MOLECULAR CONCEPT OF ORGANIZATION IN THE CONTEXT OF DEVELOPMENTAL BIOLOGY

BY

Name of the teacher

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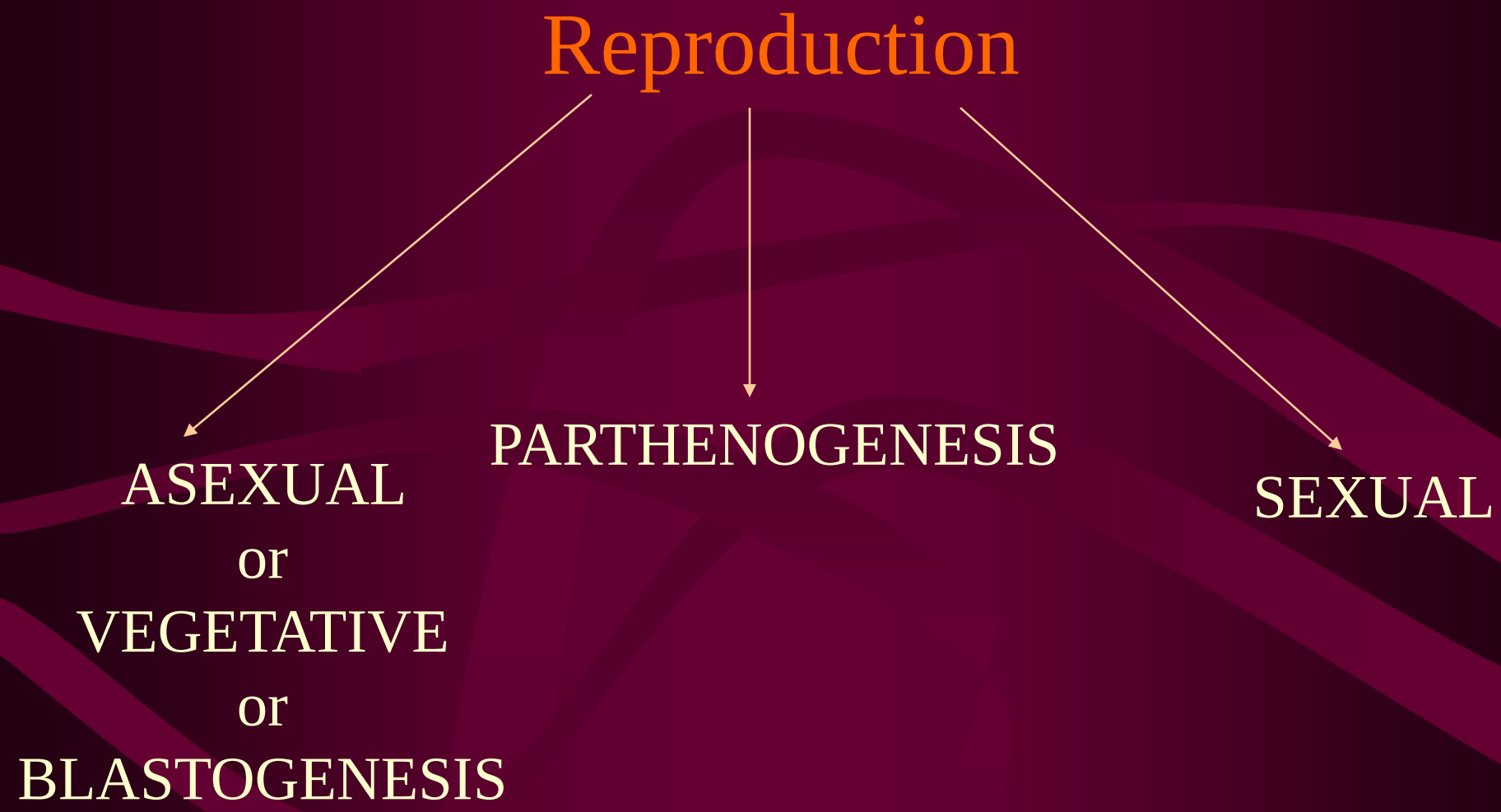
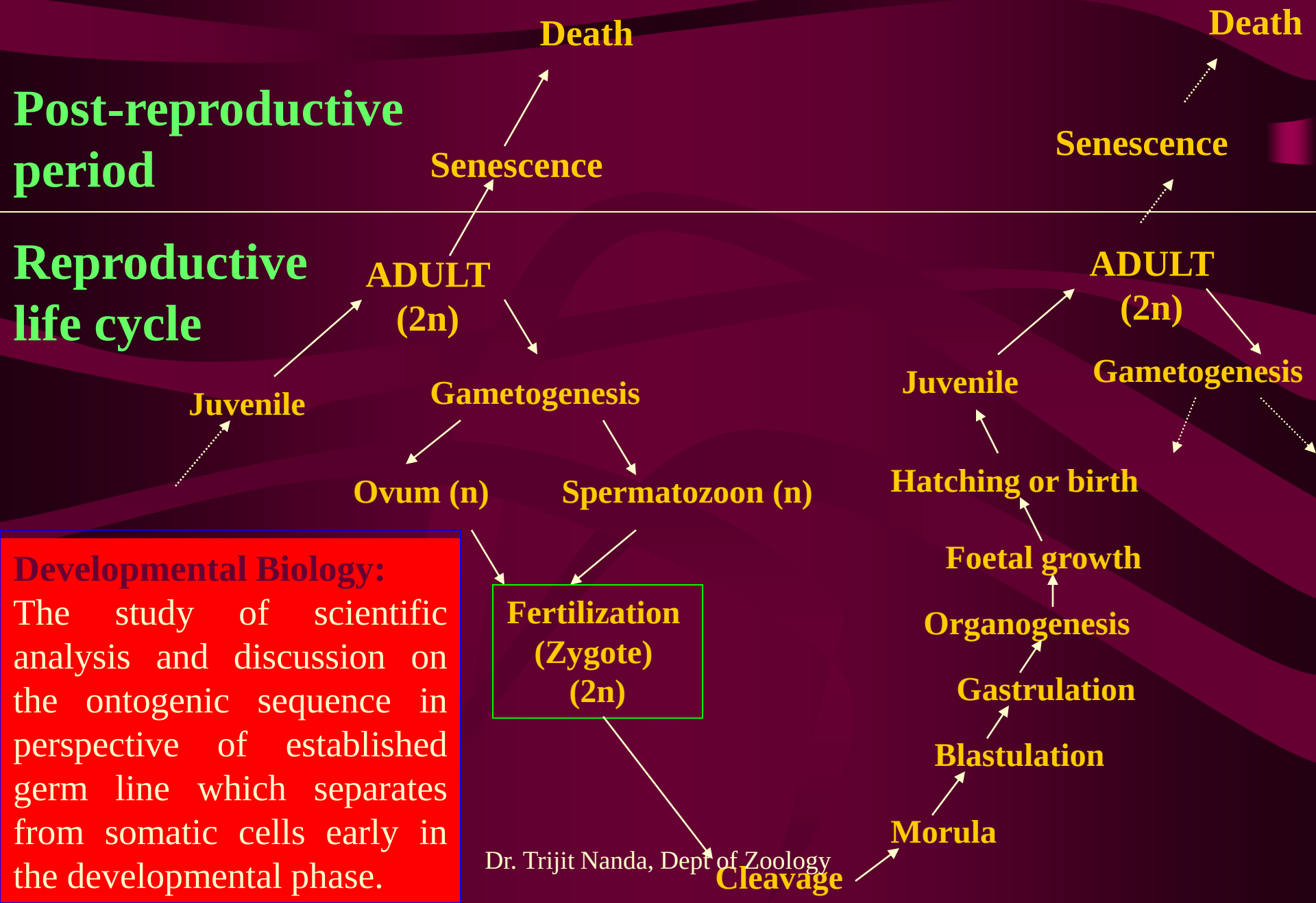
Reproduction – CONTINUTY OF GENERATION



Major Phases in the life cycle of a typical vertebrate



Developmental Biology:
The study of scientific analysis and discussion on the ontogenic sequence in perspective of established germ line which separates from somatic cells early in the developmental phase.

Organizer Concept

♂ Male + Female ♀

Fertilization

Zygote

Repeated cleavage

Blastomeres

Grow Divide Differentiate

Complex Organism

Early gastrulation blue print of the future organ system established

Depending upon

Specific relationships of a particular (assigned) group of tissues of the developing embryo

Inductor or organizer

Cluster of cells in one part of embryo

Transmits chemical stimulus

EVOCATOR

To differentiate

Responsive tissues/ cells

PARTICULAR DEVELOPMENTAL FATE

MORPHOGENETIC EFFECT PRODUCED IS COINED AS EMBRYONIC INDUCTION

INDUCTION AND COMPETENCE

The kind of interaction at close range between two or more cells/tissues of different histories and properties - *Induction*

INDUCTION

INDUCER

Tissue A ⇢ **Tissue B**

RESPONDER

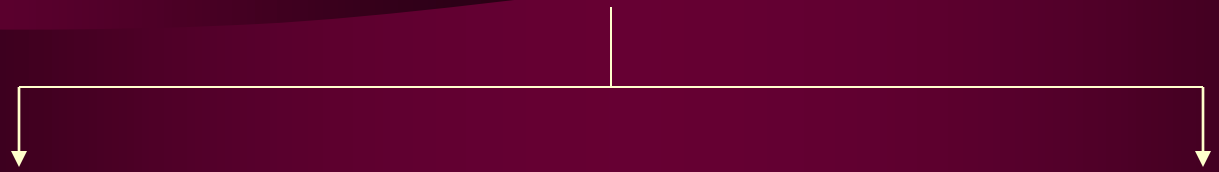
Induced tissue

Changes the cellular behaviour

The ability to respond to a specific inductive signal - Competence – *Actively acquired condition*

PAX 6 protein in the developing mammalian eye competent to respond to the inductive signal coined as *Competence factor*

INDUCTIVE INTERACTION



INSTRUCTIVE

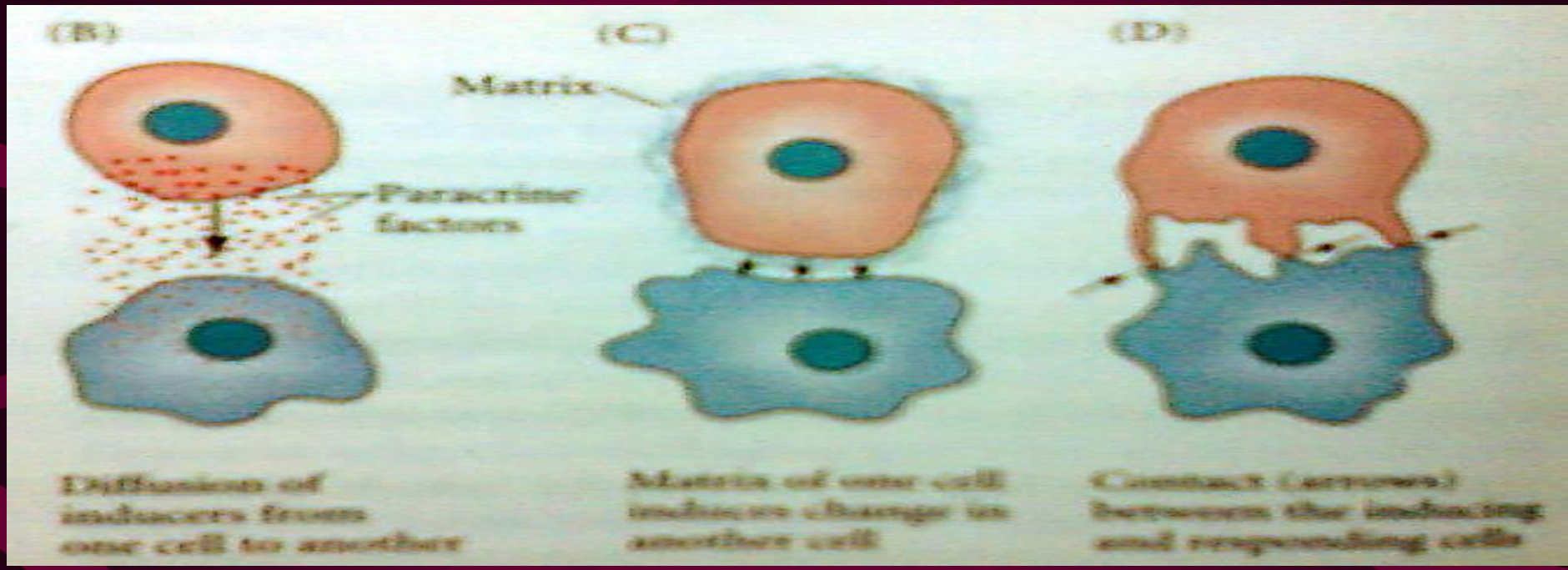
Responsive tissue has the option of forming more than one type of tissues depending upon the nature of inductive stimulus

PERMISSIVE

Responding tissue contains all the potentials that are to be expressed and needs only an environment that allows the expression of these traits

PARACRINE FACTORS

How are the signals between inducer and responder transmitted?



Diffusion of inducers from one cell to other

Matrix of one cell induces change in other cell

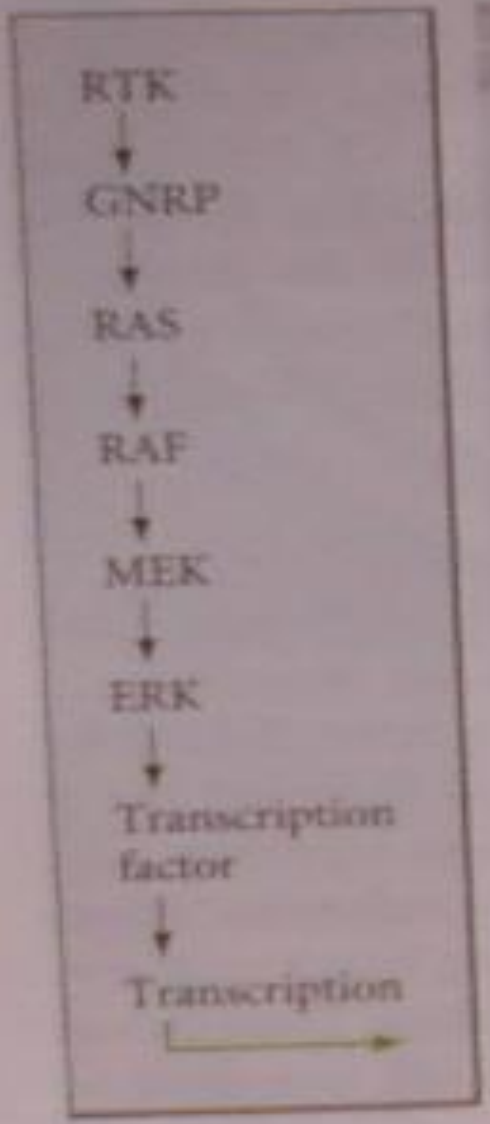
Contact (arrows) between inducing and responding cells

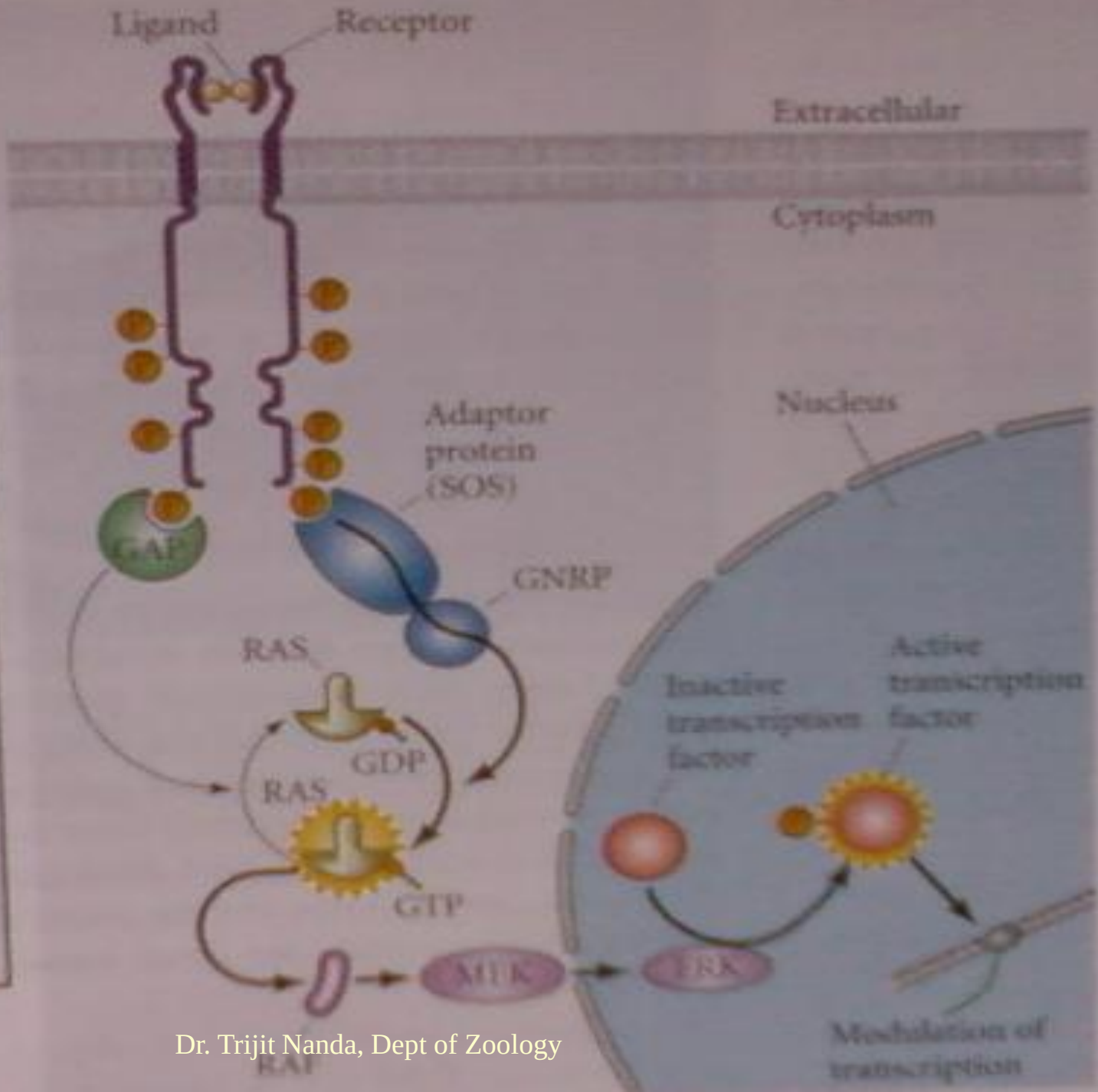
CELL SURFACE RECEPTORS AND THEIR SIGNAL TRANSDUCTION PATHWAYS

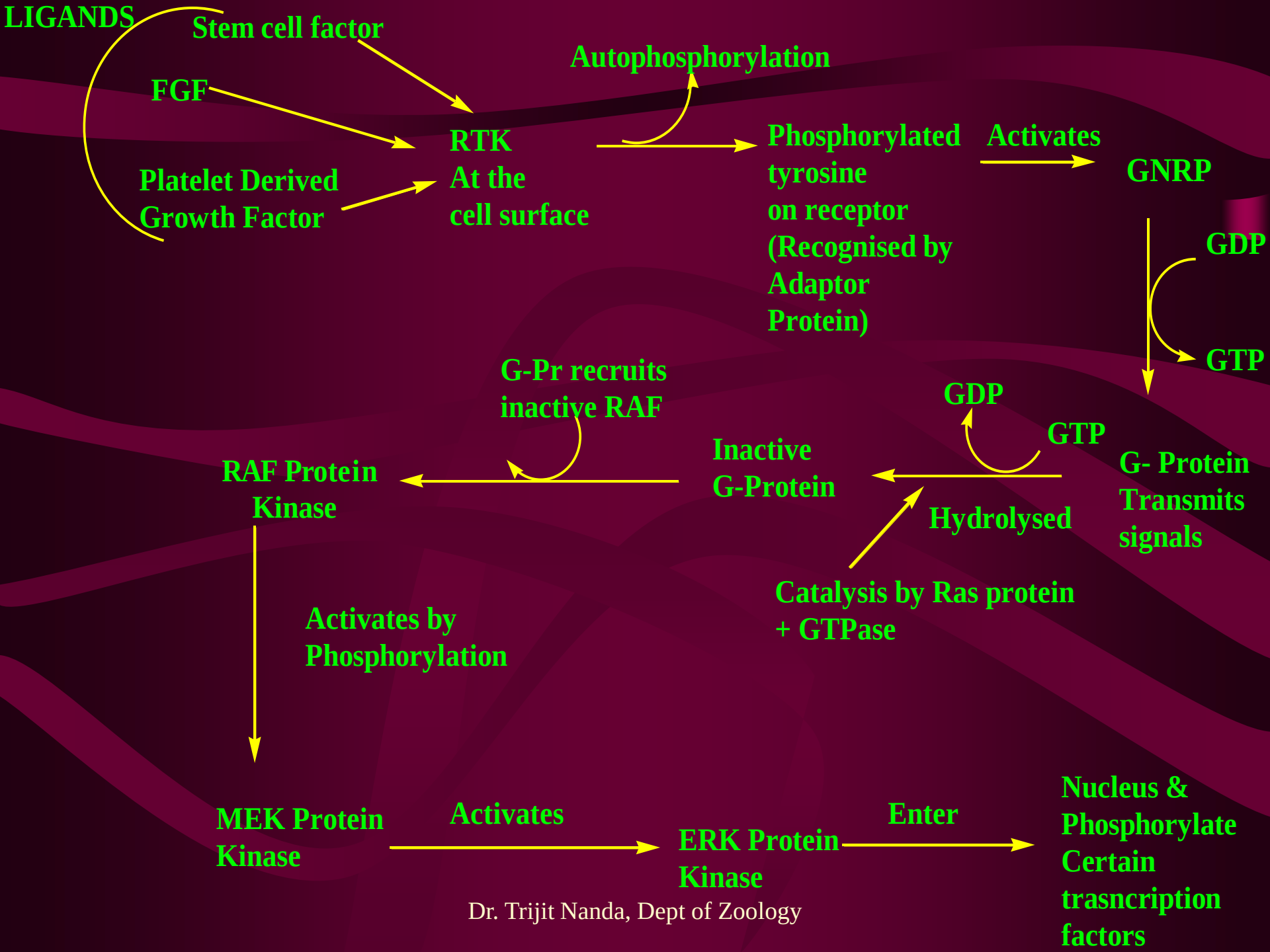
The pathways between cell membrane and genome

Steps involved:

- Ligand (paracrine factor) binds its receptor in the ECS
- Ligand induces conformational changes in the receptor structure
- Transmission of transmembrane information to the cytoplasmic domain
- The conformational change in the cytoplasmic domain-induces enzymatic activities


RTK
GNRP
RAS
RAF
MEK
ERK
Transcription factor
Transcription


Ligand
Receptor
Extracellular
Cytoplasm
Adaptor protein (SOS)
GAP
GNRP
RAS
GDP
RAS
GTP
MEK
ERK
Nucleus
Inactive transcription factor
Active transcription factor
Modulation of transcription


LIGANDS
Stem cell factor
FGF
Platelet Derived
Growth Factor
RTK
At the
cell surface
Autophosphorylation
Phosphorylated
tyrosine
on receptor
(Recognised by
Adaptor
Protein)
Activates
GNRP
GDP
GTP
G-Pr recruits
inactive RAF
GDP
GTP
RAF Protein
Kinase
Inactive
G-Protein
G- Protein
Transmits
signals
Hydrolysed
Catalysis by Ras protein
+ GTPase
Activates by
Phosphorylation
MEK Protein
Kinase
Activates
ERK Protein
Kinase
Enter
Nucleus &
Phosphorylate
Certain
trasncription
factors

"A TRIBUTE TO THE TRUE ORGANIZERS"

A piece of the upper blastopore lip of an amphibian embryo undergoing gastrulation exerts an organizing effect on its environment in such a way that, if transplanted to an indifferent region of another embryo, it causes there the formation of a secondary embryonic anlage. Such a piece can therefore be designated as a Organizer.

Hans Spemann

Hilde Mangold

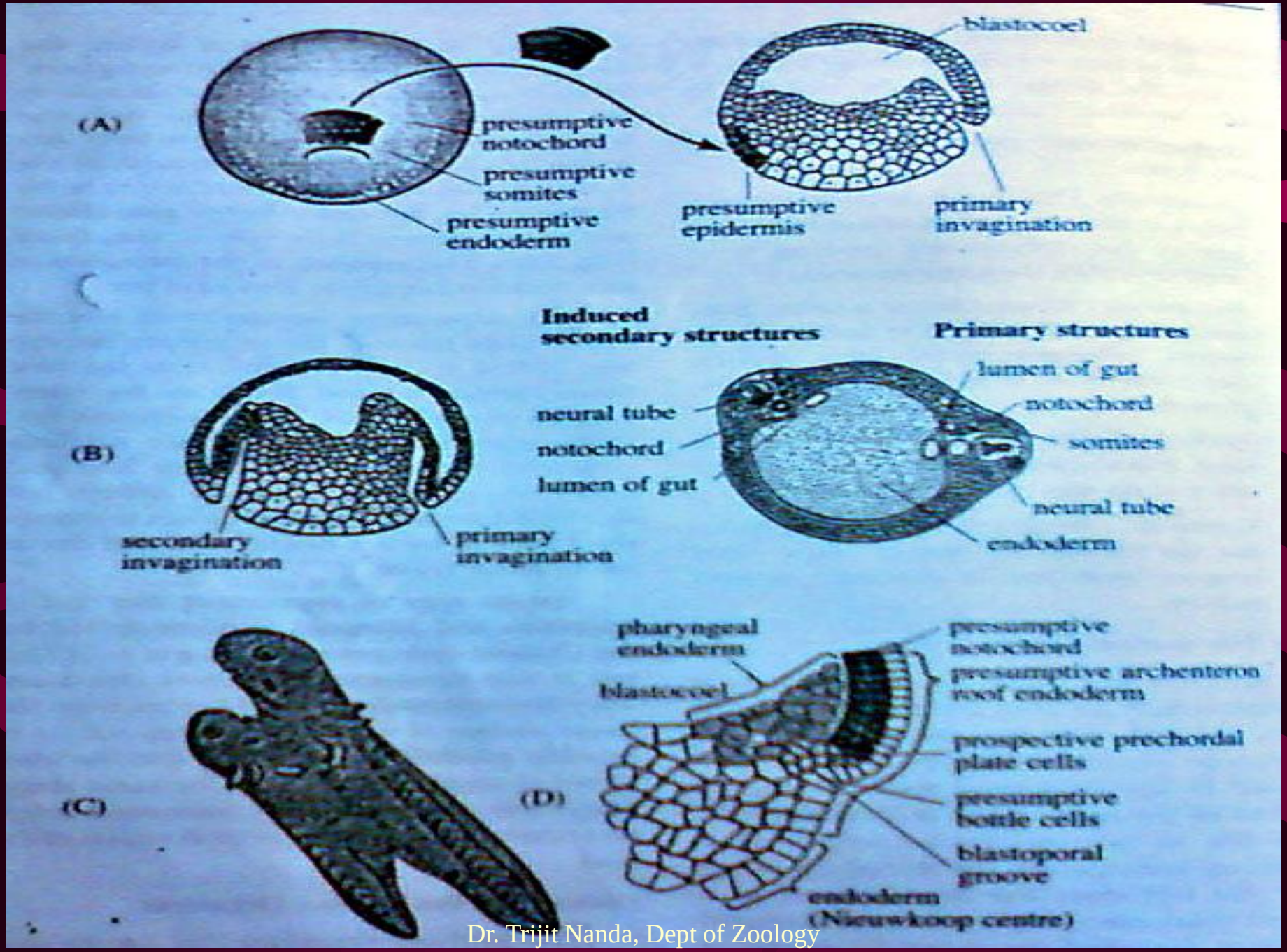
The Primary Embryonic Induction

The transplantation experiment conducted in 1924 by Hans Spemann and his pupil Hilde Mangold

- Showed that, of all the tissues in the early gastrula, only one has its fate determined - the dorsal lip of the blastopore, which was derived from the gray crescent cytoplasm.

- When this dorsal lip material was taken from pigmented *Triturus taeniatus* and transplanted into the presumptive belly skin region of the non-pigmented *T. cristatus* of the same age, then it not only continued to be the blastopore lip, but also initiated gastrulation and embryogenesis in the surrounding tissue

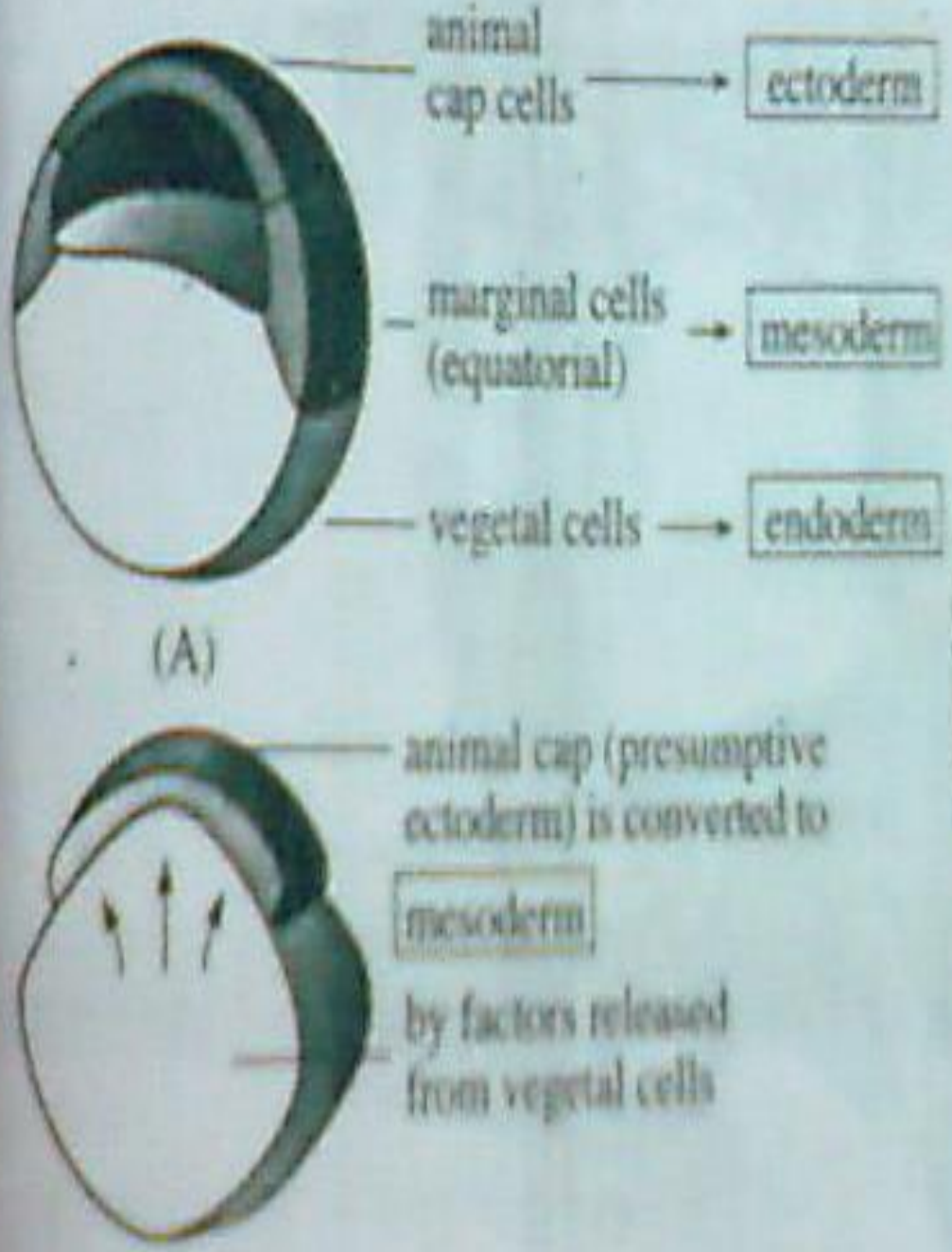
  This resulted in the formation of two conjoined embryos instead of one.


(A)
presumptive notochord
presumptive somites
presumptive endoderm
blastocoel
presumptive epidermis
primary invagination
(B)
Induced secondary structures
Primary structures
neural tube
notochord
lumen of gut
secondary invagination
primary invagination
lumen of gut
notochord
somites
neural tube
endoderm
(C)
(D)
pharyngeal endoderm
blastocoel
presumptive notochord
presumptive archenteron roof endoderm
prospective prechordal plate cells
presumptive bottle cells
blastoporal groove
endoderm (Nieuwkoop centre)

The Nieuwkoop center

Peter Nieuwkoop **demonstrated how the dorsal blastoporal lip obtained its properties.**

- Demonstrated that the properties of the newly formed mesoderm were induced by vegetal (presumptive endoderm) cells lying beneath it.
- Nieuwkoop removed the equatorial cells (presumptive mesoderm) from a blastula and showed that neither the animal cap (presumptive ectoderm) nor the vegetal cap (presumptive endoderm) produced any mesodermal tissue.
- When the two caps were applied one against the other, the animal cap cells were induced to form mesodermal structures such as notochord, muscles, kidney cells and blood cells.
- The dorsal most vegetal cells of the blastula are capable of inducing the organizer. These cells are called the Nieuwkoop center.


animal cap cells
ectoderm
marginal cells (equatorial)
mesoderm
vegetal cells
endoderm
(A)
animal cap (presumptive ectoderm) is converted to
mesoderm
by factors released from vegetal cells
(B)
organizer
dorsal mesoderm-inducing signals
Nieuwkoop centre
mesoderm-inducing signals
(C)

Molecular setup of the Nieuwkoop center

1. The endoderm in *Xenopus*, induces the formation of mesoderm due to the presence of *Xenopus brachyury* (Xbra) gene.
2. The Xbra protein is a transcription factor that activates the genes that produce mesoderm specific proteins.
3. All the cells of the vegetal area are able to induce the overlying marginal cells to become mesoderm.
4. Only the dorsal most marginal cells become the organizer.
5. The factor that forms the Nieuwkoop center at this region is a multifunctional protein, called β-catenin, that acts as a nuclear transcription factor.
6. β-catenin in *Xenopus* embryos, begin to accumulate at the dorsal region of the egg during the cytoplasmic movements of fertilization.
7. Initially the cells containing β-catenin is present both in the Nieuwkoop center and the organizer regions, but by late cleavage it comes to lie specifically in the Nieuwkoop center.
8. β-catenin is essential for forming the dorsal axis.

Conclusion:

The organizer tissue serves the following five major functions

It has the ability to become dorsal mesoderm (pre – chordal plate, chordamesoderm etc.)

It has the ability to dorsalize the surrounding mesoderm into lateral mesoderm.

It has the ability to induce the dorsal ectoderm into neural ectoderm.

It has the ability to subsequently transform the neural ectoderm into the neural tube.

It initiates the movements of gastrulation.

Recently it is found that the endoderm releases a signal protein called activin that induce the formation of mesoderm prior to gastrulation. This is evidenced through experimentation - when isolated ectoderm cultured with activin and consequently ectoderm turned mesoderm in gastrulation. The ingracing notochordal cells later release another signal protein follistatin which otherwise inactivating activin available in the endoderm. Therefore a mechanism is being pursued wherein notochord has the ability to maintain follistatin secretion and surmounts the effects of activin. There after an inducer coming out from the notochord itself which is known as noggin to produce neural plate only.

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