Regulations in the induction of the organized neural system in amphibian embryos

TUNEO YAMADA
Swiss Institute for Experimental Cancer Research, 1066 Epalinges, Switzerland

Summary

Some of the recent data on the induction of the neural system in amphibian embryos are reviewed, utilizing a model, according to which two basic events regulate in this system: (1) ectodermal dorsalization, which occurs all over the induced region of the ectoderm and is responsible for the neural and mesectodermal pathways and (2) caudalization, which occurs only on the posterior level of dorsalized ectoderm and is responsible for the posterior mode of induced differentiation, functioning as a gradient with the apex at the posterior end of the embryo. Dorsalization of ectoderm can be caused by treatment with Con A or TPA, both of which are potential mitogens. Not only after the treatment with TPA, but also during normal dorsalization, the activation of protein kinase C occurs in responding cells. The possibility is suggested that an early step of mitogenic transmembrane signal transduction induced by a growth factor regulates dorsalization in intact embryos. Ectodermal dorsalization is responsible for the appearance of neuronal and glial cell lineages, and independent of the ECM network formed on the internal surface of the responding ectoderm during gastrulation. In caudalization, a series of experiments suggests that the regulatory role is played by the transcript of the mesodermal posterior homeobox gene, XhoX 3. The expression of this gene in time and location closely coincides with the pattern of convergent extension, one type of morphogenetic movement, which is expressed in a posterior–anterior gradient. This directed cell mobility is responsible for the formation of the body axis of vertebrates, and was shown to be involved in caudalization by earlier induction experiments in urodele embryos. Thus clues have been obtained for regulation in dorsalization and caudalization, paving the way for understanding the inductive action of the organizer.

Key words: induction, regulation, neural system, amphibia.

Introduction

The purpose of this article is to review some recent progress made on different research fronts of the induction of the neural system in amphibian embryos, and organize the data into a coherent view of regulations operating in the emergence of CNS. Some general contemporary reviews on embryonic induction are available (Gurdon, 1987; Saxen, 1989). In the present review, for coordinating various data, a model of the induction of the neural system is used, in which two distinct events operate in combination (Yamada, 1950, 1978). (1) Ectodermal dorsalization. This is basic for induction and proceeds all over the responding part of the ectoderm. When dorsalization alone occurs, the affected area assumes the anterior-most dorsal property (archencephalic). However, in the explanted condition, dorsalization may produce unorganized neural structures. It is proposed that strong dorsalization of ectoderm leads to neural differentiation, while milder dorsalization to mesectodermal differentiation. The conventional expression, neuralization, is almost equivalent to ectodermal dorsalization. However, the latter emphasizes the axial connotation of the event and embraces the induction of mesoderm. (2) Caudalization. If caudalization accompanies dorsalization, the affected ectoderm expresses structures of posterior levels. Caudalization functions as a gradient. Weak caudalization of dorsalized ectoderm leads to deuterencephalic structures, medium one to trunk structures and strong one to tail structures. In a similar model of the induction of CNS proposed by Nieuwkoop (1955), terms activation and transformation are used, which are equivalent to dorsalization and caudalization, respectively. According to Toivonen (1979), if competent ectoderm and the dorsal lip are confronted in the transfer filter arrangement with Nuclepore filter of 0.05 μm pore size, only the induction of archencephalic or non-specifiable neural tissue together with noses and lenses is transmitted. If the pore size is increased to 0.6 μm, in addition to the above reported tissues, hindbrain, spinal cord, ear vesicle, myotomes and notochord are expressed. It is possible that, in the latter case, a mesodermalizing factor of dorsal lip was transmitted to the ectoderm and produced dorsal mesodermal tissues,
which in turn induced posterior neural tissues in the surrounding ectoderm, without passing through the filter. The mesodermalizing factor is known to be transmitted through Nuclepore filters of 0.2–0.4 μm pore size (Minuth, 1978; Grunz and Tacke, 1986). That the dorsal lip contains the mesodermalizing factor is not surprising. The posterior part of the archenteron roof induces posterior myotomes in normogenesis (Spofford, 1945, 1948), and the dorsal lip sample often contains endodermal cells, which should have mesodermalizing effects. Thus above cited transfilter experiments imply that ectodermal dorsalization can be transmitted through the filter of 0.05 μm pore size, while caudalization is blocked by the filter. Whether caudalization can be transmitted through 0.6 μm pore size filter remains questionable. This keeps the possibility open that the transfilter condition blocks the transmission of caudalization. In any case, these studies show that the physical properties of factors involved in dorsalization and caudalization are distinct.

Ectodermal dorsalization

Although the identification of the dorsalizing factor that is transmitted from the dorsal mesoderm to responding ectoderm during the induction of the neural system in the intact embryo has not been achieved, the dorsalizing effect of partially purified proteins separated from amphibian eggs and embryos has been repeatedly demonstrated (Janecek et al. 1984a, b; Born et al. 1989). There exist at least two types of dorsalizing proteins from those sources: a basic protein present in ribonucleoprotein particles and an acidic protein or glycoprotein contained in a fraction of small vesicles and high-speed supernatant. The inducing frequency of both microsomes and high-speed supernatant increases after autolysis or treatment with dissociating agents (Born et al. 1989). It was suggested that the dorsalizing factors are synthesized in oocytes, stored in a masked form, and activated in part during gastrulation. When both types of dorsalizing proteins indicated above are covalently bound to CNBr-Sepharose or cross-linked CNBr-Sepharose particles, the inducing activity of both proteins remains intact, showing that they act on the cell surface (Born et al. 1986).

While studies of factors derived from embryos have failed so far to cast further light on the nature of regulation occurring in dorsalization, the use of artificial inducers has been rather successful in this respect. In a series of experiments using isolated Cynops presumptive ectoderm as the responding tissue, the dorsalizing effect of Concavalin A (Con A) was analyzed (Takata et al. 1981; Yamazaki-Yamamoto et al. 1981, Takata et al. 1984a, b). When ectoderm is treated with Con A at the concentrations of 100–500 μg ml⁻¹ for 2–3 h, archencephalic or non-specified neural tissues are induced. The effect is blocked by alpha-methyl-D-mannoside or alpha-L-fucose. Con A binds to the inner surface of ectoderm and is successively incorporated into cytoplasm. However, when it is conjugated with Sepharose beads the neuralizing effect is unaffected, suggesting that Con A acts at the cell surface for neuralization, in agreement with the mitogenic effect of Con A on lymphocytes (Paul et al. 1973). Con A treatment causes specific ultrastructural cell surface changes distinct from those induced by non-dorsalizing lectins. [³H]Thymidine incorporation is suppressed in treated ectoderm in the first 30 h period, and enhanced in the subsequent 30 h period. To test the hypothesis that the receptor for Con A on ectodermal cells is a glycoprotein, ectodermal explants were first treated with neuraminidase to remove sialic acid, and then treated with almond glycopeptidase, which releases oligosaccharide from glycoprotein. Such an explant does not respond with neuralization when Con A is added, while the neuraminidase treatment alone does not affect the response. Grunz (1985a) showed that Xenopus ectoderm is induced to form archencephalic or non-specified neural structures after treatment with Con A, and this effect is enhanced by pretreatment with Cytochalasin B. An influence of the latter on the binding of Con A is suggested. In the double layer of Xenopus ectoderm, Con A binds mainly to the inner layer and induces neural tissue only in this layer. Whether the receptor of Con A on ectodermal cells functions as the receptor for the normal dorsalizing factor is a crucial question. Relevant in this context is the report that treatment of a sandwich of ectoderm and dorsal lip with tunicamycin, an inhibitor of glycosylation, does not inhibit ectodermal dorsalization (Grunz, 1985b). However, the modification of the cell surface pattern of glycoprotein that occurs with tunicamycin is a complex process dependent on many factors, above all on the pool size, as mentioned by the author, and a definite conclusion from this observation cannot be drawn without information on essential parameters. When Con A is applied to isolated presumptive ectoderm of Rana temporaria, well-organized archencephalon with retina, lens and cartilage are induced (Mikhailov and Gorgolyk, 1988). In this work, Con A bound to Sepharose failed to dorsalize ectoderm. The discrepancy between this observation and that of Takata et al. (1981) has not been cleared up. The report that Con A is able to dorsalize ventral mesoderm opens a new perspective into the research of dorsosventral organization in amphibian development (Diaz et al. 1990).

Duprat et al. (1982) showed that when Pleurodeles ectoderm is pretreated with soybean lectin (SBA) or Pisum sativum lectin, both of which are non-dorsalizing, and then combined with dorsal lip for 4 h, the dorsalization that occurs in control ectoderm is inhibited, suggesting that the structural integrity of cell membrane is required for a response to the normal dorsalizing signal. If, however, pretreated ectoderm is kept combined with dorsal lip for 24 h, dorsalization occurs, probably due to turnover of glycoconjugates.

Davids et al. (1987) reported that treatment of early gastrula ectoderm of Triturus alpestris with 75 nm phorbol 12-myristate 13-acetate (TPA) leads to differ-
entiation of neural tissue, mesenchyme and melanophores. The number of mitotic cells is greatly increased. Since TPA is known to affect the cells by directly activating protein kinase C (PKC) (Castagna et al. 1982; Nishizuka, 1986), the observation implies an involvement of this enzyme in ectodermal dorsalization. In a subsequent report, an enhancement of PKC activity was demonstrated in isolated ectoderm after treatment with TPA or a partially purified neuralizing protein obtained from Triturus embryos (Davids, 1988). Endogenous substrates, which are phosphorylated more intensely after dorsalization, are proteins of approximately 31, 21 and 14×10^3 M_. According to Otte et al. (1980), an enhancement of PKC activity occurs in Xenopus presumptive neural ectoderm when it becomes underlain by dorsal mesoderm in intact gastrula. The PKC activation was found associated with translocation of the enzyme from cytosol to cell membrane. During stages 10–13, a threefold increase in membrane-bound PKC activity and twofold decrease in cytosolic PKC activity occurs in whole embryos, while in partial embryos composed of endoderm, mesoderm and ventral ectoderm, neither PKC activity shows significant changes, suggesting that the translocation and activation of PKC is associated with neural induction. It is reported that in TPA-treated Xenopus ectoderm, in addition to the more frequent occurrence of neural tissue, muscle develops in rare cases (Davids, 1988). This can be related to the fact that a prolonged treatment of cells with TPA inhibits the PKC activity (Rodriguez-Pena and Rozengurt, 1984). A negative control of the PKC activity has been suggested as the possible regulation in mesoderma lization of presumptive ectoderm (Yamada, 1989).

N-CAM RNA, which has a localized expression in the neural plate and neural tube in Xenopus development, is reported to increase its amount during stages 10–12 (Kinter and Melton, 1987), and N-CAM protein can be detected in stage 14 (Jacobson and Rutishauser, 1986). This seems to imply that N-CAM is one of the first genes expressed as a consequence of the PKC activation induced by the normal dorsalizing factor. It is probable that the neuralizing effect of Con A is also associated with the PKC activation, because in human T lymphocytes Con A induces a rapid degradation of phosphatidylinositol 4,5-bisphosphate, and a transient accumulation of two messengers, d-inositol 1,4,5-trisphosphate and sn-1,2-diaclyglycerol (Hasegawa-Sasaki and Sasaki, 1983). The latter messenger activates PKC (Downes and Michell, 1985). Con A is known also to cause an increase in protein phosphorylation in human lymphocytes (Chaplin et al. 1980). Both Con A and PTA are potential mitogens, and the PKC activation is one of the main pathways of mitogenic signal transduction (Rozengurt, 1985; Rozengurt et al. 1988). The observation that during the induction of neural plate PKC is activated is in accord with the assumption that a transmembrane signalling involving a growth factor receptor is the basic regulation of dorsalization, as well as with the observation that the network of extracellular matrix present on the internal surface of ectoderm during gastrulation (Boucaut et al. 1990) does not play a basic role in dorsalization (Duprat and Gualandros, 1984). Furthermore, most of agents or cellular events, other than those discussed above, that have been reported as effective in dorsalizing competent ectoderm are potentially mitogenic. For example, Heps in the protonated form causes dorsalization of Triturus ectoderm, and the enhancement of the Na^+/H^+ antiport system is proposed to be the regulation (Tiedemann, 1986). The activation of Na^+/H^+ exchange is caused by a number of mitogens (Pouysségur et al. 1982), and is responsible for cytoplasmic alkalization, which is a precondition for mitogenesis. cAMP derivatives are effective in dorsalizing Amblystoma ectoderm, which is prone to auto-neuralization (Wahn et al. 1975), but ineffective in Triturus ectoderm, which is more stable (Grunz and Tiedemann, 1977). The enhancement of cAMP level is regarded as one pathway of mitogenic signal transduction, which functions in synergy with other pathways (Rozengurt, 1985).

The idea has been proposed that in the late-stage embryonic induction, where the mature cell lineage responds to the inductive stimulus, a growth factor functions as the exogenous inducing factor and the pathway of responding cells is decided by the mode of cell-cycle progression of responding cells, which is altered by the inducing factor (Yamada, 1989). In contrast, in the early-stage embryonic induction, where the determination of pathway occurs more quickly, the pathway of responding cells may be mediated by an early step of mitogenic transmembrane signalling evoked by a growth factor acting as the exogenous factor. According to this speculation, the activation of PKC or subsequent phosphorylation of specific proteins may decide the dorsal pathway of responding cells. The other obvious possibility is that the growth factor receptor on the competent cells carries a specific signal for dorsalization unrelated to that for mitogenesis. However, the neuralizing effect of TPA, which does not depend on such a receptor in activating PKC (Castagna et al. 1982), contradicts this possibility.

Under various conditions the presumptive ectoderm becomes neuralized in the absence of an inducing factor (Holtfreter, 1944; Suzuki, 1983; Siegel et al. 1985; Duprat et al. 1990). The tendency of autoneuralization varies according to species. But even in Xenopus laevis known to be free from such tendency, the ectoderm becomes neuralized when kept disaggregated for a certain period and then reaggregated in the absence of an inducing factor (Grunz and Tacke, 1989). Autoneuralization has been traditionally interpreted to be due to the presence of masked neural determinant in ectodermal cells, which is activated under subcytolytic conditions. However, this is certainly not the only theoretical possibility. It is possible, for instance, that neuralization is always regulated by a certain event in the ectodermal cells, which in normogenesis is activated by the inducing factor from dorsal mesoderm, but can be also activated by subcytolytic conditions. If the PKC activation is such an event, one could raise the question...
whether autoneuralization caused by disaggregation is due to the activation of PKC by proteases, reported by Kishimoto et al. (1983), which in turn may be activated by the subcytolytic condition of disaggregation. In any case, it is relevant to find out whether PKC is activated during autoneuralization. Duprat et al. (1990) demonstrated that, when Pleurodeles early gastrula ectoderm is dissociated and then cultured, cells express neuronal and glial differentiation. This raises the question whether the non-induced ectoderm represents a heterogeneous cell population containing cells predisposed to neuronal and glial cell lineages.

Caudalization

In the past few years, some homeobox genes have been reported that are expressed in the posterior part of early Xenopus embryos, either restricted to the mesoderm (Ruiz i Altaba and Melton, 1989b), or to the ectoderm (Sharpe et al. 1987), or common to both germ layers (Condie and Harland, 1987; Carrasco and Malacinski, 1987). In the case of mesodermal posterior homeobox gene, Xhox 3, studies implicate a role regulating the posterior differentiation which coincides with that of caudalization in the present model (Ruiz i Altaba and Melton, 1989c, 1990). The pertinent points of these studies will be reviewed. The possibility is also open that other genes of this group have similar or related roles. The transcription of Xhox 3 starts with MBT, peaks at the early neurula stage and sharply decreases later (Ruiz i Altaba and Melton, 1989b). During gastrulation and neurulation Xhox 3 RNA is distributed in a gradient in the dorsal mesoderm with the apex at the posterior end. In the tail-bud and early larval stages, the same RNA is localized at the tip of the tail, and in neural tissue (Ruiz i Altaba and Melton, 1989b; Ruiz i Altaba, 1990). In a number of experimental series, the possible role of Xhox 3 transcript in regulating the anteroposterior level of induced differentiation was studied (Ruiz i Altaba and Melton, 1989c, 1990). The correlation between the amount of Xhox 3 RNA present in the mesoderm, which has been produced by various polypeptide growth factors in ectoderm (Ruiz i Altaba and Melton, 1989a), and the expressed level of anteroposterior differentiation induced by the mesoderm in the blastocoel test in the host embryo was well demonstrated. For instance, the mesoderm induced by XTC-MIF has a low level of Xhox 3 RNA and induces, in the blastocoel test, brain, while the mesoderm induced by bFGF with a high level of Xhox 3 RNA induces spinal cord with trunk and tail characteristics. The experimentally induced perturbation of anteroposterior differentiation is associated with a change in Xhox 3 RNA amount that is not always correlated with the expressed anteroposterior level. For instance, the Li⁺-treated embryo, which lacks trunk and tail axial structures but has a well-formed head, has a very low level of Xhox 3 RNA. On the other hand, the UV-produced headless embryo with weak posterior axis shows a very high level of Xhox 3 RNA. The injection of Xhox 3 RNA into the fertilized egg leads to an embryo with various degrees of head inhibition. Neither the enhancement of posterior structures of the primary axis nor formation of a secondary posterior axis occurs after the injection. According to the present model, the formation of the posterior axis depends on both the dorsalizing factor and caudalizing factor, hence, if we assume that Xhox 3 transcript is the caudalizing factor, the injection of Xhox 3 RNA alone should not greatly affect the morphogenesis of the embryo. Similarly, in the UV-treated embryo, primary dorsalization is inhibited, leading to the suppression of ectodermal dorsalization; hence the presence of a large amount of Xhox 3 RNA is neither correlated with the exaggeration of primary posterior axis nor with multiple posterior axis formation. On the other hand, the mesoderm contains the dorsalizing factors as well as the caudalizing factors, and is able to produce secondary posterior axis in the blastocoel test. One vigorous test for the caudalizing role of Xhox 3 transcript may be the demonstration that the dorsalized ectoderm, which tends to develop archencephalic structures, can be diverted into trunk-tail formation under the influence of the transcript. It may be possible to realize this demonstration by combining Con A treatment of ectoderm with the injection of Xhox 3 RNA. An uneven distribution of the transcript may be required in the test. The above-cited results suggest that the anteroposterior value of neural tissue is determined by the level of Xhox 3 transcript present in the inducing mesoderm. This is at variance with the prevailing theory of the induction of neural system, according to which the anteroposterior differentiation is decided by the gradient in the extent of mesodermalization with the maximum at the posterior end (Saxén and Toivonen, 1955; Saxén, 1989).

The obvious developmental event that distinguishes different anteroposterior levels of the embryonic axis at the time of inductive interaction between dorsal mesoderm and presumptive neural ectoderm in the intact embryo is convergent extension (C–E), one type of morphogenetic movement. C–E is a directed cell motility that causes streaming of cells along the anteroposterior axis, converging them toward the dorsal midline (Vogt, 1929, Keller et al. 1985). In the localized vital staining experiment, when a circular mark is made on the surface of a germ layer, the mark later assumes an elongated form and is shifted toward the dorsal midline. Recently, C–E has been shown to be associated with mediolateral cell intercalation (Keller and Tibbetts, 1989). Although there exists good evidence for the essential role played by fibronectin-rich EM on the internal surface of ectoderm for the forward migration of dorsal mesoderm during amphibian gastrulation (Boucaut et al. 1990), C–E appears to be regulated independently from this EM (Smith et al. 1990). C–E has a moulding effect on the embryo, and is involved in the transformation of the spherical or discoidal embryos into an axiated structure, probably in all vertebrates. When the anterior end of the neural system (the archencephalic region) is induced, the anterior archenteron roof involved in the induction is
not expressing C-E. On the contrary, when all more posterior levels of the neural system are induced, the part of archenteron roof involved in the induction is expressing C-E, and the induced ectoderm expresses C-E for a certain time interval. There exists a gradient in the extent of C-E expression in the presumptive neural ectoderm and the archenteron roof along the anteroposterior axis: C-E is not expressed in the archencephalic region, weakly expressed in the deuterencephalic region, moderately expressed in the trunk region and strongly expressed in the tail region. In the tail bud, C-E persists a long time after it has terminated in other regions. The extent of C-E expression in the whole embryo is maximum during the late gastrula stage to the early neurula stage. While in the ectoderm, C-E becomes expressed from the middle or late gastrula stage in the posterior levels of neural ectoderm as it is dorsalized by mesoderm, in the mesoderm the expression of C-E begins in the late blastula stage when the mesoderm ring is descending towards the vegetal pole and converging toward the dorsal midline in preparation for invagination. In this phase, not only the presumptive posterior archenteron roof, but also the presumptive anterior archenteron roof participates in C-E in Urodèles. The latter part of the archenteron roof however stops C-E as it invaginates at the dorsal lip and comes in contact with the ectoderm. It is possible that in Anura the participation of the presumptive anterior archenteron roof in C-E before invagination is weak or absent. The above described pattern of C-E during inductive interaction of ectoderm and dorsal mesoderm in the intact embryo supports the view that caudalization is mediated by C-E. C-E expressed by the mesoderm may be responsible for C-E expressed by the induced ectoderm, which in turn mediates caudalization of ectoderm. However, if this is the case, the anterior archenteron roof before invagination should induce posterior structures, because it is expressing C-E. Spemann (1931) showed that the *Triturus* anterior archenteron roof induces head structures even if it is tested before invagination, utilizing the blastocoel test. However, a series of subsequent studies using *Cynops* embryos revealed a quite different situation (Okada and Takaya, 1942a, b; Takaya, 1978; Hama, 1950, 1978). Putting together these studies demonstrated that if the presumptive anterior archenteron roof before invagination is tested for an inductive effect under conditions that enable an immediate and direct contact of the mesoderm with the ectoderm, posterior differentiation is expressed. If a test method is used in which some time interval is required for the direct contact, like the conventional blastocoel test, then head structures including the archencephalic ones are expressed. On the other hand, the presumptive posterior archenteron roof always induces posterior differentiation, whether tested before or after invagination, and irrespective of the test methods. Thus expression of C-E always correlates with posterior differentiation. These observations led to the proposal that caudalization is mediated by the gradient of C-E (Yamada, 1950, 1978).

In timing and localization, the expression of posterior homeobox genes, mentioned above, closely coincides with the pattern of C-E described here: (1) in the neurula, the gradient of activity along the anteroposterior axis with the apex at posterior end; (2) the peak of activity in the late gastrula to the early neurula; (3) the persistence of activity at the tail tip after termination of the activity in all other regions; (4) the start of appearance of mesodermal Hox 3 RNA at MBT in harmony with the start of mesodermal C-E at late blastula and (5) the expression of ectodermal Xihbox 6 only after the induction (dorsalization) (Sharpe et al., 1987) also in harmony with the pattern of ectodermal C-E. However, the expression of some posterior homeobox genes in neural tissues (Carrasco and Malcinski, 1987; Ruiz i Altaba and Melton, 1989b; Ruiz i Altaba, 1990) cannot be correlated with the C-E pattern. Furthermore both posterior homeobox genes and C-E have independent evidence for their connection with caudalization. Thus the question should be asked whether posterior homeobox genes are involved in the control of C-E. It is also important to find out whether the contact of dorsalized ectoderm with the mesoderm expressing Xhox 3 leads to the expression of Xihbox 6 in the ectoderm as suggested by the C-E pattern.

The ability of divergent vertebrate tissues to induce in competent amphibian ectoderm the embryonic axis of various anteroposterior levels has been interpreted as due to the presence of factors controlling the anteroposterior levels of induction in those tissues that were called the heterogenous inducers (HI). This is the reason that in the past those HI have been extensively used for the analysis of anteroposterior differentiation, replacing the organizer. From the present standpoint, and in terms of the present model, the induction caused by HI can be interpreted in the following way. First the presence in HI of the dosalizing factor, which is widely distributed among tissues, enables the induction to occur in responding ectoderm. Second, the mesoder-malizing factors probably in the form of specific polypeptide growth factors are distributed in most HI and mesoderntalize a part of responding ectoderm. The induced mesoderm should contain dorsalizing factors. But more importantly, it may express the mesodermal posterior homeobox gene at various levels, depending on the type of growth factor involved, as demonstrated by the cited work of Ruiz i Altaba and Melton (1989b, 1990). The caudalization, which is obvious in the induction by many HI, should be attributed to the transcript of the gene in the inducing mesoderm. Thus, the caudalization factor is probably not present in HI itself. This means that HI cannot replace the organizer.

**Concluding remarks**

The concept inherent in the present model that the induction of different anteroposterior levels of CNS is not due to a number of independent, level-specific inducing factors as generally believed at the time of
proposal, but due to the combinatorial effects of two factors, one affecting the level of the dorsoventral axis, and the other affecting the level along the anteroposterior axis, is well supported by the cited experiments of Ruiz i Altaba and Albers (1990b, 1990) as well as by the recent morphogenetic analysis of Nieuwooji and Albers (1990). One question to be raised is why dorsalization is required in the expression of posterior differentiation mediated by the caudalizing factor. Is phosphorylation of some specific proteins caused by dorsalization essential in this regulation? Another aspect of the function of Xhox 3 transcript to be mentioned here is that its primary role may be to determine the posterior mode of mesodermal differentiation, and its role in ectodermal caudalization discussed in this review may be a secondary one.

As has been recently pointed out by Duprat et al. (1990), in order to understand embryonic induction one should look more closely at the nature of response. In this respect some progress is being made. In this review, PKC activation has been discussed as a candidate for the essential response in dorsalization, and the induced expression of ectodermal posterior homeobox gene has been proposed as a possible candidate for the response to caudalization. The transcript of Xhox 6 may directly mediate the posterior mode of neural differentiation.

The understanding of the inductive action of the organizer that is responsible for the emergence of CNS is an unfulfilled agenda for developmental biology for last 66 years. We are now in the exciting phase where the first clues for such an understanding are being furnished.

References


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