggs directly opened the trail towards the organizer concept. Ligatures that bisected pre-gastrulation stages completely rather than allowing a bottleneck to persist yielded two alternative results: either a complete larva forming in each half, or a larva in one half only and a mere *Bauchstück* or belly piece in the other (Fig. 2C). Spemann noticed that the former result was only obtained when the prospective blastopore had been bisected by the ligature (Fig. 2B). It was only on this condition that both parts could gastrulate and neurulate.



A

Apart from keeping the lens controversy very alive, Spemann from 1908 onward was busy as Professor of Zoology at Rostock. The administrative and teaching obligations attached to this post reduced the time he could spend on research, yet he made the best also of his Rostock years. He won several students for doctoral work, among them Horst Wachs who continued to study the lens, now with respect to regeneration rather than induction. However, the first and most esteemed Ph.D. student was Otto Mangold (Fig. 4), Spemann's life-long friend and ultimately his successor at Dahlem and Freiburg. With the amphibian organizer Mangold is linked in three ways: (1) In his Ph.D. project, he studied regulation and determination after combining various parts of early newt embryos, fusing for instance two embryos at the two-cell stage. (2) After 1924, he was to analyze the organizer effect in more detail than any other person during Spemann's lifetime. (3) Last but not least, in 1921 he married Spemann's Ph.D. student Hilde Pröscholdt (Fig. 4), who was busy performing and documenting the experiments that gave birth to the organizer paper.

fully concentrate on research. When the Great War broke out in 1914, he luckily was no longer fit for military service. So he could spend the next few years in surroundings as congenial for research as any nowadays; these years proved the most creative of his life. Missing all his younger collaborators, who had been called to arms, he all by himself performed a variety of pioneering operations that were to break the ground for the ultimate organizer experiment.

C

means for distinguishing, in transplantation experiments, between the structures contributed by host and graft, respectively. The latter approach, in addition to yielding important information by itself, perfected the technical expertise required for the organizer experiment.

With the chimeric embryos, the main aim was to see whether and how embryonic cells from different newt species would cooperate during embryogenesis. As for the “whether”, the cooperation was found to be nearly perfect. As for the “how”, the chimeric embryos provided further evidence for gastrulation as a key event in organizing the future body plan. This was indicated for instance when blastula halves, each comprising the future blastopore, were fused with opposite axial polarities so that the invaginating archenterons would meet head-on. Their tips apparently split up as in Siamese twinning, but each half was then deflected laterally by its heteropolar opponent, with whom it finally fused to form a chimeric head sticking out at right angles on each flank (Fig. 6). Spemann named this cross-shaped malformation *duplicitas*

cruciata. In this, as in the Siamese twins of a decade earlier, the neural plates and tubes apparently followed the courses that the invaginating archenterons had taken.

The lip transplantations, in turn, provide a marvellous example of how a wrong working hypothesis can severely delay a crucial discovery: with the right hypothesis in mind, Spemann should have recognized the organizer effect in 1916 at the latest. If so, however, he might not have won the Nobel prize at all, because W. H. Lewis (of lens induction fame) had done a few similar experiments on frog embryos as early as 1907. Both Lewis and Spemann found neural structures at the implantation site, but neither was surprised or alerted by this finding, because the then current wisdom derived the neural plate from the lips of the blastopore - exactly from where the transplants were taken! The German legend of 1918, reprinted in Fig. 7 and translated in the legend, unambiguously states that the transplant *formed* the incomplete supernumerary neural tube seen in the Figure, and the lab notes of 1916 state the same. Lewis saw in some of his results “an indication of how the neighbouring parts

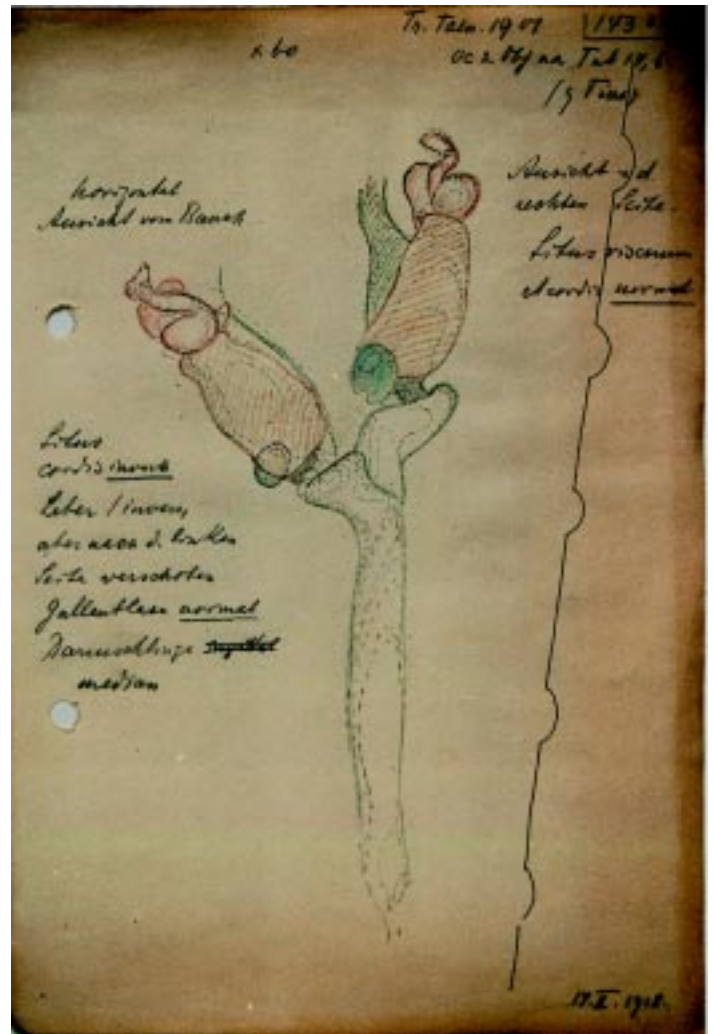
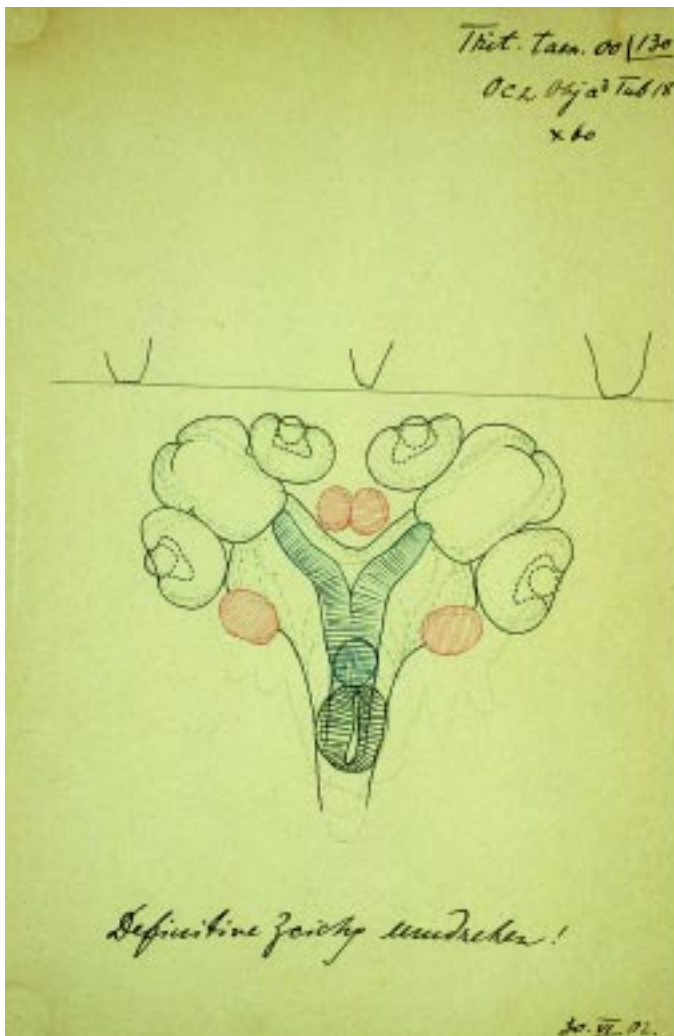


Fig. 3. Siamese twin embryo drawings (*Duplicitas anterior*) by Hans Spemann 1900/1901. (Left) Ventral view showing notochord (hatched), CNS and otic placodes; cross section of spinal cord inserted below. **(Right)** Another embryo, situs in the branching region seen from ventral. The two livers (hatched, with gall bladders attached caudally) cover the two branches of the gut. The hearts (top left and right) reveal a unilateral situs inversus that also includes the viscera where however it is less easily recognized. The wavy line on the right is a mark for adjusting the serial sections on which the reconstructions are based. (UAF).

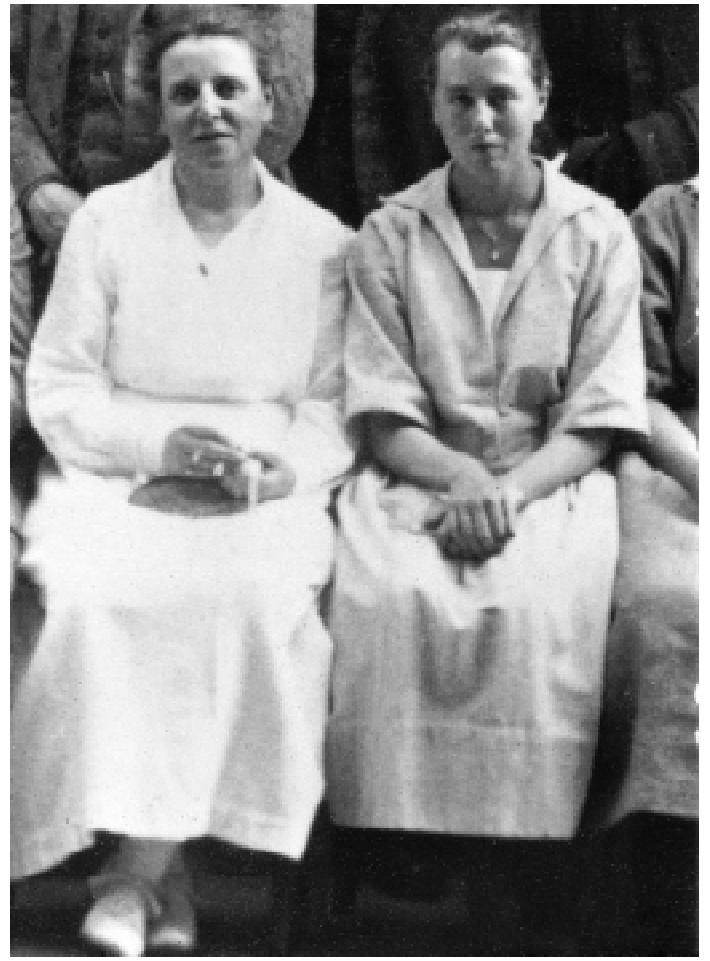
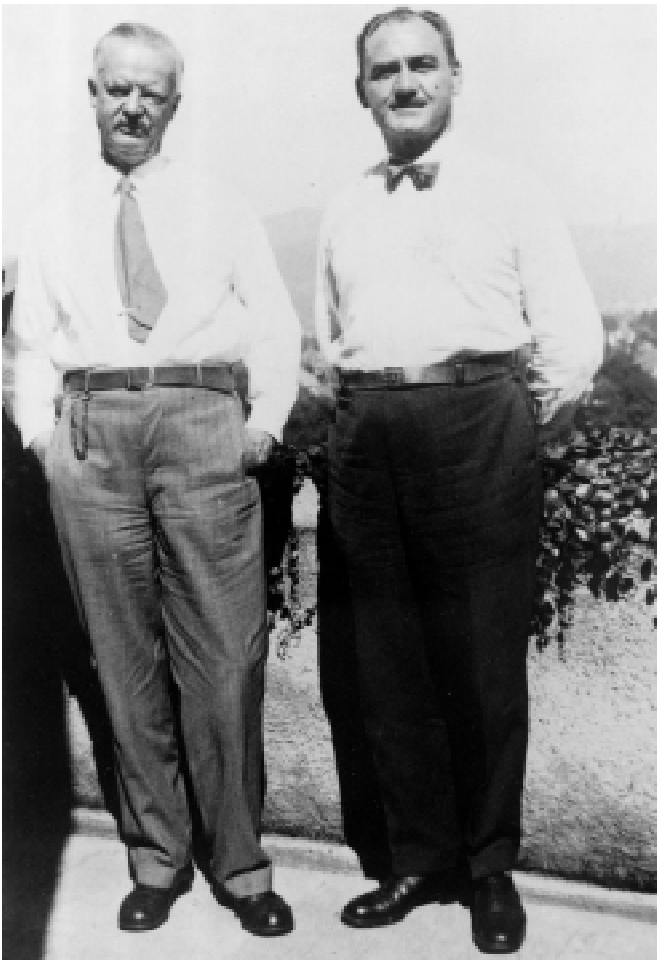


Fig. 4. Hans Spemann and Otto Mangold on the balcony at Spemann's home, about 1930. On the right, Hilde Pröscholdt (subsequently Hilde Mangold after her marriage to Otto Mangold) seated to the left of Mrs. Spemann in early June 1922, when she had completed the experiments for her thesis. It is a stamp-size cutting from the group photograph of participants in the 1922 meeting of German zoologists. Incidentally, at this meeting Walter Vogt first presented his fate mapping data, revealing for instance the previously unsuspected dorsal extension of the invaginating mesoderm (Vogt, 1922). Hans Spemann glued the photograph to a well-wishing card he sent to Hilde's mother, dated Dec. 19, 1928. (Courtesy of Yale University, Sterling Library, Ross G. Harrison papers and SAF).

in a normal embryo must interact upon each other" (1907, p. 140) - but this remark alluded to a quantitative effect, the hypertrophy of the notochord in some transplants, and not to a qualitative shift in developmental fate; this should be noted in context with an unjustified priority claim to be mentioned below.

The erroneous location of the neural anlage in the blastoporal lip (Fig. 8A), on which Spemann based his interpretation, had been conceived and aggressively advertised in 1888 by Wilhelm Roux, the conceptual founder of developmental biology, and was accepted by celebrities like Oscar Hertwig and Thomas Hunt Morgan (Sander 1991a,b). In this context, it should be remembered that the first fate map based on dye marks (Fig. 8B) was not published before 1924. Spemann might perhaps have learned of it earlier, because Vogt was a good friend and had begun his experiments in 1914 (Vogt 1922). However, there is no evidence to indicate that Spemann was aware of Vogt's map before 1922, when Hilde Mangold had completed the experiments on which the organizer paper rests.

Apparently, Spemann himself had earlier missed at least one chance to correct Roux's claim. The case shown in Fig. 8C (published 1919) could have shown him - but apparently did not -

that the prospective neural plate derives from far above the dorsal lip. So, Roux's (and Spemann's) error dawned first on a thoughtful and helpful colleague. This was the anatomist Hans Petersen of Heidelberg, who apparently warned Spemann in 1919 that some of his results were speaking against a neural fate for the lip (we know this from Spemann's letter of thanks to him). Spemann had observed both ectodermal and mesodermal structures at the implantation site of some lip grafts, and thought that the graft had given rise to both. He now reconsidered his arguments, and in a paper submitted on January 11, 1921 - that is, before Hilde Mangold started experimenting - he proposed the *experimentum crucis* for proving neural induction:

"Maybe the entire transplanted [lip] piece belongs to the region bound to invaginate, and hence would represent prospective endomesoderm [...]. Consequently, if one would take this piece from a taeniatus embryo and transplant it onto a cristatus host, then notochord and somites should belong to the former [species] but the neural plate to the latter." (Spemann 1921).

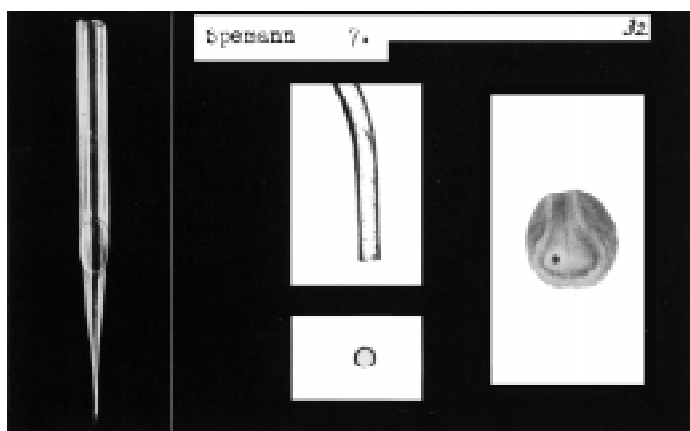


Fig. 5. Spemann's pipette for transplanting small cell groups from early newt embryos. The hole in the pipette on the left was covered by a stretch of rubber tubing slid over the shaft; pressure on it would eject or (at relaxation) suck up minute volumes. (Middle and right) Copy of a lantern slide (8.5 x 10 cm) prepared by Spemann, showing the tip and an embryo from which the prospective optic vesicle had been removed (UAF).

Obviously, these lines embody the strategy that was to reveal the organizer effect. Spemann's expectations, however, fell quite short of this effect - he expected neural induction but apparently failed to foresee that mesodermal structures could be induced in the host as well!

In any case, Spemann most likely would have sat down in the 1921 spawning season to perform the heteroplastic lip transplantations envisioned, which should have revealed the organizer effect. However, the events took a different turn. In 1918, towards the end of the Great War, living conditions in Berlin-Dahlem had deteriorated to a degree nearly stalling all research activities. In particular, the military and social upheavals in and around the Dahlem Institutes worried Spemann much. So he gladly accepted the offer to take over Weismann's chair at Freiburg, where he

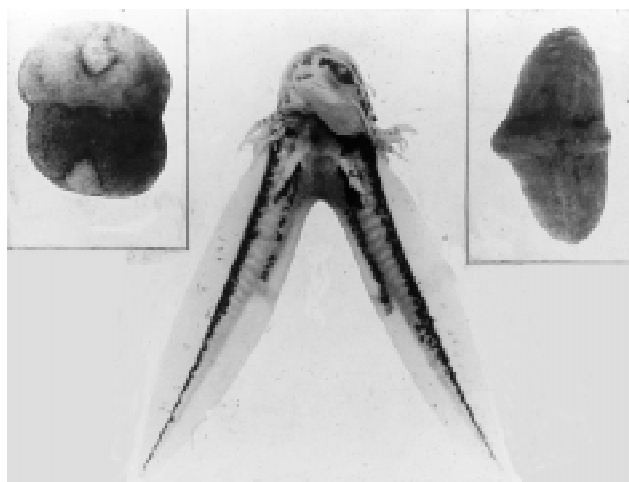


Fig. 6. Gastrulating halves of newt embryos fused so that the archenterons would meet head-on. The result is a *duplicitas cruciata*, shown after neurulation (on the right) and after hatching (center). Notice that the chimeric head at the junction is seen from ventral; its counterpart is hidden on the far side. Poster prepared for the Chicago World Fair of 1933, signed H. Spemann (Courtesy of Theo Peters, Giessen; SAF).

moved in 1919. His first years there were filled by time-consuming obligations in both teaching and administration, on top of the strenuous everyday struggle for survival in starving postwar Germany. So research had to stand back. The administrative duties culminated in 1923/24 after Spemann had been elected the university's *Rektor*, and it was only after his one-year term in this top position that he could return to his beloved experiments. To the historian, Spemann's *Rektorat* offers a boon, because during that

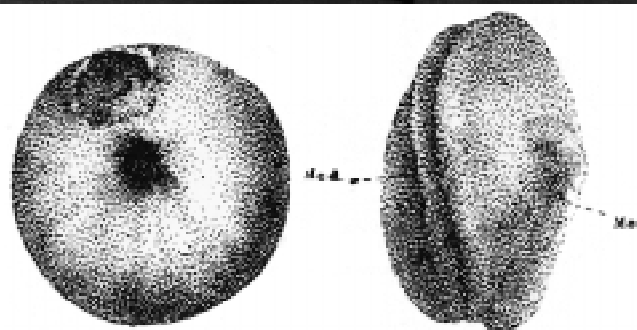
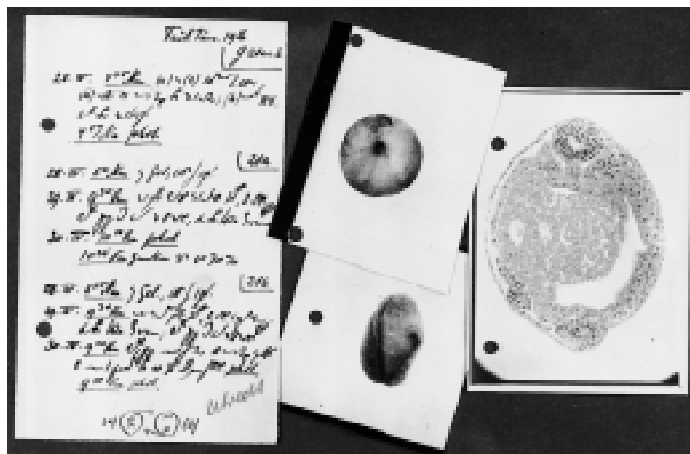


Fig. 15 und 16. Nahe über dem Urmund (näher als beim Keim der Fig. 8) ein Stück herausgenommen und einem anderen gleich alten Keim in die Gegend der späteren Epidermis verpflanzt. Dort entwickelt es sich neben dem normalen (Med) zu einem kleinen überzähligen Medullarrohr (Med).

Fig. 7. Unrecognized neural induction in a 1916 experiment by Spemann. From left to right, lab notes in Spemann's shorthand, filed photomicrographs of donor embryo (top) and recipient (bottom) at neurulation, and microscopic section after neurulation (UAF). (Below) The drawings in Spemann's "Figs. 15 and 16" in his 1918 paper, were based on such photographs. The legend reads: "Close to the blastopore (and closer than shown in 'Fig. 8') [of the 1918 paper], a piece was removed and transplanted into the prospective epidermal region of another embryo of the same age. There it developed next to the normal one (Med), into a small supernumerary medullary tube (Med)." (Translation by K.S.). Note that the two "Med" should probably have been numbered 1 (on the left) and 2 (on the right).

period he felt obliged to maintain a diary that listed his activities by the hour. This record is crucial when it comes to evaluating his and Hilde Mangold's relative contributions to the organizer paper that appeared in print a few months later.

In 1920, the young and vivacious Hilde Pröscholdt (1898-1924) had come to Freiburg, lured there probably by a guest lecture of

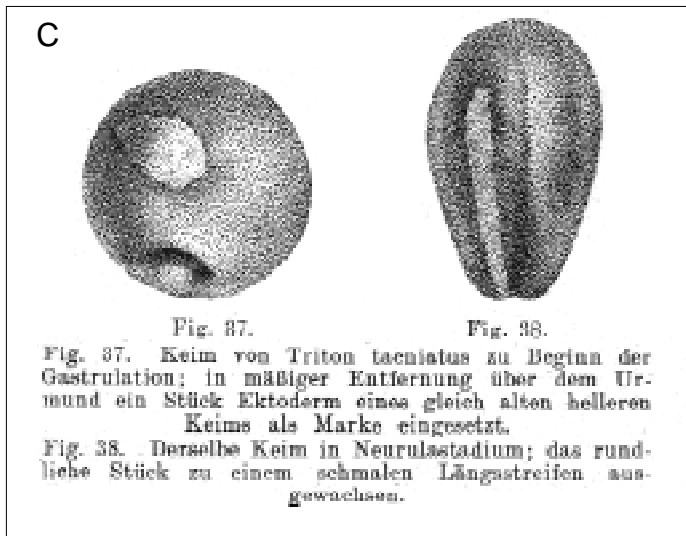
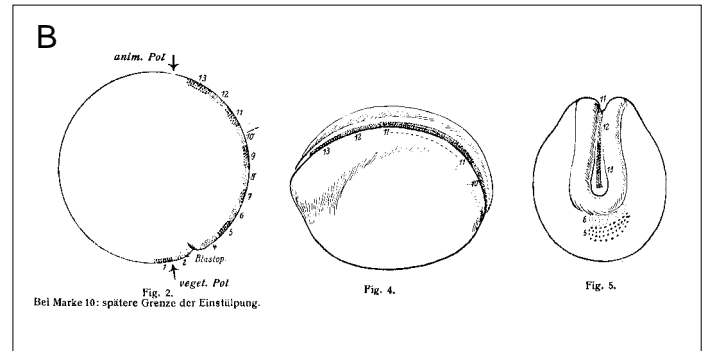
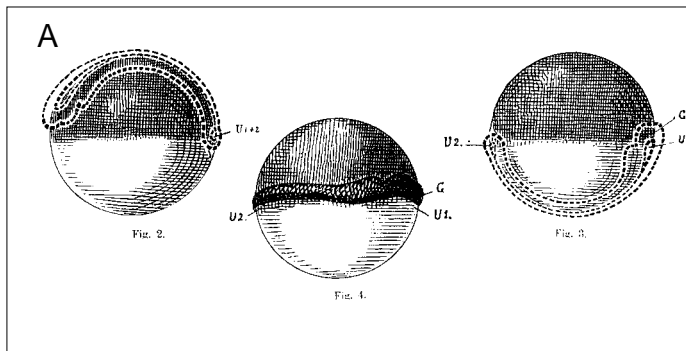


Fig. 8. (A) The “ring embryo” anomaly of frog embryogenesis that caused Wilhelm Roux to locate the neural anlage in the blastoporal rim (Figures from Roux 1888, rearranged). (Left), pregastrulation embryo with the prospective medullary plate superimposed in its “traditional” position, rejected by Roux (U, blastopore; 1 and 2, its locations at the onset and end, respectively, of gastrulation). (Middle), when epiboly gets blocked, the blastoporal lips form a swollen ring around the white yolk plug; this ring transforms into separate halves of the medullary plate, connected anteriorly by the brain (G). (Right), Roux claimed that in normal development, the left and right halves of the blastoporal rim would progress - due to “bilateral epiboly” - down the yolk plug until meeting on the midline where they would form the medullary plate as indicated. (For further explanations, see Sander, 1991, 1996). **(B) Fate mapping by colour marks in newt embryogenesis.** The lateral view (“Fig. 2” in the series) shows where the various marks were placed at the onset of gastrulation. The marks above no. 10 (bar) will end up in the neural tube (“Fig. 4”), and those below in the archenteron from where they shine through the epidermis (“Fig. 5”) (from Vogt 1924, Figures rearranged). **(C) An experimental result that might have raised doubts** (but did not) about attributing the neural anlage to the dorsal lip - see text. The legend reads “Fig. 37. Triton taeniatus embryo at the onset of gastrulation; some distance above the blastopore, a piece of [prospective] ectoderm from a less pigmented embryo of the same age has been inserted as a mark. Fig. 38. The same embryo at the neurula stage; the roundish piece has grown to form a narrow longitudinal strip.” (from Spemann 1919; translation by K.S.).

some distance above the blastopore, a piece of [prospective] ectoderm from a less pigmented embryo of the same age has been inserted as a mark. Fig. 38. The same embryo at the neurula stage; the roundish piece has grown to form a narrow longitudinal strip.” (from Spemann 1919; translation by K.S.).

Spemann in Frankfurt where she had studied Zoology for two semesters. She soon entered the *Großpraktikum* (the obligatory full-time practical work in Zoology), where she met two fellow students whose names must be known to almost every embryologist the world over: Viktor Hamburger and Johannes Holtfreter. After one semester, Hilde asked Spemann to fix a topic for her doctoral thesis. Impressed by her drive and intellect, he suggested that she repeat with modern methods one of the first developmental experiments ever, published in 1744: Abraham Trembley’s turning the *Hydra* polyp inside-out.

During some preliminary exercises (Fig. 9) she tried hard, but failed, as did the master himself when he came to assist her. With time beginning to run short - doctoral students paid considerable fees as well as their personal upkeep in those days - Hilde probably got nervous and, in any case, Spemann gave her his most attractive experiment: chimeric transplantations of the blastoporal lip. She mastered the technique very quickly and after two spawning seasons had amassed 274 experiments involving altogether four newt species (Faessler 1997). Two in every three operated embryos died early for unknown reasons (no Holtfreter solution in those days as yet!), but about 15% survived to stages suitable for histological assessment. At least 29 among these showed neural structures of host origin at the implantation site, accompanied in 13 cases by somites. Hilde’s lab notes and microscopic slides (Fig. 10) have survived to this day by a chain of fortunate events

(Faessler 1994, 1997; Faessler and Sander 1996). This has enabled us to present in Fig. 11B part of the very section which Hilde Mangold had drawn for “Fig. 24” in the joint paper, and also a section of another embryo (Fig. 11E) that shows the distinction between host and graft cells particularly well; this was published after Hilde’s death by her husband in the five-volume *Festschrift* for Spemann’s 60th birthday (H. Mangold 1929).

Of the 29 embryos that had visibly formed neural structures in reaction to the implant, Spemann selected a sample of six that between them illustrated the points to be made in the paper. We can ascribe the choice to him, not Hilde, for various reasons, most notably: (1) Some lab file notes of 1922 suggest that Hilde felt

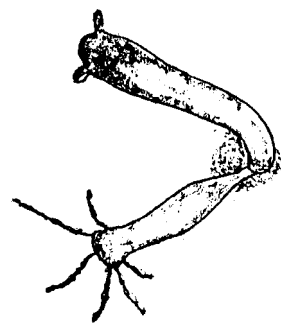
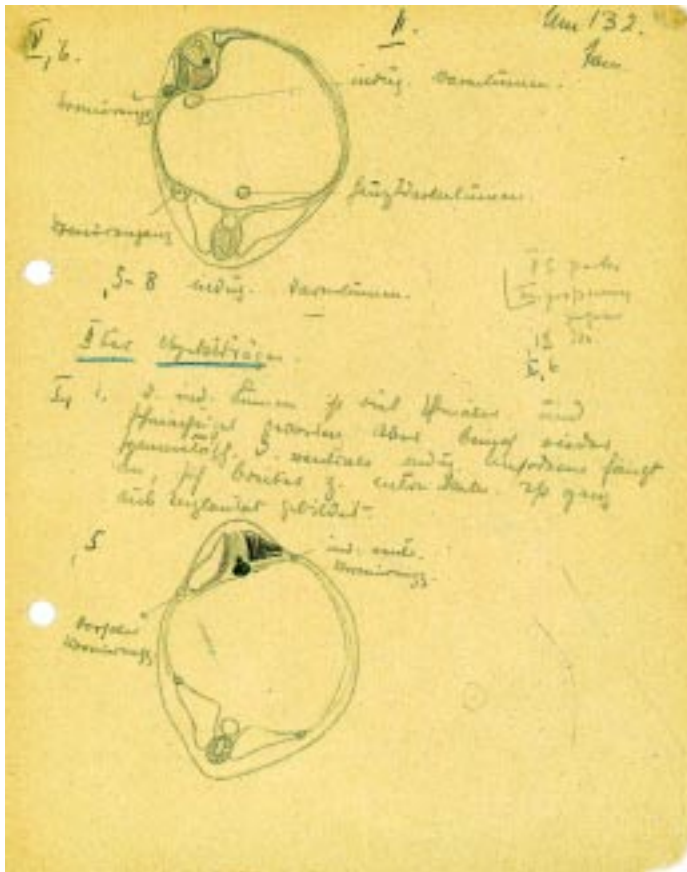


Fig. 9. Hydra doublet produced by Hilde Mangold and drawn on 4th March, 1921. Two individuals, one of them marked by staining, were cut below the tentacles and the isolated “heads” joined with opposite polarities. Within 12 days, two complete body columns had been intercalated and were about to separate. (Courtesy Embryological Collection, Hubrecht Laboratory, Utrecht/NL).



difficulties seeing her results in a larger context, which is no surprise when one considers that she was 23 and had just completed her third year as a biology student. (2) According to his diary, Spemann in 1924 spent altogether at least 50 hours discussing with Hilde the

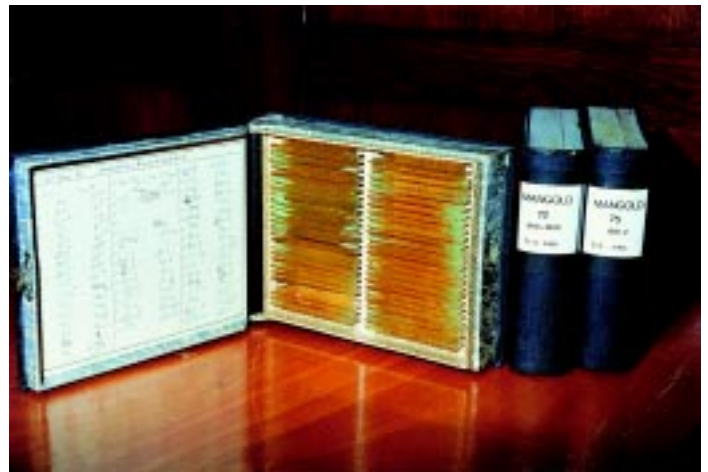


Fig. 10. Hilde Mangold's Lab notes on the famous heteroplastic lip transplantation (Um. 132) and her own slide boxes labelled "Mangold" by the curator of the Embryological Collection of the Hubrecht Laboratory (Utrecht/The Netherlands). Hilde's name does not appear in the register! Obviously the slides and the corresponding files were considered part of Otto Mangold's work donated to the collection. (Courtesy Embryological Collection / Gesineke Bangma, Hubrecht Laboratory, Utrecht/NL).

manuscript to be published jointly. (3) Most importantly, Spemann (as outlined above) had developed all by himself the conceptual approach as well as the techniques required. Early in 1921, he actually had predicted two possible outcomes of the chimeric experiment, one of them - as mentioned above - the induction of neural plate by the archenteron roof. Notwithstanding Spemann's conceptual contributions, Hilde got her Ph.D. with nearly the best marks (Fig. 12).

With these facts and judgements, a fair attribution of merit to each author of the organizer paper would credit Spemann with

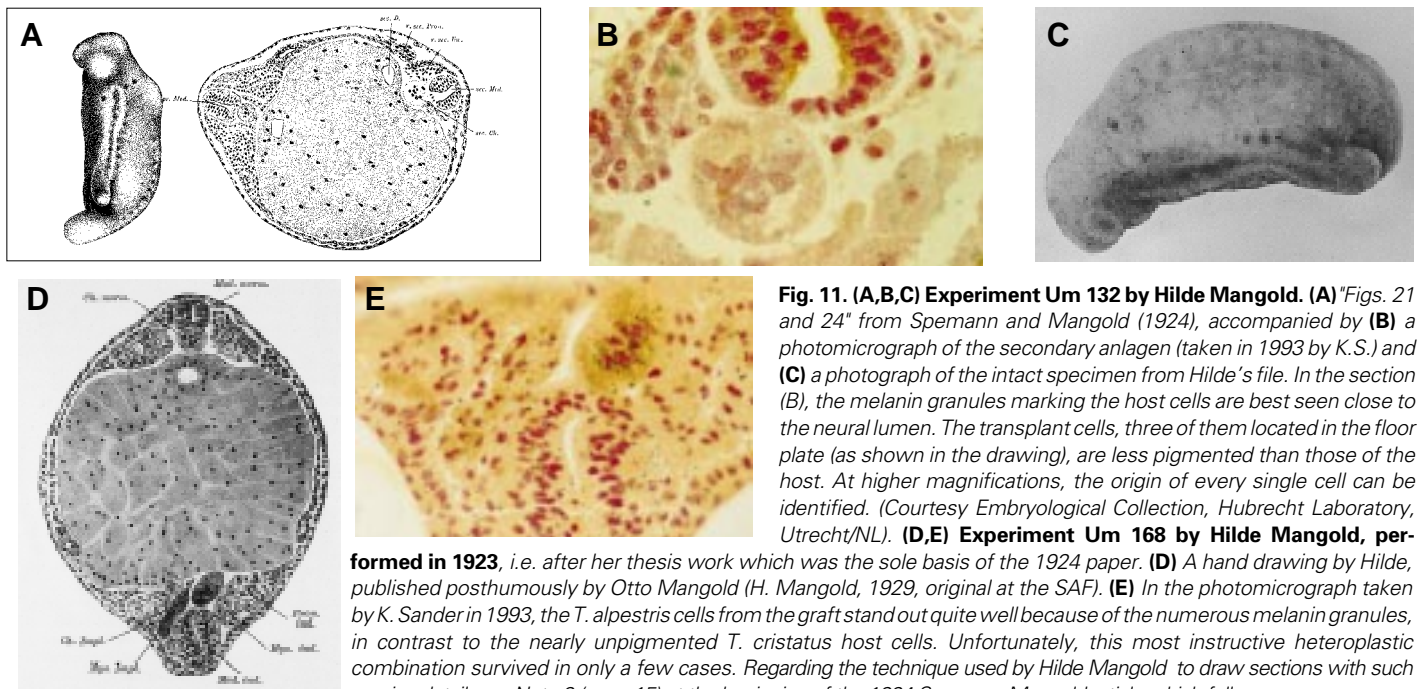


Fig. 11. (A,B,C) Experiment Um 132 by Hilde Mangold. (A) "Figs. 21 and 24" from Spemann and Mangold (1924), accompanied by (B) a photomicrograph of the secondary anlagen (taken in 1993 by K.S.) and (C) a photograph of the intact specimen from Hilde's file. In the section (B), the melanin granules marking the host cells are best seen close to the neural lumen. The transplant cells, three of them located in the floor plate (as shown in the drawing), are less pigmented than those of the host. At higher magnifications, the origin of every single cell can be identified. (Courtesy Embryological Collection, Hubrecht Laboratory, Utrecht/NL). (D,E) Experiment Um 168 by Hilde Mangold, performed in 1923, i.e. after her thesis work which was the sole basis of the 1924 paper. (D) A hand drawing by Hilde, published posthumously by Otto Mangold (H. Mangold, 1929, original at the SAF). (E) In the photomicrograph taken by K. Sander in 1993, the *T. alpestris* cells from the graft stand out quite well because of the numerous melanin granules, in contrast to the nearly unpigmented *T. cristatus* host cells. Unfortunately, this most instructive heteroplastic combination survived in only a few cases. Regarding the technique used by Hilde Mangold to draw sections with such precise detail, see Note 2 (on p. 15) at the beginning of the 1924 Spemann-Mangold article which follows.

Auf Grund menschlicher Experimente sollte bei der Bildung eines Organismus, daß eine bestimmte Stelle des jungen Amphibienembryo vor den übrigen durch eine gewisse Eigenschaft ist, daß man sie auch in anderen Tieren in ihrer weiteren Entwicklung beeinflussen kann. Versucht wurde, ob es in einer bestimmten Stelle aus diesem „Organisationszentrum“ die Fähigkeit besitzen, in fremdem, indifferentem Gewebe einen anderen Keim hervorzubilden. Von der Bildung eines Embryonalkeims. Von der menschlichen „Organisationsstelle“, daß, was aus ihr selbst wird, von dem übrigen zu kommen, was es indifferente, weißt ein solches Transplantation müssen Keime menschlichen hervorgebracht werden.

Die große unerwartet tiefen Spemann'schen dieser Arbeit sind von Frau Hilde Mangold mit selbstem Gefühl. Auch dieses abweisende Antwort hat positive Bedeutung der Mensch ist hoch auf der großen Bedeutung.

Die Arbeit verdient die Note 1-2.

Freiburg, 14. Feb. 1923.

Spemann.



Fig. 12. Evaluation of Hilde Mangold's dissertation by Hans Spemann, for the Faculty Dean (written on a form which routinely provided just a single page for this purpose!). The best rating would have been "1". The text reads as follows:

"Various experiments have permitted the conclusion that in a young amphibian embryo, a limited region is distinguished before the others by determining the development of the indifferent other parts. From this followed the task of testing whether, and to what degree, small parts of the "organization center" possess the capacity, when transplanted into foreign indifferent tissue of another embryo, to call forth there the formation of an embryonic rudiment. To permit a distinction between the transplanted "organizer", and what it develops into, from that which it has induced, it was necessary to perform such transplantations between embryos of different species. The large, especially technical, difficulties of this task were overcome by Mrs. Hilde Mangold with rare dexterity and perseverance. The positive result of the experiment is of great theoretical importance. The thesis deserves the rating 1-2. Frbg. [=Freiburg], 14. February 1923. Spemann". (Translation K.S.) (UAF).

To the right, the Bronze plate commemorating Hilde Mangold, unveiled in the new Zoology building at Freiburg University on her 100th birthday. It was cast from the plate on Hilde's tombstone at Gotha, Poland. (Photograph K.S., 2000).

paving the conceptual and technical way to the chimeric lip transplantations and with having predicted neural induction on this basis, while Hilde Mangold did the demanding experiments and thereby demonstrated that the lip's potential is much more dramatic, organizing as it does the basic structure of almost the entire body. Spemann always acknowledged Hilde's contributions. Yet, whether she would have shared the Nobel Prize in 1935 must remain an open question, because she died tragically before the organizer paper had come out (Sander 1985; Faessler and Sander 1996).

Some fellow biologists, however, felt prompted to give the credit elsewhere. First among these was Gavin de Beer (1927), who suggested that W.H. Lewis had discovered the organizer effect in 1907, but - as mentioned above - Lewis at best had observed neural

inducts without recognizing them as such. At worst, he had transplanted neurally determined cells - note that by new standards his frog embryos were too old to respond. Gavin de Beer's mistaken proposal was reiterated by Sven Hörstadius in 1928. Spemann quipped on both in 1931:

"You may well make a discovery without intending to do so, but not without noticing it".

A more recent claim for priority is harder to dismiss, especially since it involved *Hydra*, the organism that Hilde Mangold had studied for a few weeks in preparation for the abortive doctoral project. Howard Lenhoff (1991) has suggested that the organizer effect was discovered in this animal, not the newt, when Ethel

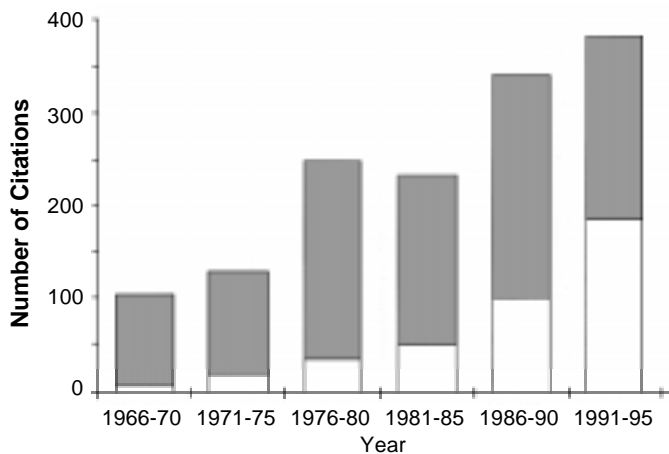


Fig. 13. Number of references made, during successive five-year periods, to the organizer paper of H. Spemann and H. Mangold (1924) (white part of columns); the grey parts refer to other publications by Spemann. Based on the ISI Citation Index, ending with the October entrances for 1995. (Faessler and Sander 1997).

Browne (later Ethel Harvey, of sea urchin fame) transplanted peristomes into the trunc's flank. Indeed, the peristomes acted as inductors in so far as they caused the flank to sprout an entire body column - clearly a proven case of induction. But whether a striking degree of organization was achieved thereby is a matter of taste: to parallel the outgrowth of an epithelial tube with the incomparably more complex organization of secondary newt embryos may not find support from all quarters.

In any case, neither the experiments of Lewis nor those of Browne were to usher in a new epoch, as the work of Spemann and Hilde Mangold did - witness Fig. 13 and the series of papers presented in this issue.

Summary

The «organizer paper», published by Hans Spemann and Hilde Mangold in 1924, initiated a new epoch in developmental biology. Also it marked the climax of Spemann's life-long research which began at the end of the nineteenth century. This introduction retraces some of the steps by which Spemann arrived at the organizer concept: The problem of amphibian lens induction including the so-called lens controversy, the early constriction experiments creating double headed malformations, and the homeo- and heteroplastic transplantations during gastrula stages of the newt. Furthermore this paper will - based on historical documents - repudiate some objections raised to the contribution of Spemann and Hilde Mangold to the discovery and interpretation of the organizer effect.

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