نموذج أجابة للفرقة تشريح مقارن وكيمياء انسجة تمهيدى ماجستير لمادة التشريح الجزيئى.

اسم الأمتحان:- التشريح الجزيئى (ح ت 602) .

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Benha University
Faculty of Science
Zoology Department

May Session,2016
Molecular Anatomy.
Time Allowed: 3hrs.

Premaster year students

Please illustrate your answers with a clear labeled diagrams whenever possible.

Answer the following questions:-

1.Give a brief account about <u>Three</u> of the followings:-
a. Animal cell. (15 marks).
b. Bacteria. (15 marks).
c. Bacteriophage.(15 marks).
d. Yeast.(15 marks).

2.In the light of your study about the molecular anatomy , give examples about using of mutants (36 marks).

3.Explain in detail how the genes play an important role in each of the formation (specifying and inducing) of limb fields, early limb bud and finally specifying of fore limb or hind limb. (39 marks)

With my best wishes,
Prof. Dr. Salwa Ibrahim.

اجابة السؤال الاول الجزيئية(ا)

Animal cell:

As more information about fundamental mechanisms in bacteria has been gained, increasing efforts have been made to study animal cells. Research with animal cells is exciting because we are beginning to understand such complex processes as hormonal regulation and the development of an egg into an adult organisms, and to gain some insight into the differences between normal cells and cancer cells. However, research with animal cells has proceeded much more slowly than work wit bacteria. There are two reasons for this. First, animal cells divide every 24 to 48 hours, whereas many bacteria divide every 25 to 50 minutes, so experiments with animal cells often take much longer than experiments with bacteria. Second, bacteria growing in culture are not significantly different from bacteria in nature, but experiments with animal cells require that the cells be removed from the animal and often separated from one another. Cells treated in this way have lost the normal route for receiving nutrients and are definity in an unnatural state. Many growth media that enable cells to grow in culture have been developed. They have been designed to keep the cells alive as long as possible, but they do not always maintain a normal state for the cell. The most obvious difference is that most cells taken from an organisms die within a few weeks. Furthermore, during that period of time the cells grow and divide, which differs from the normal quiescent (or inactive) state of cells in living organisms. A few cells survive and grow indefinitely; these are said to have been immortalized and have generated an established cell line. In time, these cells develop abnormalities in chromosome number (often extra chromosomes) and behave somewhat like tumor cells.

اجابة السؤال الاول الجزيئية (ب)

Bacteria

Bacteria are free- living unicellular organisms. They have a single chromosome, which is not enclosed in a nucleus (they are prokaryotes), and compared to eukaryotes they are simple in their physical organization. For all practical purposes, a bacterium can be thought of as a solution of several thousand chemicals and a few organized particles enclosed in a rigid cell wall.

Bacteria have many features that make them suitable objects for the study of fundamental biological processes. For example, they are grown easily and rapidly and, compared to cells in multicellular organisms, they are relatively simple in their needs. The bacterium that has served the field of molecular biology best is Escherichia coli (usually referred to as E. coli), which divides every 20 minutes at 37^{o}C under optimal conditions. Thus, a single cell becomes 10^{9} bacteria in about 20 hours. Bacteria can be grown in a liquid growth medium or on a solid surface. A population growing in a liquid medium is called a bacte3rial culture. If the liquid is a complex extract of biological material, it is called a broth. If the growth medium is a simple mixture containing no organic compounds other than a carbon source such as a sugar, it is called a minimal medium contains each of the ions Na+, K+, Mg2+, NH4+, Cl- , HPO2-4, and SO2-4, and a source of carbon source must be added for growth to occur, the bacterium is termed an auxotroph. For example, if the amino acid leucine is required in the growth medium, the bacterium is a leucine auxotroph; the genetic symbol for such a bacterium is Leu.l a prototroph the genetic symbol for such a bacterium is leu. A protocroph would be indicated leu. Bacteria are frequently grown on solid surfaces. The earliest surface used for growing bacteria was a slie of raw potato. This was later replaced by media solidified by gelatin. Because many

bacteria exrete enzymes that digest gelatin, an inert gelling agent was sought. Agar, which is a gelling agent obtained from a variety of seaweed and used extensively as a thickening agent in Japanese cuisine, is resistant to bacterial enzymes and has been universally used. Solid growth medium is called a nutrient agar if the agar was added to a broth rich in nutrients. Otherwise, it is called minimal agar. Solid media are typically laced in a petri dish. In lab jargon a petri dish containing a solid medium is called a plate and the act of depositing bacteria on the agar surface is called plating.

A bacterium growing on an agar surface divides. Since most bacteria are not very motile on a solid surface, the progeny bacteria remain very near the location of the original bacterium. The number of progeny increases so much that a visible cluster of bacteria appears. This cluster is called a bacterial colony formation allows one to determine the number of bacteria in a culture. For instance if 100cells are spread over the surface of a plate, 100 colonies will appear the next day.

Plating is a method for determining if a bacterium is an auxotroph. This is done in the following way. Minimal agar and nutrient agar plates are prepared. Several hundred bacteria are plated on each plate and the plates are incubated overnight in an oven. Several hundred colonies are subsequently found on the nutrient agar because it contains so many substances that it can satisfy the requirements of nearly any bacterium. If colonies are also found on the minimal agr, the bacterium is a protroph; ; if no colonies are found, it is an auxotroph and some required substance is not present in the minimal agar. Minimal plates are then prepared with various supplements. If the bacterium is a leucine auxotroph, the addition of leucine alone will enable a colony to form if both leucine and hisidine must be added, the bacterium is auxotrophic for both of these substances.

اجابة السؤال الاول الجزيئية (ج)

Bacteriophage

Bacteria are subject to attack by viruses. These small particles are called bacteriophage, or simply phage, and they are capable of growing only inside bacteria. Phag have been the object of choice for a great many types of experiments because they are much simpler than bacteria in their structures (usually having between two and ten components) as well as their life cycles and yet possess the most essential, if minimal, attributes of life.

Most phages contain only a few different types of molecules, usually several hundred protein molecules of one to ten types (depending on the complexity of the phage) and one nucleic acid molecule. The protein molecules are organized in one of three ways. In the most common mode the protein molecules form a protein shell called the coat or phage head, to which a tail is generally attached; the numceic acid molecule is contained in the head. Another form of a phage is a tailless head. The least common form is a filament in which the protein molecules form a tubular structure in which the nucleic acid is embedded. Phages are known that contain double stranded DNA (the most common variety), single stranded dna single stranded rna, and double stranded rna (least common).

Phage are parasites and cannot multiply except in a host bacterium. Thus, a phage must be able to enter a bacterium, multiply, and then escape. There are many ways by which this can be accomplished. However, a basi life cycle is outlined below and depicted.

The life cycle of a phage begins when a phage particle adsorbs to the surface of a susceptible bacterium. The phage nucleic acid then leaves the phage particle through the phage tail (if the phage has a tail) and enters the bacterium through the bacterial cell wall. In a complicated but understandable

way the phage essentially converts the bacterium to a phage synthesizing factory. Within about an hour, the time varying with the phage species, the infected bacterium bursts o lyses and several hundred progeny phage are released. The suspension of newly synthesized phage is called a phage lysate.

Phage multiply faster than bacteria. A typical bacterium doubles in about half an hour, while a single phage particle gives rise to more than 100 progeny in the same time period. Each of these phage can then infect more bacteria, and those released in this second cycle of infection can infect even more. Thus, in two hours there are four cycles of infection for both a bacterium and a phage yet a single bacterium has become 2 = 16 bacteria and a single phage becomes 100 = 10 phage particles.

By using procedures that make the bacterial cell membrane and cell wall permeable, infection can be initiated with free dna rather than by phage particles. This technique, which is called transfection, is exceedingly useful, as it allows an experimenter to alter the dna molecule either chemically or physically and then study the effect of the change by infecting a cell with the altered dna. Transfection is an essential procedure in genetic engineering and has been widely used in studying animal and plant viruses.

The life cycle of a phage is highly regulated, but in a slightly different way from the metabolic regulation of a bacterium. Phages are totally dependent on the metabolism of their host bacteria, so the regulatory systems of the hosts usually control the phage basi metabolic processes such as energy generation and synthesis of the precurors of dna, rna, and proteins. The job of an infecting phage is to reproduce itself by synthesizing its own nucleic acid and structural proteins, and finally to cause the bacterial cell wall to break so that progeny phage can escap. This requires that the various steps in phage production be regulated in time. Study of this regulation has been an important part of molecular biological research and has yielded a great deal

of information about baic processes in all cells. Some examples will be seen in.

Phage are counted by a technique called the plaque assay about 10 bacteria plus a phage sample are added to warm liquid agar, which is then poured onto solid agar where it hardens. The bacteria multiply, forming a turbid layer in the agar called a lawn. While the bacteria are multiplying, each phage adsorbs to one cell, which remain localized in the agar. These progeny phage adsorb to nearby bacteria and multiply again; several cycles of infection occur, giving rise to a clear transparent hole in the tubid layer. This clear area is called aplaque since each phage forms one plaque, the individual phage can be counted. Different phage mutants often produce characteristic identifiable plaques, making the technique useful for genetic analysis.

اجابة السؤال الاول الجزيئية (د)

Yeasts are unicellular organisms that have been used for millennia for producing wine and beer a great deal of early biochemical research was carried out with yeasts rather than bacteria, work stimulated mainly by interest in understanding and improving beer.

Yeast ells are propagated in the laboratory and counted in much the same way as bacteria. They grow in liquid suspensions in either chemically defined media or in complex broths. They also grow on a solid surface to form colonies. The multiplication mechanism of all but the fission yeasts differs from the simple splitting of a mature bacterium in that yeast ells do not divide but multiply by budding.

That is, each mother cell produces a daughter cell (a bud) by outgrowth from the cell wall of the mother. The daughter cell grows and matures and

can then also produce progeny by budding. The mother ell can bud many times.

In the past, most of the research effort in molecular biology has been with bacteria and viruses, because of their simplicity compared to eukaryotes. In recent years technological advances have made possible efficient and informative study of eukaryotes. The yeast saccharomyces cerevisiae has been an important object of study it has the genetic organization of eukaryotes and uses many regulatory strategies that are similar to higher organisms, yet the ease of handling and speed of growth are those encountred with typical microorganisms. Of particular interest also is the fact that saccharomyces has both haploid and diploid phases. Haploid cells are of two types, which can mate sexually to form a stable diploid cell line. In particular nutritional conditions diploids undergo meiosis, generating haploid sexual spores. This mating system allows detailed genetic experiments to be performed and makes yeast a useful system for the study of both genetic recombination and the mechanisms of meiosis.

Other unicellular eukaryotes, namely the alga chlamydomonas and the protozoan tertrahymena, also possess many of the attributes of yeast and are being used more frequently in eukaryotic molecular biology.

اجابة السؤال الثانى

Some examples for uses of mutants:-

Some of the most significant advances in molecular biology have come about through the analysis of mutants. In the following paragraphs the kinds of approaches that have been taken are described.

1-a mutant defines a funcitonn. For example, the intake of fe3+ ions by bacteria might be by passive diffusion through the cell membrane, or some

system might be responsible for the process. Wild type e. coli can take in the fe3+ ion from a 10-5 m solution, but mutants have been found that cannot do so unless the ion concentration is very high. This finding indicates that a genetically determined system for fe3+ intake exists, although the observation does not tell what this system is. Temperature sensitive mutants (mutants that exhibit a defect only above a particular temperature) are especially useful in defining functions. For example, temperature sensitive mutants of e. coli have been isolated that fail to synthesize dna. These mutants fall into at least then distinct classes, suggesting that there may be at least ten different steps, each involving separate proteins, which are required for dna synthesis. One of those mutants lacks a particular protein that is normally located in the cell membrane; the interpretation of such an experimental results is not unambiguous but does suggest that there is some connection between dna synthesis and the cell membrane.

2-mutants can introduce biochemical blocks that aid in the elucidation of metabolic pathways. The metabolism of the sugar galactose, for example, requires the activity of three distinct genes called galk, galt, and gale. If radioactive galactose c gal is added to a culture of gal cells, may different different radioactive comounds cana be found as the alactose is metabolized. At very early times after addition f c) al, thre relatd cmpoudsre detectable © galcose 1-phosphate (gal 1-1p), (C) uridnediphospogalato UDP- al), and (C) uridine diposphogcose UDP glu) diferenmutnt genes wil block difesteps of themetaboli pathway. I h cl is a galk muant, the c gal labelsifound only in galactse. S thegalk gene isknown to b eresponsiblefor the mabolic pahay. If the cell is gal kmutant, the c allabel if found noly in galctose. Tus he galk gene is known tobe responsible or te fst metaboli tep. If thmuant gal is usd, al-p ccmulates. Tus the frst step in te eracitn sequence s found to be the conversion of glatose to gal – 1- by the galk gene product (namely, the

enzyme galactokinase). If a gale mutant is used, some gal 1-p is found but the principal radiochemical is udp- gal. thus the biochemical pathway must be

3-mutants enable one to learn about metabolic regulation. Many mutants have been isolated that alter the amount of a particular protein that is synthesized or the way the amount synthesized responds to external signals. These mutants define regulatory systems. For example, the enzymes corresponding to the galk, galt, and gale genes are normally not present in bacteria but appear only after galactose is added to the growth medium. However, mutants have been isolated in which these enzymes are always present, whether or not galactose is also present. This indicates that some gene is responsible for turning the system of enzyme production on and off, and this regulatory gene must be responsive to the presence and absence of galactose.

4-mutants enable a biochemical entity to be matched with a biological function or an intracellular protein. For many years an e. coli enzyme called dna polymerase I was studied in great detail. Purified polymerase I is capable of synthesizing dna in vitro, so it was belived that this enzyme was also responsible for in vivo bacteria dna synthesis. However, an e. coli mutant (pol a) was isolated in which the activity of polymerase I was reduced 50-fold yet the mutant bacterium grew and synthesized dna normally. This observation suggested strongly that polymerase I could not be the only enzyme that synthesized intracellular dna. Indeed, biochemical analysis of cell extracts of the pola mutant showed the existence of two other enzyme polymerase II and polymerase III, which could, when purified, also synthesize dna. In further study, a temperature senstivie mutantion in a gene called dnae was found to be unable to synthesize dna at 42oC, although synthesis was normal at 30c. the three enzymes, polymerases I, II, and III, were isolated from cultures of the dnae mutant and each enzyme was assayed.

Although polymerases I and II were active at both 30C and 42C, polymerase III was active at 30C but not at 42C, so that polymerase III was determined to be the product of the dnae gene and the enzyme responsible for intracellular dna synthesis.

5-mutants locate the site of action of external agents. The antibiotic rifampicin prevents synthesis of rna. When first discovered, it was precursor molecules (by binding to dna and thereby preventing the dna from being transcribed into rna or by binding to rna polymerase, the enzyme responsible for synthesizing rna. Mutants were isolated that were resistant to rifampicin. These mutants were of two types those in which the bacterial cell wall was altered so that rifampicin could not enter the cell (an uninformative type of mutant) and those in which the rna polymerase was slightly altered. The finding of the latter mutants proved that the antibiotic acts by binding to rna polymerase.

6-mutants can indicate relations between apparently unrelated systems.

Bacteriophage , which normally adsorbs to and grows in e. coli, fails to adsorb to a bacterial mutant unable to metabolize the sugar maltose. Such failure is not associated with mutants incapable of metabolizing other sugars or with anyother phages, and this knowledge implicated some product or agent of maltose metabolism in the adsorption of.

أجابة السؤال الثالث

Formation of the limb bud

Specification of the limb fields hox genes and retinoic acid

Limbs will not form just anywhere along the body axis. Rather, there are discrete positions where limb fields are generated. Using the techniques described in chapter researchers have precisely localized the limb fields of

many vertebrate species. Interestingly, in all land vertebrates, there are only four limb buds per embryo, and they are always opposite each other with respect to the midline. Although the limbs of different vertebrates differ with respect to which somite level they arise from their position is constant with respect to the level of hox gene expression along the anterior positerior axis in fishes in which the pectoral and pelvic fins correspond to the anterior and posterior limbs, respectively, amphibians, birds and mammals, the forelimb buds are found at the most anterior expression region of hoxc the position of the first thoratic vertebra. The lateraly plate mesoderm in the limb field is also special in that it will induce myoblasts to migrate out from the somite and enter the limb bud, no other region of the lateral plate mesoderm will do that.

Retinoic acid appears to be critical for the initiation of limb bud outgrowth, since blocking the synthesis of retionoic acid with certain drugs preents limb bud initiation suggested that gradient of retinoic acid along the anterior posterior axis might active certain homeotic genes in particular cells and thereby specify them to become included in the limb field. The source of this retinoic acid is probably hensen's node the specification of limb fields by retinoic acid activated hox genes might explain a bizarre observation made by mohanty hejmadi and colleagues 1992 and repeated by maden (1993). When the stails of tadpoles were amputated and the stumps exposed to retinoic acid during the first days of regeneration the tadpoles regenerated several legs from the tail stump it appears that the retinoic acid caused a homeotic transformation in the regenerating tail by respecifying the tail tissue as a limb forming pelvic region.

Inducation of the early limb bud fibroblast growth factors

Limb development begins when mesenchyme cells protliferate from the somatic layer of the limb field lateral plate mesoderm (limb skeletal

precursors) and from the somites limb muscle precursor fig. these cells accumulate under the epidermal tissue to create a circular bulge called a limb bud. Recent studies on the earliest stages of limb formation have shown that the signal for limb bud formation comes from the lateral plate mesoderm cells that will become the prospective limb mesenchyme. These cells secrete the paracrine factor fgf10 fgf10 is capable of initiating the limb forming. Actions between the ectoderm and the mesoderm. If beads comtaining FGF10 are placed ectopically beneath the flank ectoderm extra limbs emerge

Specification of forelimb or hindlimb: Tbx4 and Tbx5

The limb buds have to be specified as being those of either the forelimb or the hindlimb. How are these distinguished? In 1996 gibson brown and colleagues made a tantalizing correlation: the gene encoding the Tbx5 transcription factor is transcribed in mouse forelimbs, while the gene encoding the closely related transcription factor tbx4 is expressed in hindlmbs. Could these two transcription factors be involved in directing forelimb versus hindlimb specificity the loss of function data were equivocal humans heterozygous for the tbx5 gene have holt oram syndrome, characterized by abnormalities of the heart and upper limbs. The legs are not affected, but neither are the arms transformed into a pair of legs.

In 1998 and 1999 , however, several laboratories provided gain of function evidence the tbx4 and tbx5 specify hindlimbs and forelimbs, respectively. First if fgf secreting beads were used to include an ectopic limb between the chick hindlimb and forelimb buds, the type of limb produced was determined by the tbx protein expressed. Those buds induced by placing fgf beads close to the hindlimb (opposite sometie 25) expressed tbx4 and became hindlimbs. Those buds induced close to the forelimb (opposite somite 17) expressed tbx5 and developed as forelimbs tissue expressed tbx5 in the

anterior portion of the limb and tbx4 in the posterior protein of the limb. These limbs developed developed as chimeric structures, with the anterior resembling a forelimb and the poseterior resembling a hindlimb moreover when a chick embryo was made to express tbx4 throughout the flank tissue (by infecting the tissue with a virus that expressed tbx4 limbs induced in the anterior region of the flank often became legs insetead of wings thus tbx4 and tbx5 appear to be critical in instructing the limbs to become hindlimbs and forelimbs, respectively.

Induction of the apical ectodermal ridge

As mesenchyme cells enter the limb region, they secrete factors that induce the overlying ectoderm to form a structure called the apical ectodermal ridge (aer). This ridge runs along the distal margin of the limb bud and will be come a major signaling center for the developing limb. Its roles include (1) maintaining the mesenchyme beneath it in a plastic prodliferating phase that enables the linear (proximal distal growth of the limb; maintaining the expression of those moleules that generate the anterior posterior (thumbpinky) axis; and interacting with the proteins specifying the anterior posterior and dorsal ventral axes so that each cell is given instructions on how to differentiate.

The factor secreated by the mesenchyme cells to induce the aer is probably fgf10 fgf10 is capable of inducing the aer in the competent ectoderm between the dorsal and ventral sides of the embryo. This junction is important. In mutants in which the limb bud is dorsalized and there is no dorsal ventral junction (as in the chick mutant limbless), the aer fails to form and limb development ceases.

Generating the proximal distal axis of the limb

The apical ectodermal ridge the ectodermal component the proximal distal growth and differentiation of the limb bud is made possible by a series of interactions between the limb bud mesenchyme and the aer.

Thus, although the mesenchyme cells induce and sustatin the aer and determine the type of limb to be formed, the aer is responsible for the sustained outgrowth and development of the limb the aer keeps the mesenchyme cells directly beneath it in a state of mitotic proliferation and prevents them from forming cartilage.

The progress zone: the mesodermal component the proximal distal axis is defined only after the induction of the apical ectodermal ridge by the underlying mesoderm. The limb bud elongates by means of the profliferation of the mesenchyme cells underneath the aer. This region of cell division is called the progress zone, and it extends about 200 m in from the aer. Molecules from the aer are thought to keep the progress zone mesenchyme cells dividing, and it is now through that fgfs are the molecules responsible when the aer moved from an early limb bud only the most proximal parts of the stylopod are made. However, if an fgf containing bead is placed in the hole left by the removal of the aer, a normal limb will form.

When the mesenchyme cells leave the progress zone, they differentiate in a regionally specific manner. The first cells leaving the progress zone form proximal (stylopod) structures; those cells that have undergone numerous divisions in the progress zone become the more distal structures therefore, if the aer is removed from an early stage wing bud, the cells of the progress zone stop dividing and only a humerus forms. If the aer is removed slightly later, humerus, radius, and ulna form.

The mitoic state of the progress zone is maintained by interacitons between the fef proteins of the progress zone and of the aer fgf10 secretion by the mesenchyme cells induces the aer and it also induces the aer to express

fgf8 the fgf8 secreted by the aer reciprocates by maintating the mitotic activity of the progress zone mesenchyme cells.

Hox genes and the specification of the proximal distal axis

The type of structure formed along the proximal distal axis is specified by the hox enes. The products of the hox genes have already played role in specifying the place where the limbs will form. Now they will play a second role in specifiying whether a particular mesenchymal cell will become (abdb- like) portions (paralogues 9- stylopod, zeugopod or autopod. The 5` 13) of the hoax and hoxd complexes appear to be active in the fore limb buds of mice. Based on the expression pattern of specific genes, and on naturally occurring and gene knockout mutations, davis and colleagues (1995) proposed a model wherein 16.14) for instance, when they knocked out all four loci for the paralogous genes haxa -11 and hoxd- 11, the resulting mice lacked the unlna and radius of their forelimbs similarly knockoing out all four hoax 13 and hoxd 13 loci resulted in loss of the autopod humans homozygous for a hoxd 13 mutation show abnormalities of the hands and feet wherin the digits fuse, and human patients with homozygous mutant alleles of hoxa13 also have deformities of their autopods in both mice and humans, the autopod the most distal portion of the limb is affected by the loss of function of the most 5` hox genes.

The mechanism by which hox genes could specifify the proximal distal axis is not yet understood, but one clue comes from the analysis of chicken hoax 13. Ectopic expression of this gene which is usually expressed in the distal ends of developing chick limbs appears to make the cells expressing it stickier. This in turn would cause the cartilaginous nodules to condense in specific ways.

As the limb grows outward, the pattern of hox gene expression changes. When the styloopod is forming hoxd and hod10 are expressed in the

progress zone mesenchyme when the zeugopod bones are being formed the pattern shift remarkably, displaying a nested sequence of hoxd gene expression. The posterior region expresses all the hoxd genes from hoxd 9 to hoxd 13 while only hoxd 9 is expressed anteriorly. In the third phase of limb development, when the autopod is forming, there is a further redpolyment of hox gene products. Hoxd is no longer expressed. Rather hoax 13 is expressed in the anterior tip of the limb bud and in a band marking the boundary of the autopod. Hoxd products join those of hoax 13 in the anterior region of the limb bud, while hoax 12, hoax 11, and hoxd 10-12 are expressed throughout the posterior two thirds of the limb bud.

The action of sonic hedgehog. When sonic hedgehog was first shown to define the zpa, it was thought to act as a morphogen. In other words, it was thought to diffuse from the zpa where it was being synthesized and to form a concentration gradient from the posterior to the anterior of the limb bud. However, recent research has provided evidence that sonic hedgehog protein (or its active amino terminal region does not diffuse outside the zpa it is now thought that sonic hedgehog works by initiating and sustaining a cascade of other proteins, such as bmp2 and bmp7 a gradient of bmps may emanate from the zpa and specify the digits.

However it works, sonic hedgehog (directly or with help from the bmp cascalde regulates the expression of the 5` hoxd genes. The transition from phase I to phase II hox expression patterns is coincident with sonic hedgehog expression in the zpa moreover, transplantation of anterior margin of the limb bud at this stage leads to the formation of mirror image patterns of hoxd gene expression and results in mirror image digit patterns.

انتهت الاجابة النموذجية للاسئلة