



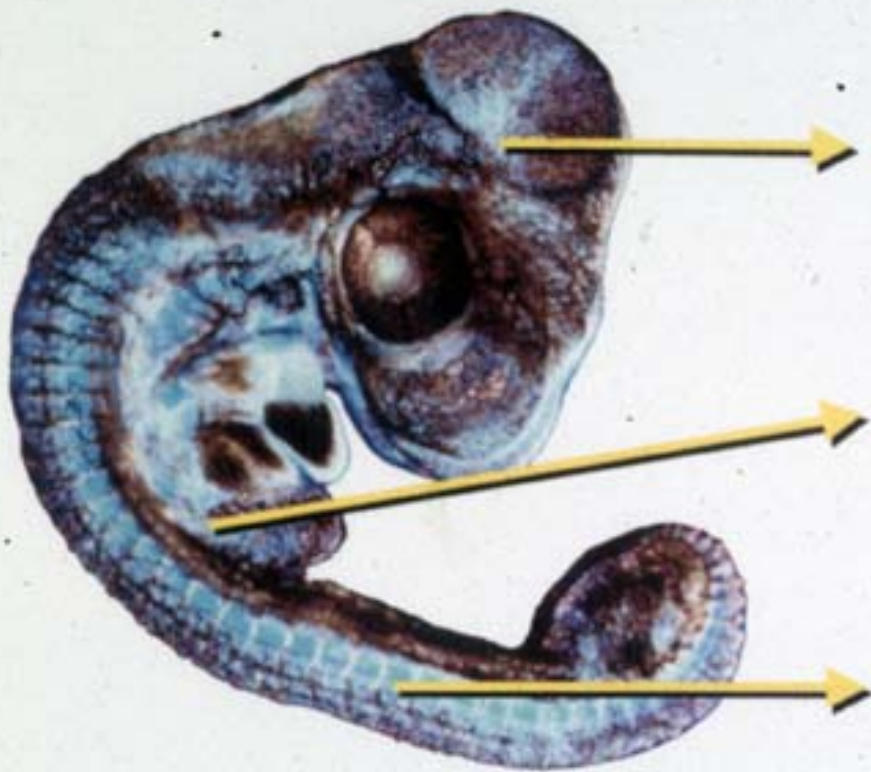
Michael W. Chapman

- **Born: Newberry, Michigan**
- **B.S. - University of California, Davis**
- **M.D. - University of California, San Francisco**
- **Residency - University of California, San Francisco**
- **Royal National Orthopaedic Hospital**
- **US Army, Belgium, Wurzburg, Germany**
- **NIH Int. Res. Fellow. AO Res. Institute**
- **1979-2000 UC Davis, Chair Orthopaedics**
- **Orthopaedic Trauma & Reconstruction**

Post-Traumatic Arthritis

- **Repo & Finlay - 1997**
- **Newberry & Haut - 1998**
- **Grodzinsky & Hunziker - 1998**
- **Zhang, Vrahas, Baratta and Rosler - 1999**





**Cranial
Neural Crest**



**Craniofacial
Skeleton**

**Lateral Plate
Mesoderm**



**Appendicular
Skeleton
(limbs)**

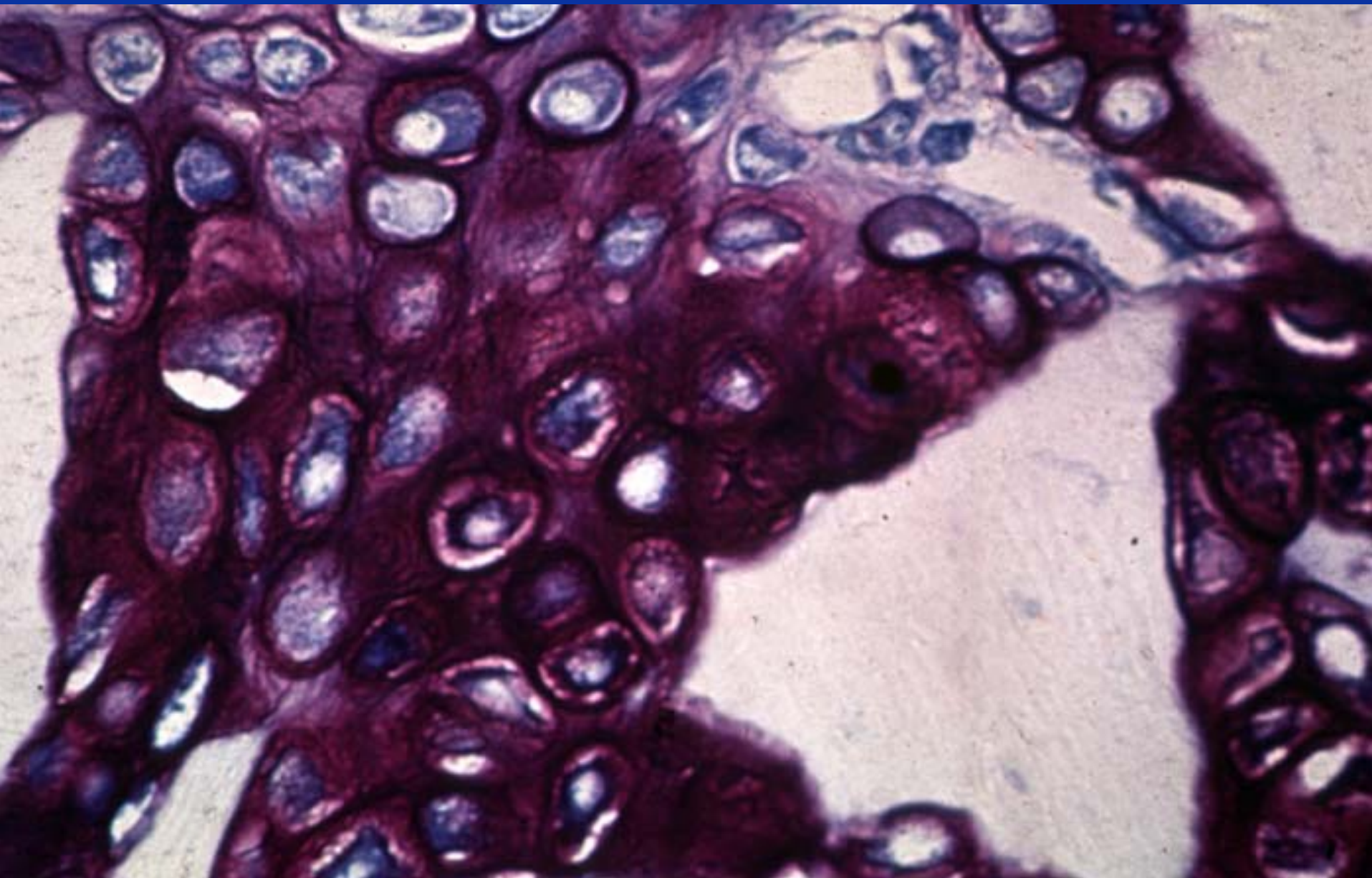
**Sclerotome
of Somite**



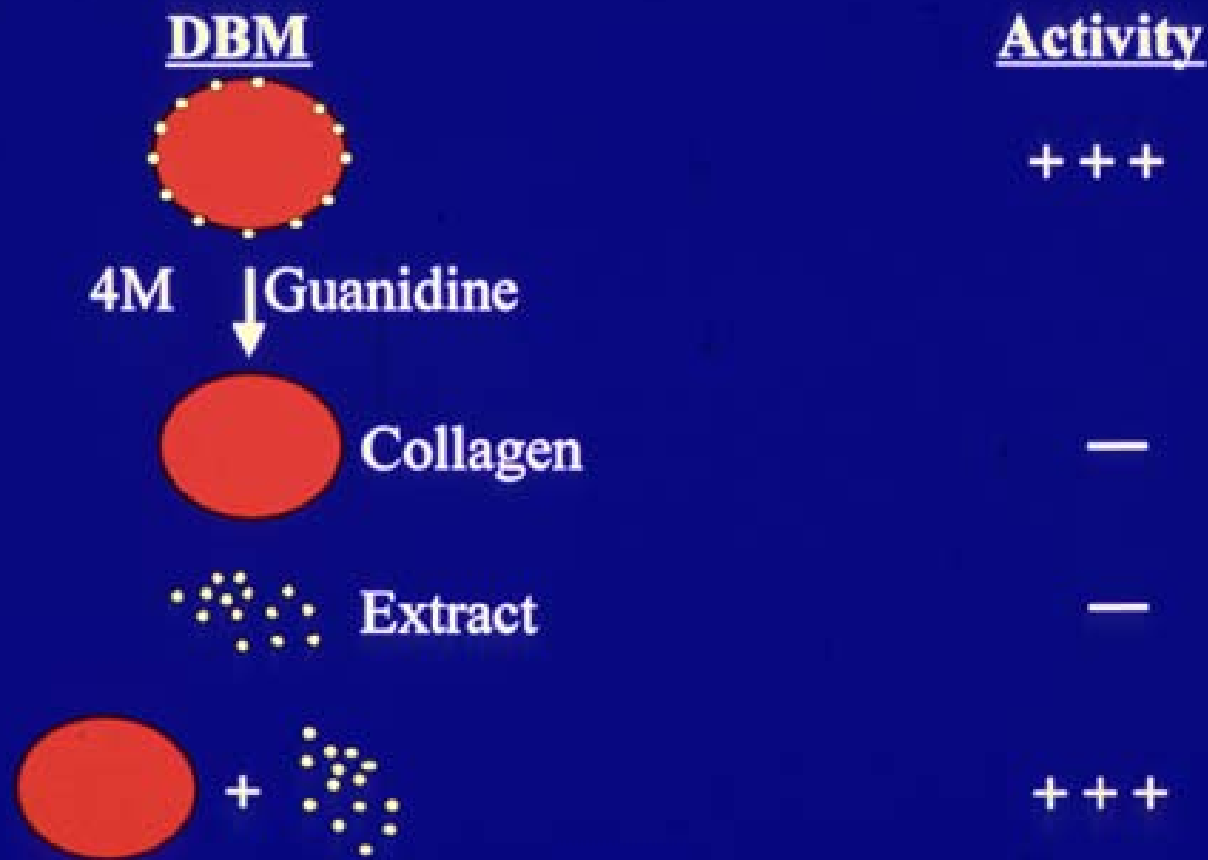
**Axial
Skeleton
(spine)**

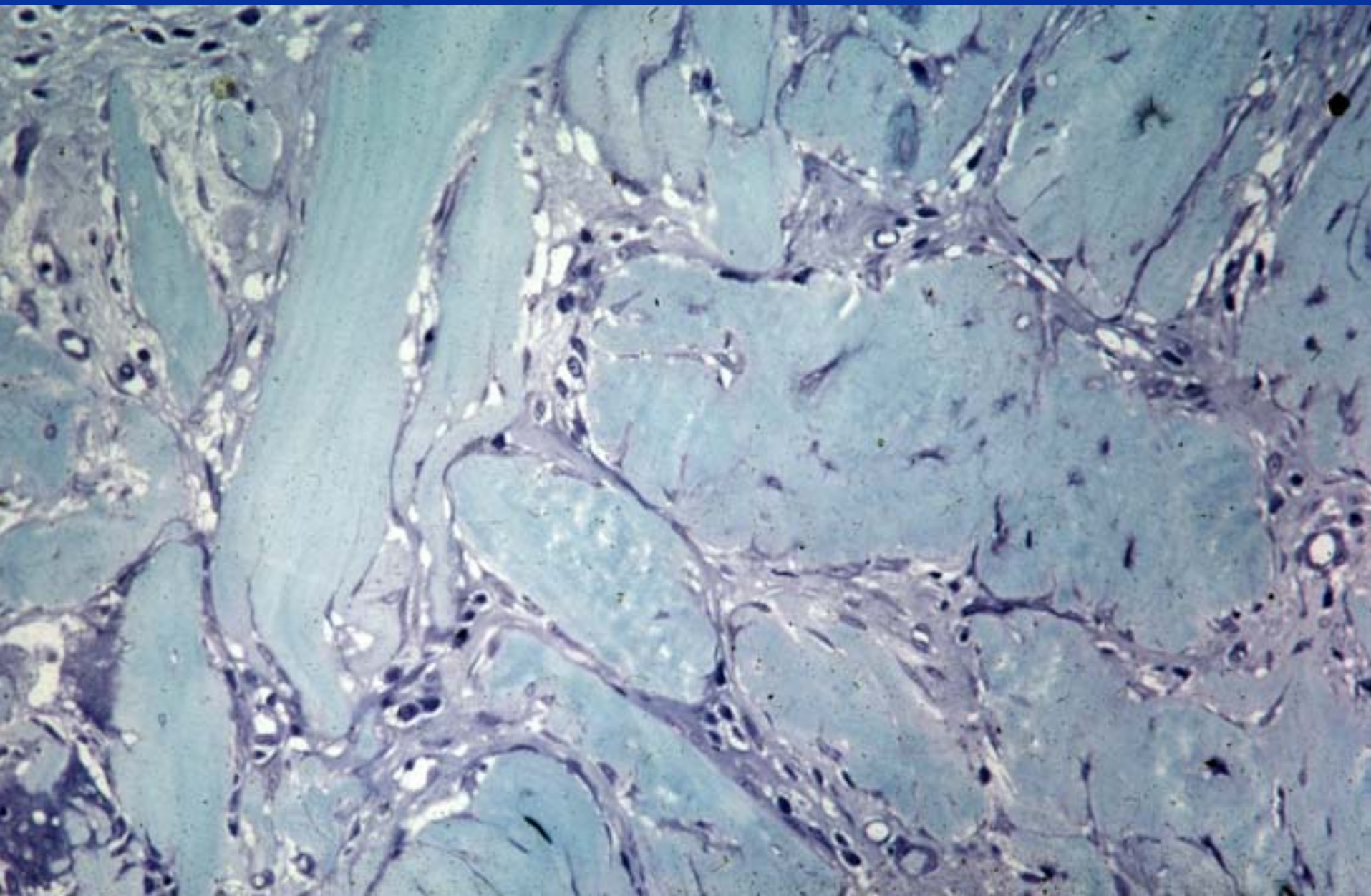
CARTILAGE DEVELOPMENT

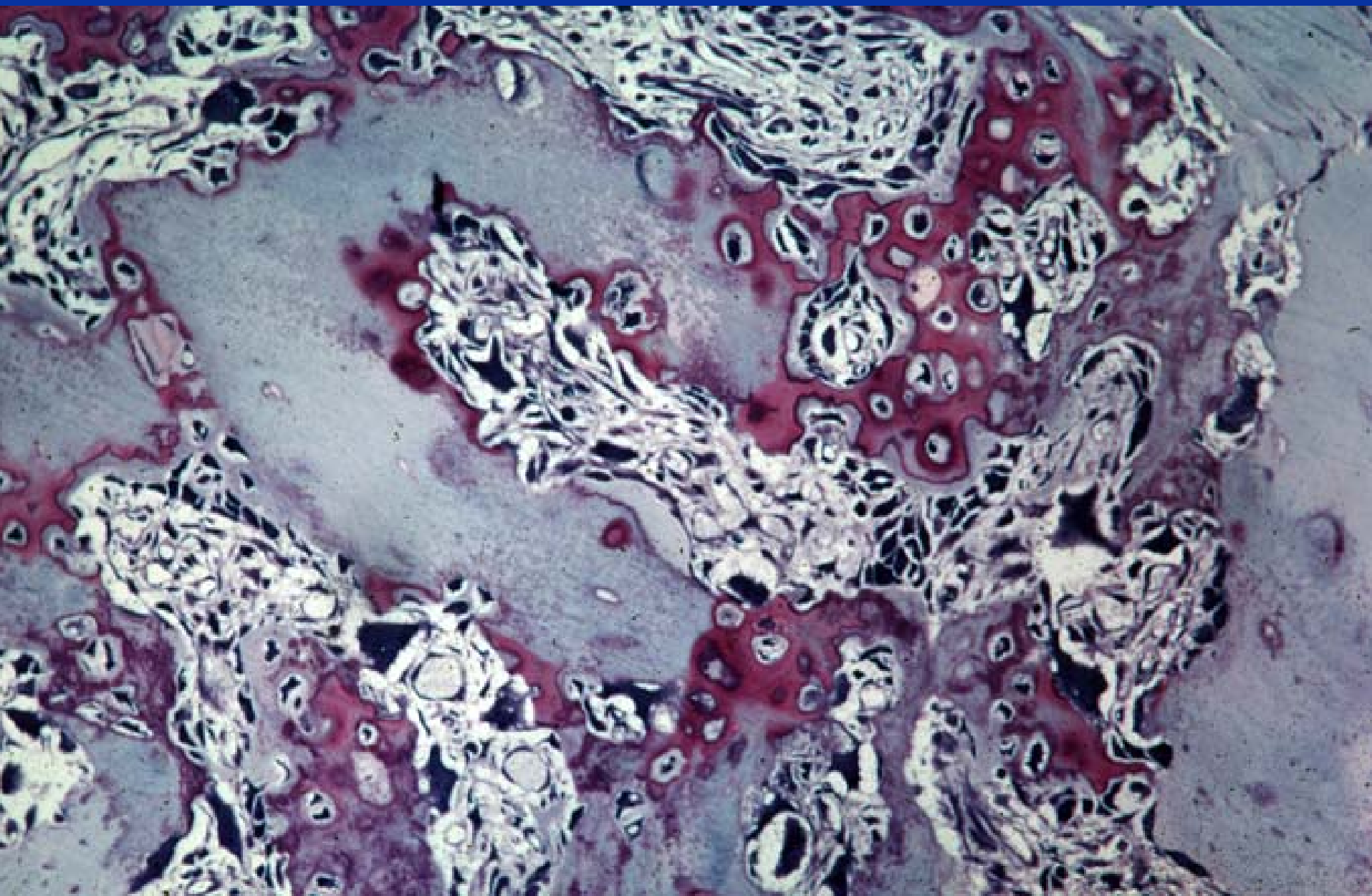
- **PATTERN FORMATION**
- **CELL DIFFERENTIATION**
- **GROWTH**
- **MAINTENANCE**
- **AGING**

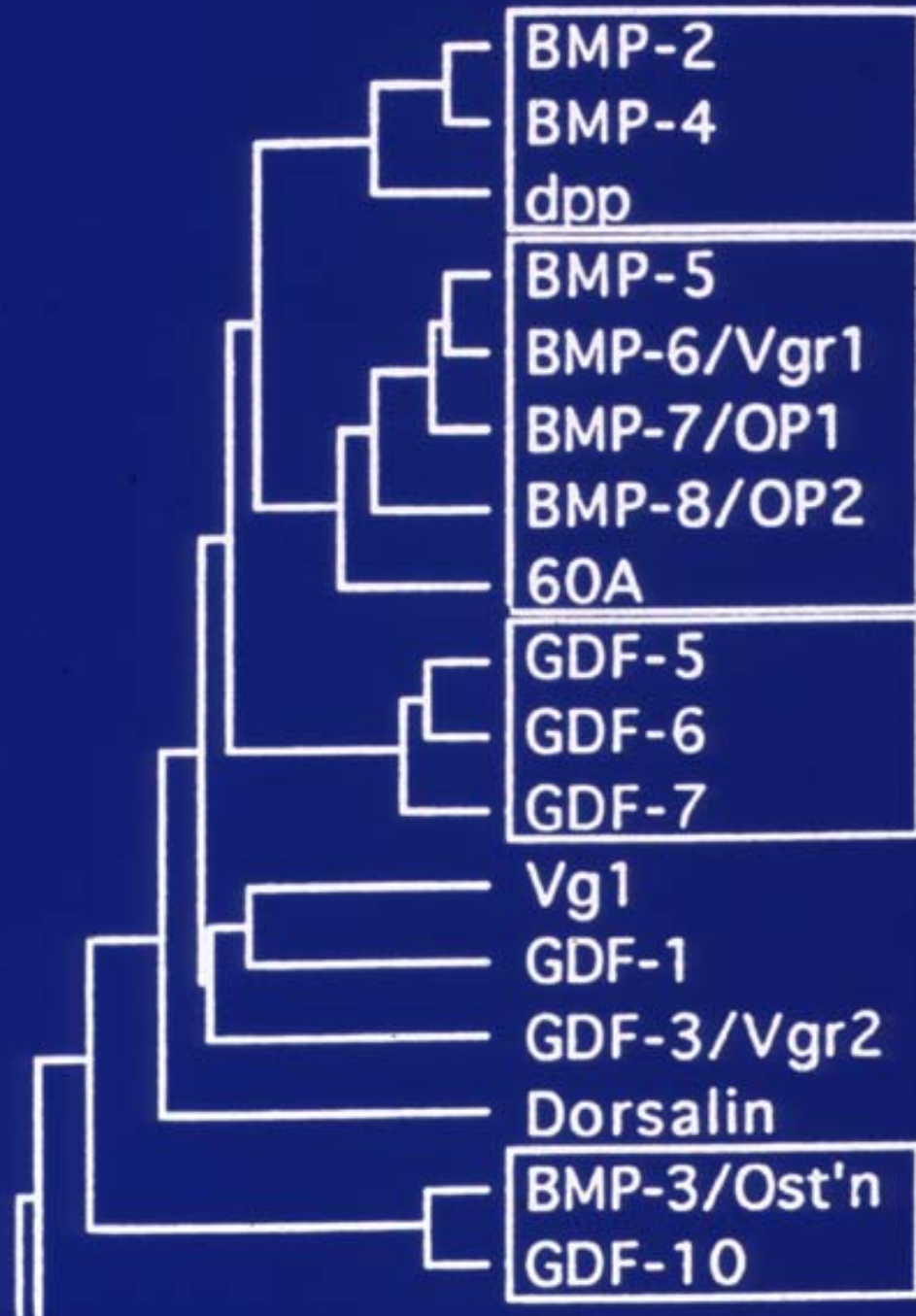


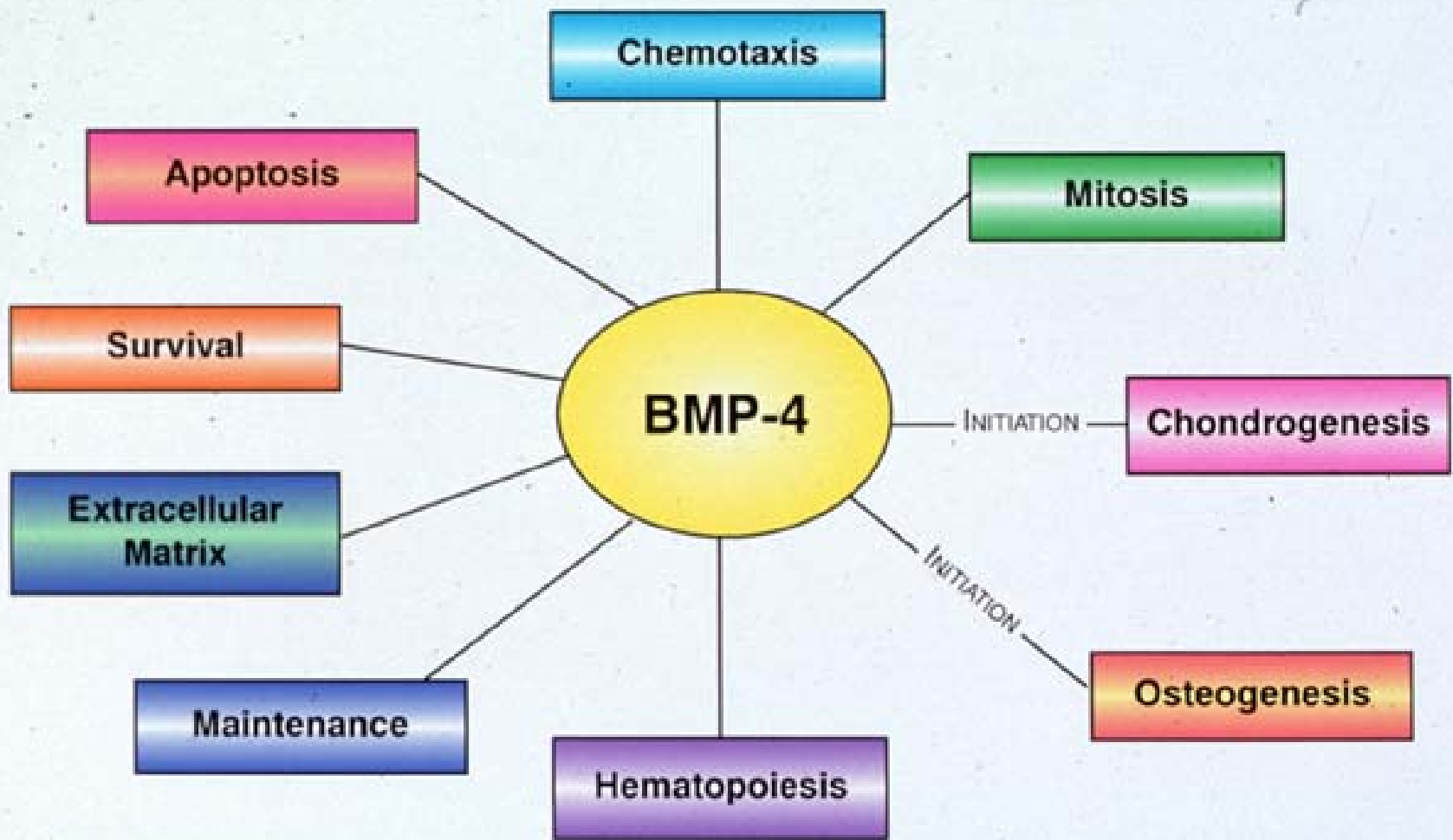
Dissociative Extraction and Reconstitution

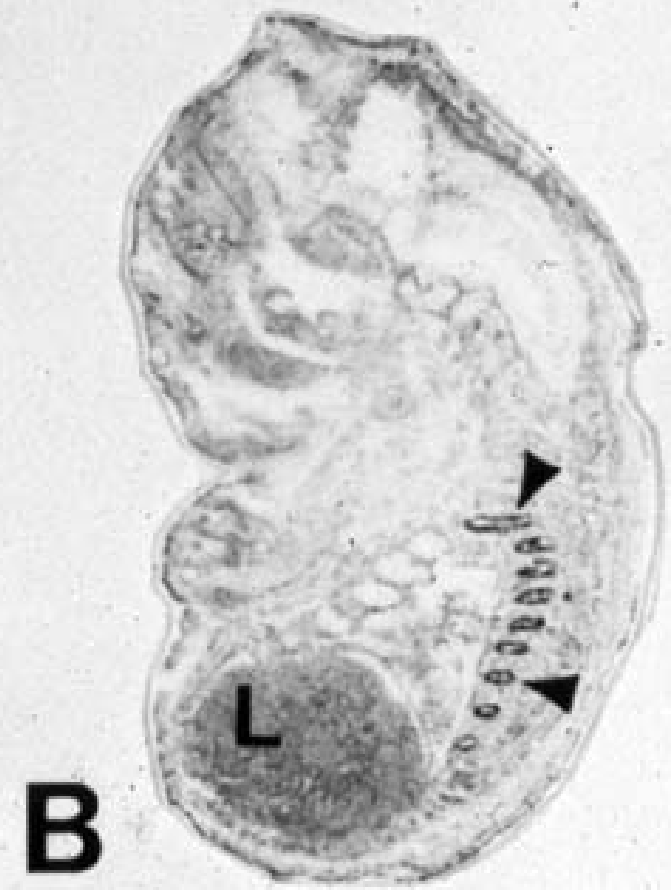
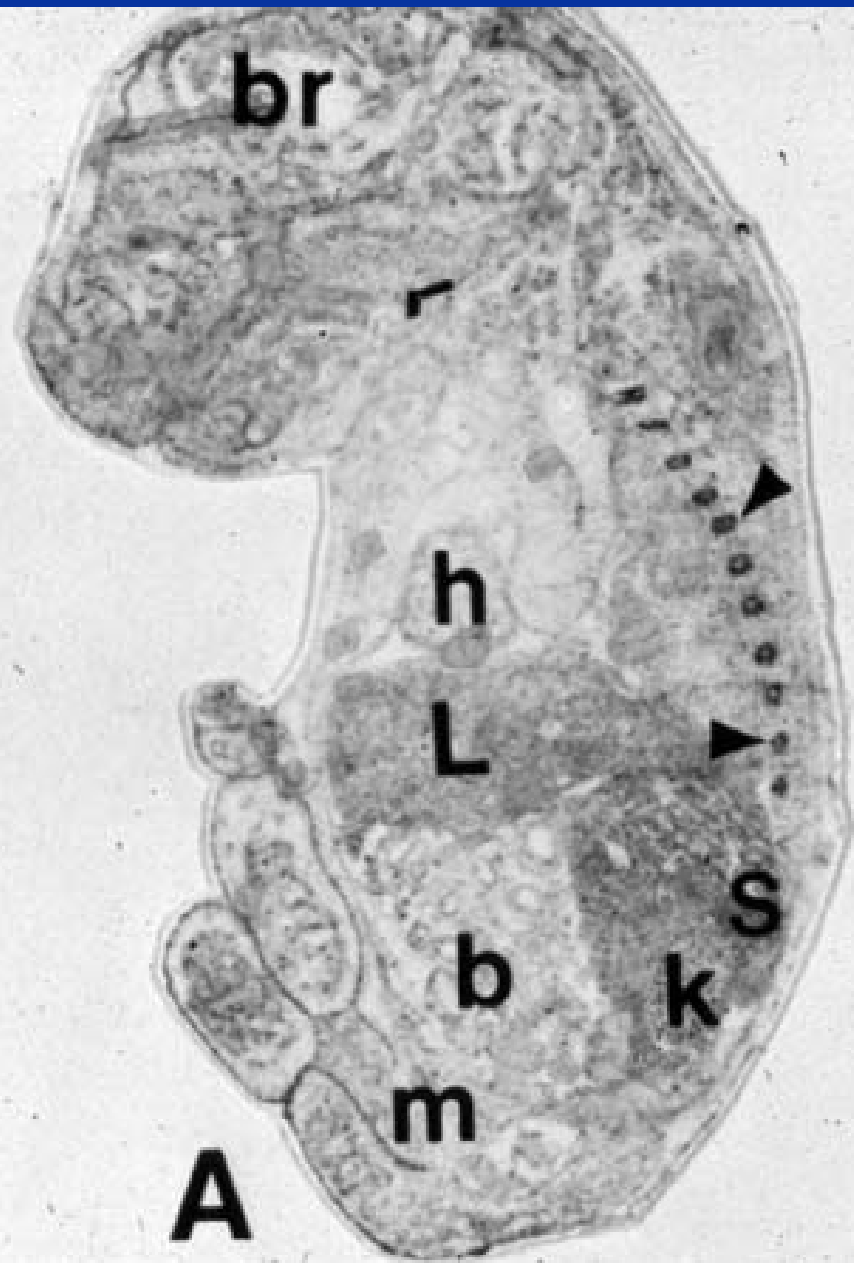












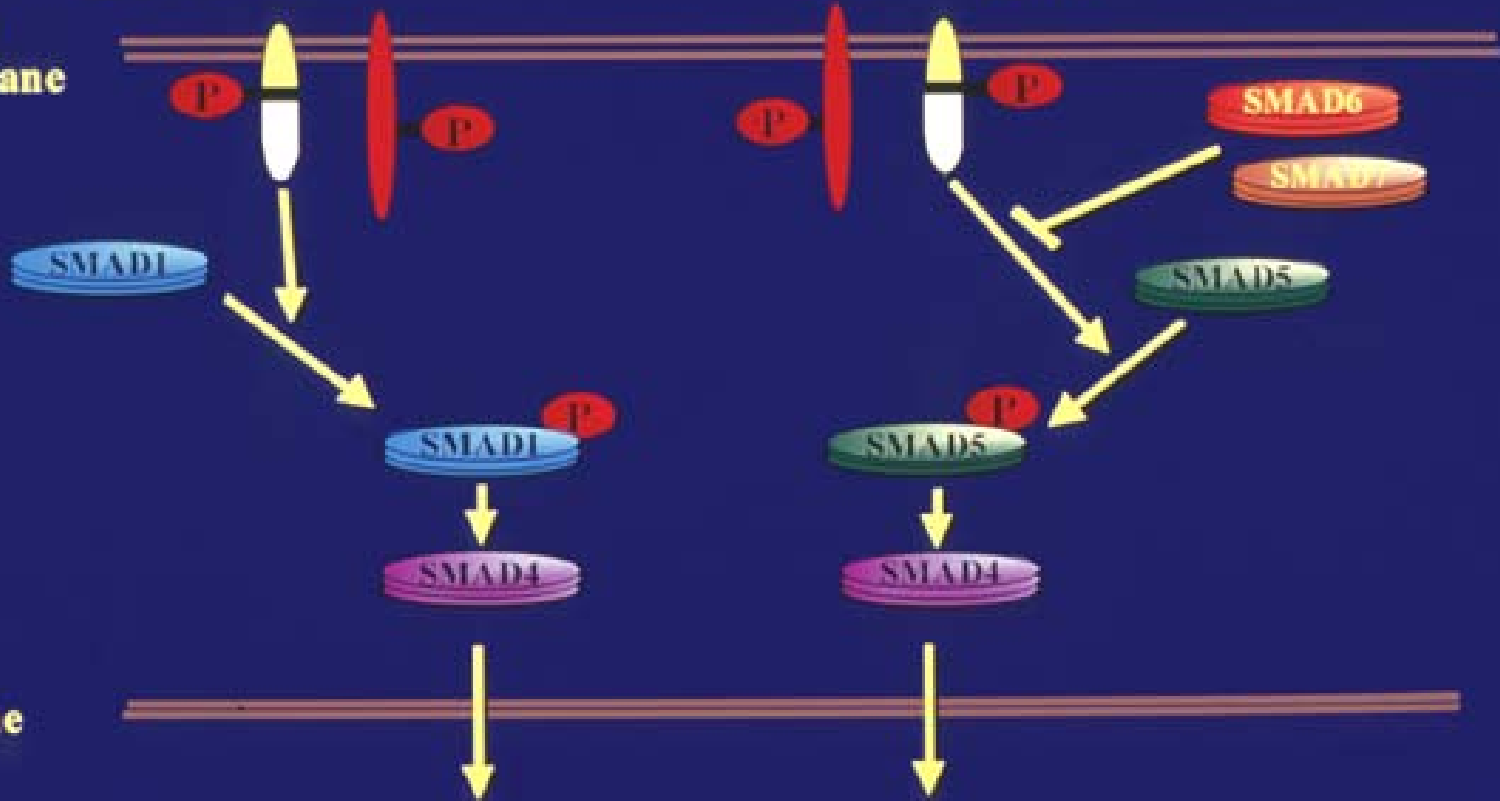
EXTRACELLULAR MATRIX
COLLAGENS I AND IV
HEPARAN SULFATE

NOGGIN
CHORDIN
FUNCTIONAL BPs

BMP 

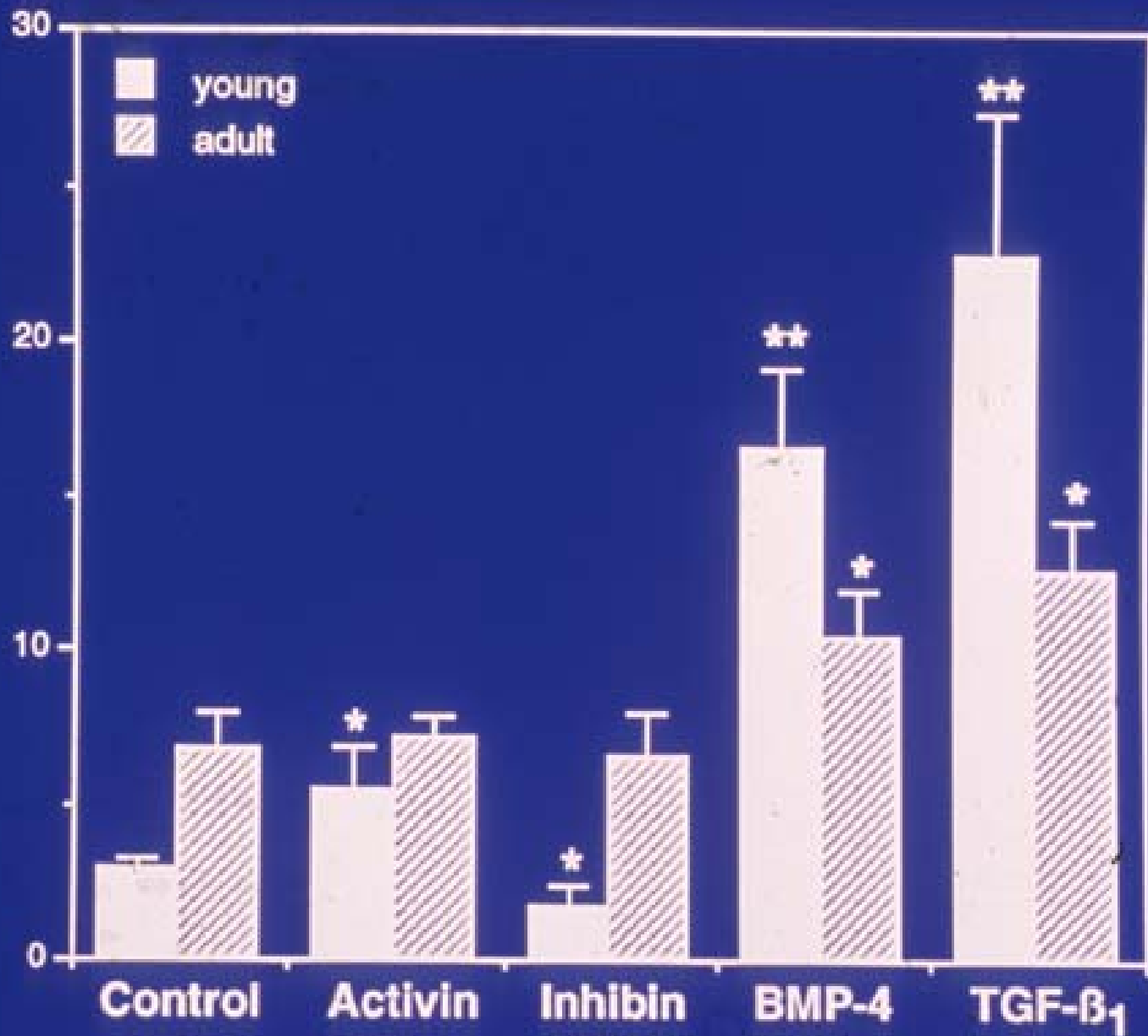
BMP 

Plasma Membrane

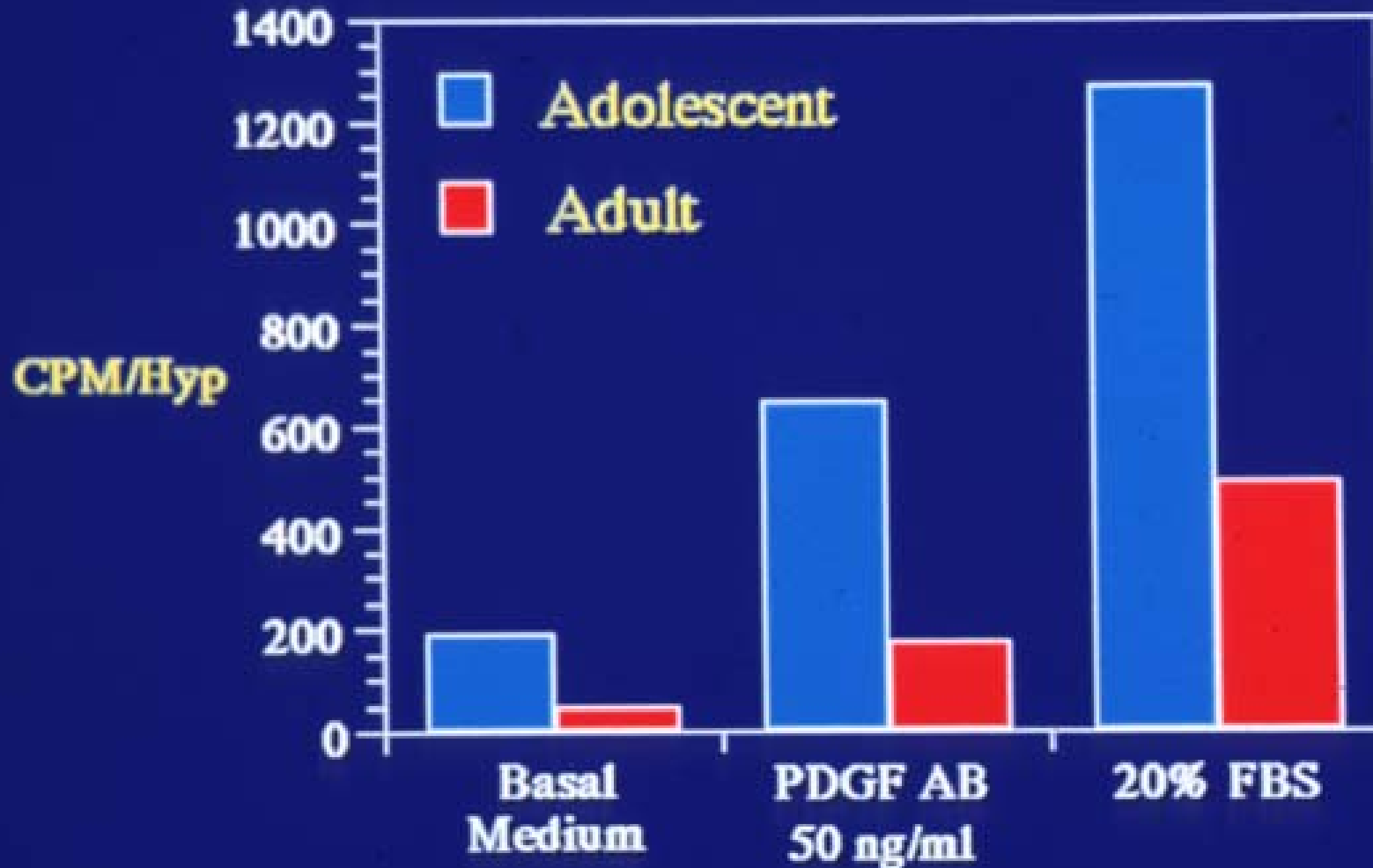


Nuclear Membrane

[35S] sulfate CPM/mg DNA ($\times 10^{-3}$)



Age-Related Biosynthesis



OSTEOARTHRITIS

- AFFLICTS 37 MILLION AMERICANS
- MOST CRIPPLING DISEASE
- COST \$20 BILLION
- ETIOLOGY NOT KNOWN
- CARTILAGE DAMAGE
- LIMITED THERAPEUTIC OPTIONS

Precartilage
(condensation
of mesenchyme)

Site of future
joint cavity
(mesenchyme
becomes rarefied)



Cartilage
(rudiment of bone)
Perichondrium
Joint capsule
Circular cleft
(joint cavity)
Perichondrium
Cartilage

F. Netter M.D.
© 1984 G&W

Periosteum
Epiphyseal cartilage
growth plate
Epiphyseal bone
Joint capsule
Synovial membrane
Joint cavity
Articular cartilages
Epiphyseal bone

Articular
menisci

Joint
cavity

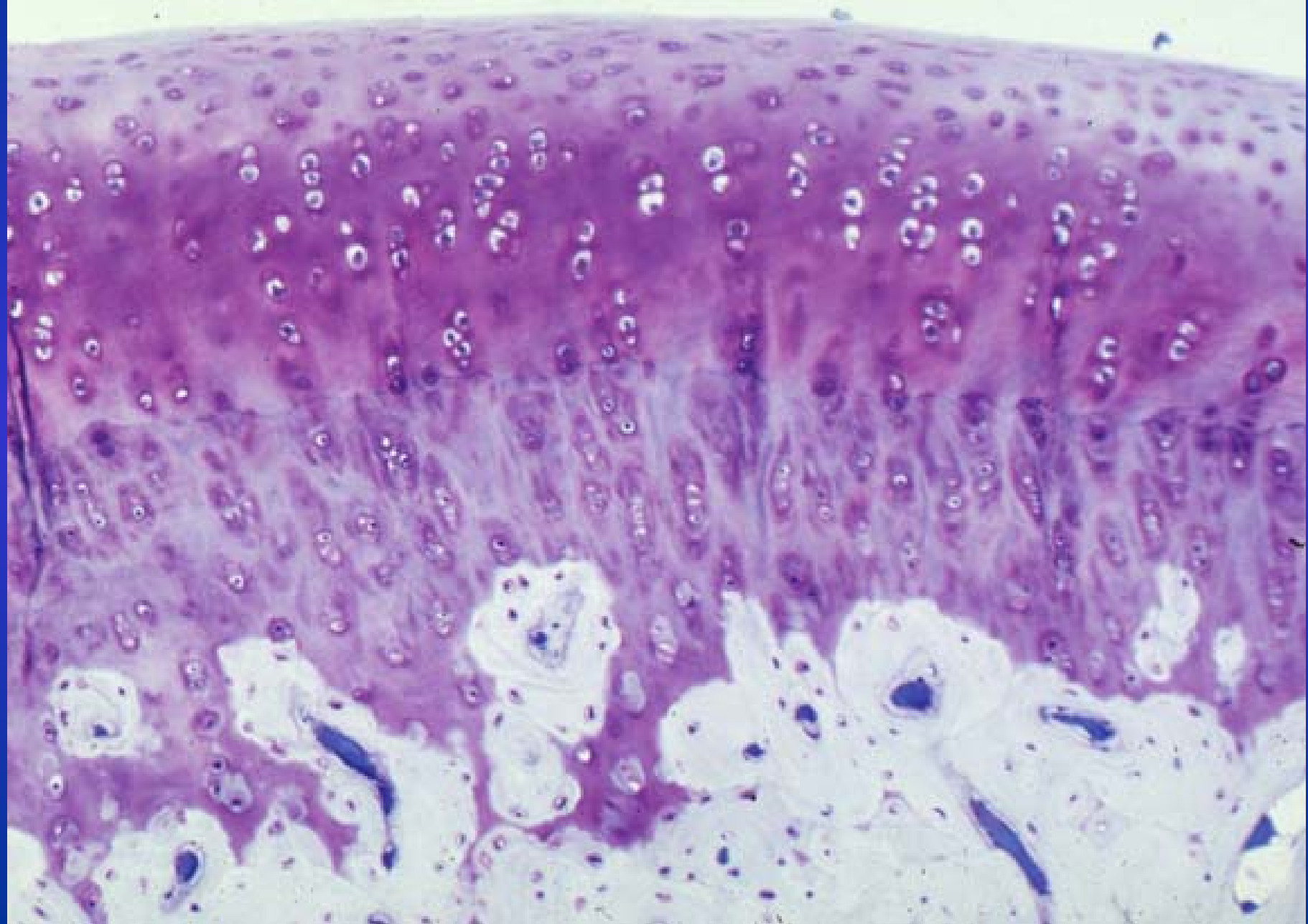
Articular
disc

Joint
cavities

Interphalangeal joint

Knee joint

Sternoclavicular



The Spectrum of Regeneration Potential of Musculoskeletal Tissues

BONE

CARTILAGE

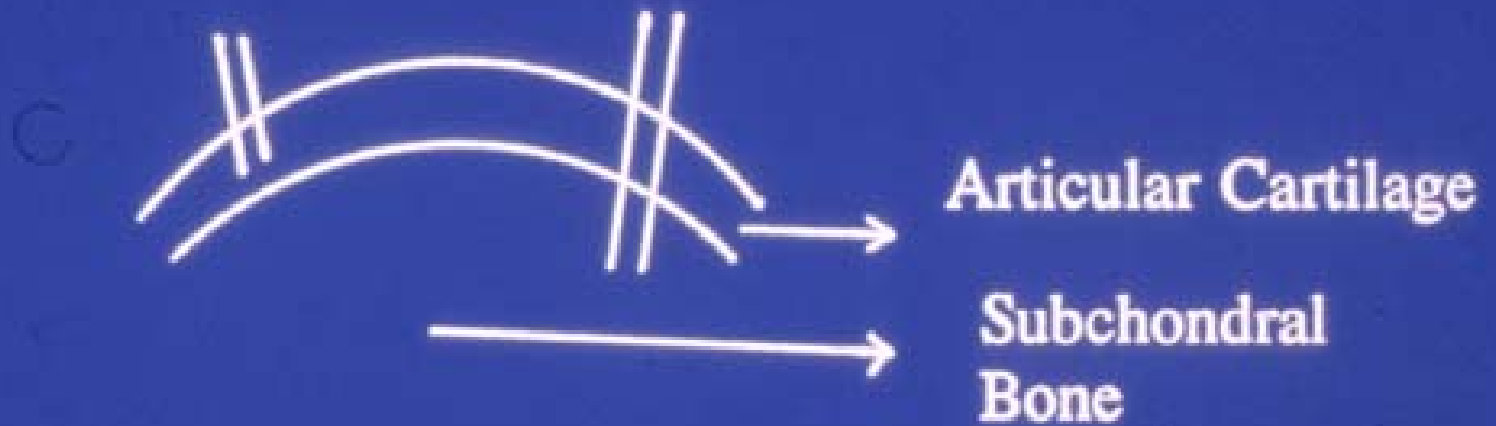


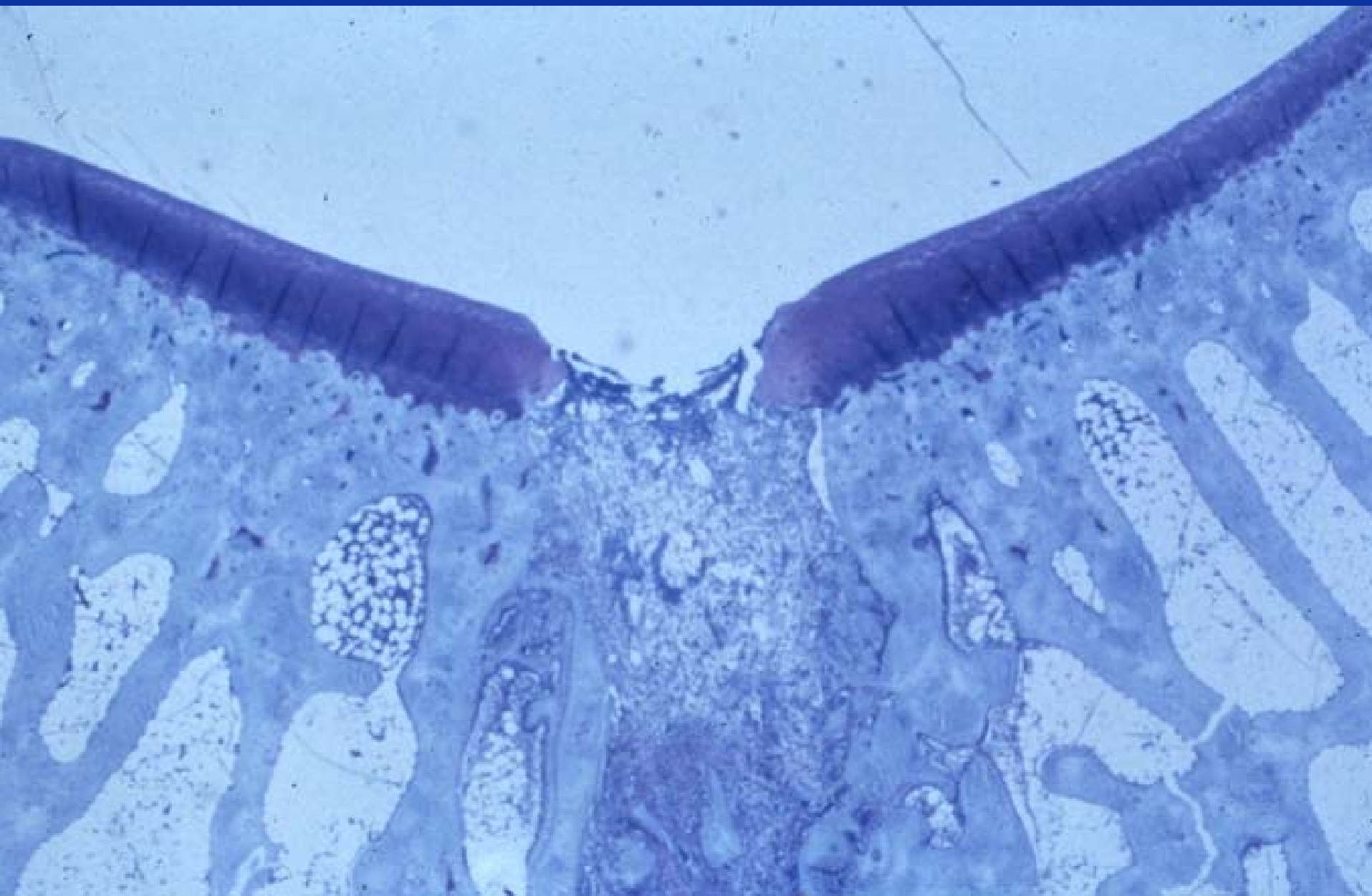
High



Low

REPAIR OF CARTILAGE







CARTILAGE - DERIVED MORPHOGENS

CDMP

OTHER NAMES

CDMP 1

GDF 5 / BMP 14

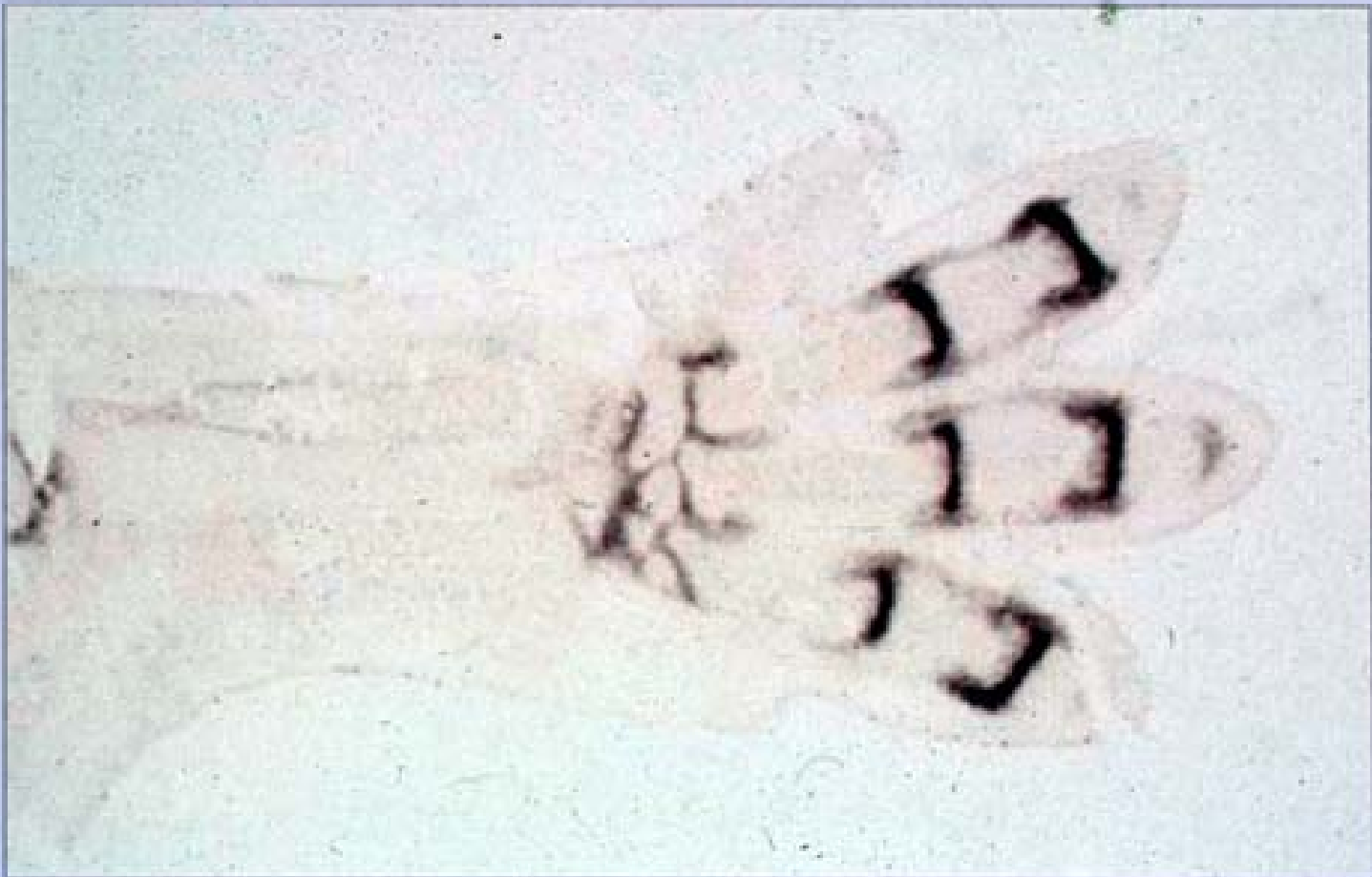
CDMP 2

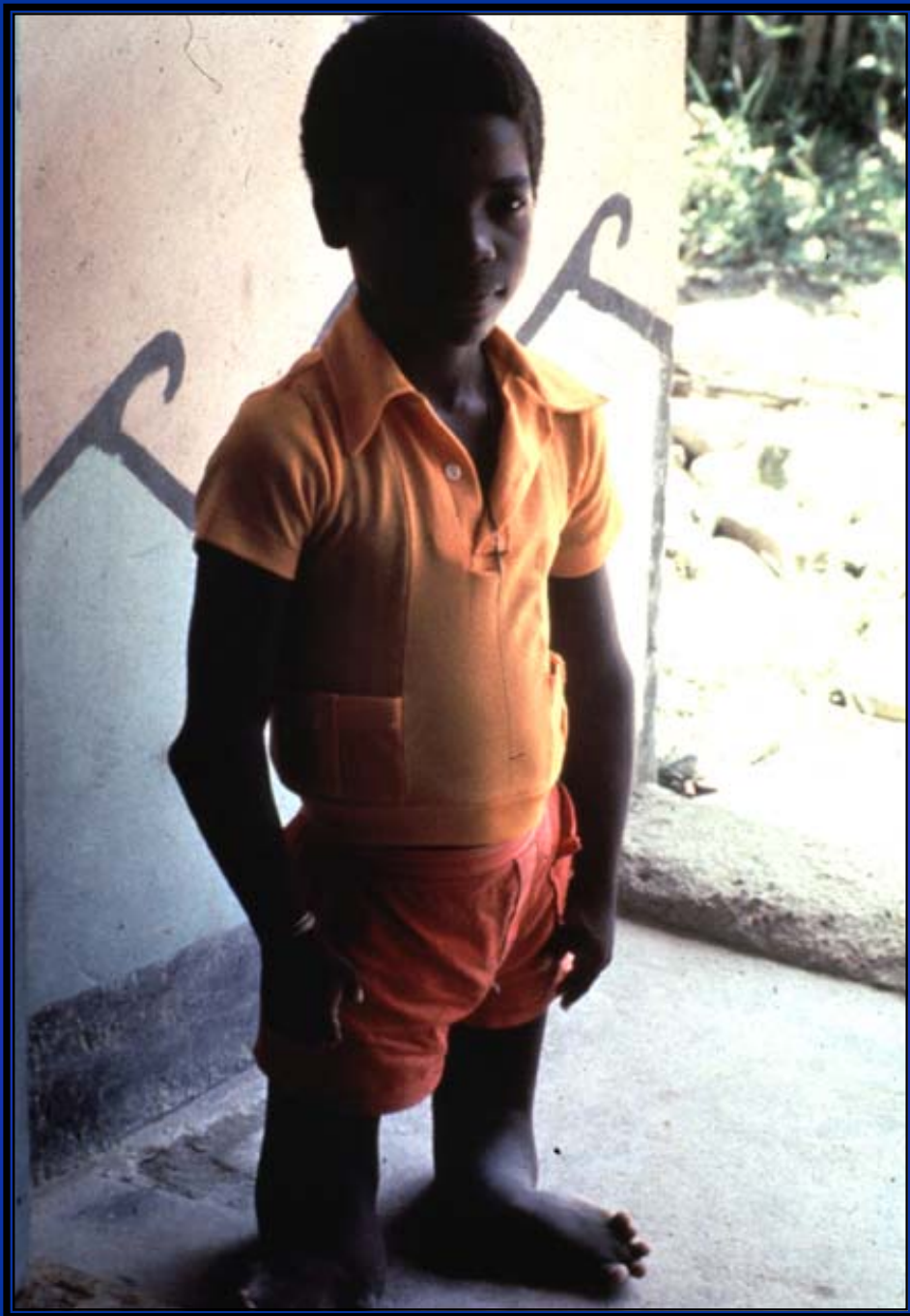
GDF 6 / BMP 13

CDMP 3

GDF 7 / BMP 12

BMP/CDMP Signaling in Joint Morphogenesis





NOVEL SEQUENCE ALIGNED WITH IL-17

hCL M D W P H N L L F L L T I S I F L G L G Q P R S P K S K R K 30
hIL-17 M T P G K T S L V S L L L L S L E A I V K A G I T I P R N

hCL G Q G R P G P L V P G P H Q V P L D L V S R M K P W A R M D 60
hIL-17 - - - P G - - - - C P N - - - - - S E D K N F P R T V

hCL E Y E R N I E E M V A Q L R N S S E L A Q R K C E V N L Q L 90
hIL-17 M V N L N I H N - - - - R N T N T N P K R S S D - - - - -

hCL W M S N K R S L S P W G Y S I N H D P S R I P V D L P E A R 120
hIL-17 - Y Y N - R S T S P W N L H R N E D P E R Y P S V I W E A K

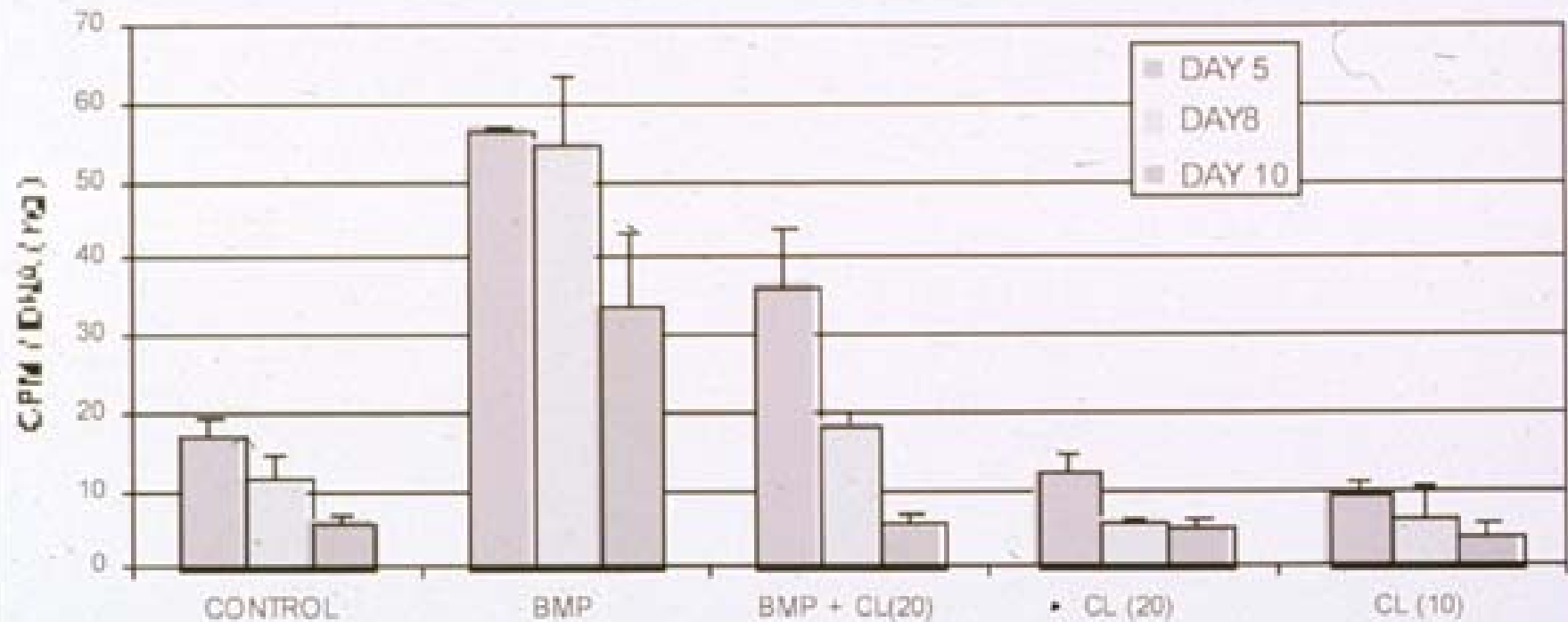
hCL C L C L G C V N P F T M Q E D R S M V S V P V F S Q V P Y R 150
hIL-17 C R H L G C I N - A D G N V D Y H M N S V P I Q Q E I L V L

hCL R R L C P P P P R T G P C R Q R A V M E T I A V G C T C I P 180
hIL-17 R R - - E P P - - H C P N S F R L E K I L V S V G C T C V T

hCL P I V H H V A 210
hIL-17

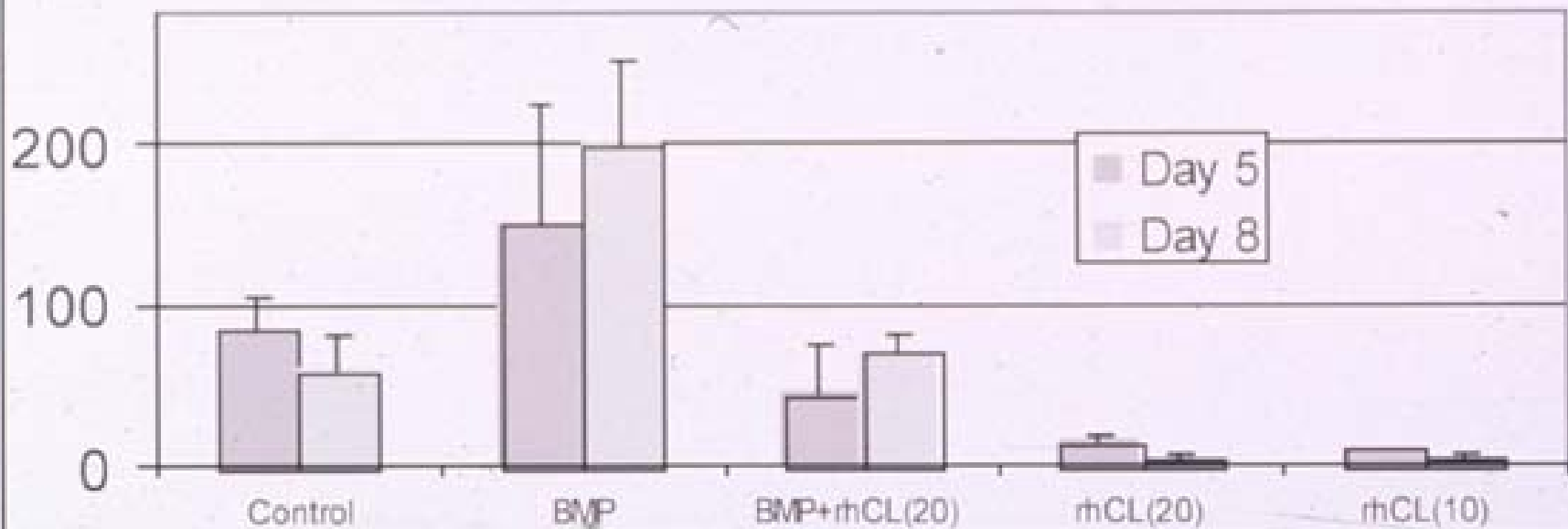
PROTEOGLYCAN SYNTHESIS

PRIMARY CALF ARTICULAR
CHONDROCYTE MONOLAYER CULTURE

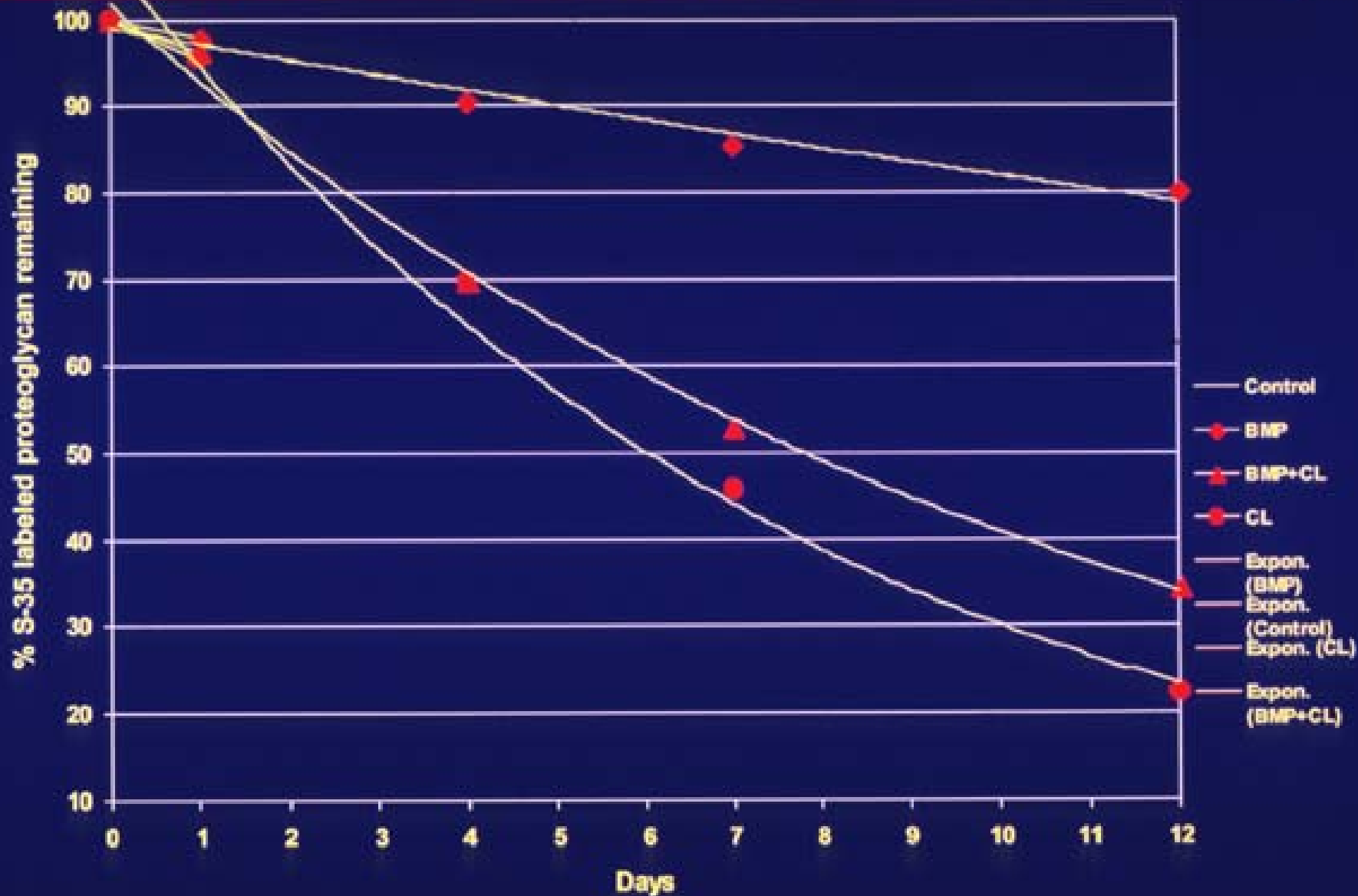


PROTEOGLYCAN SYNTHESIS

CALF ARTICULAR CHONDROCYTE EXPLANT CULTURE



PROTEOGLYCAN RELEASE



SIGNALS

GROWTH & MORPHOGENETIC FACTORS

- **INITIATION**
- **PROMOTION**
- **MAINTENANCE**
- **REMODELING**
- **TERMINATION**

GROWTH AND DIFFERENTIATION FACTORS

- **BMPs**
- **CDMPs**
- **TGF β**
- **PDGFs**
- **IGFs**
- **FGFs**

What Are Morphogens?

Morphogens are Inductive Signals that Initiate and Govern Tissue Morphogenesis Based on Tissue Interactions that are Dynamic and Reciprocal.

MORPHOGENESIS

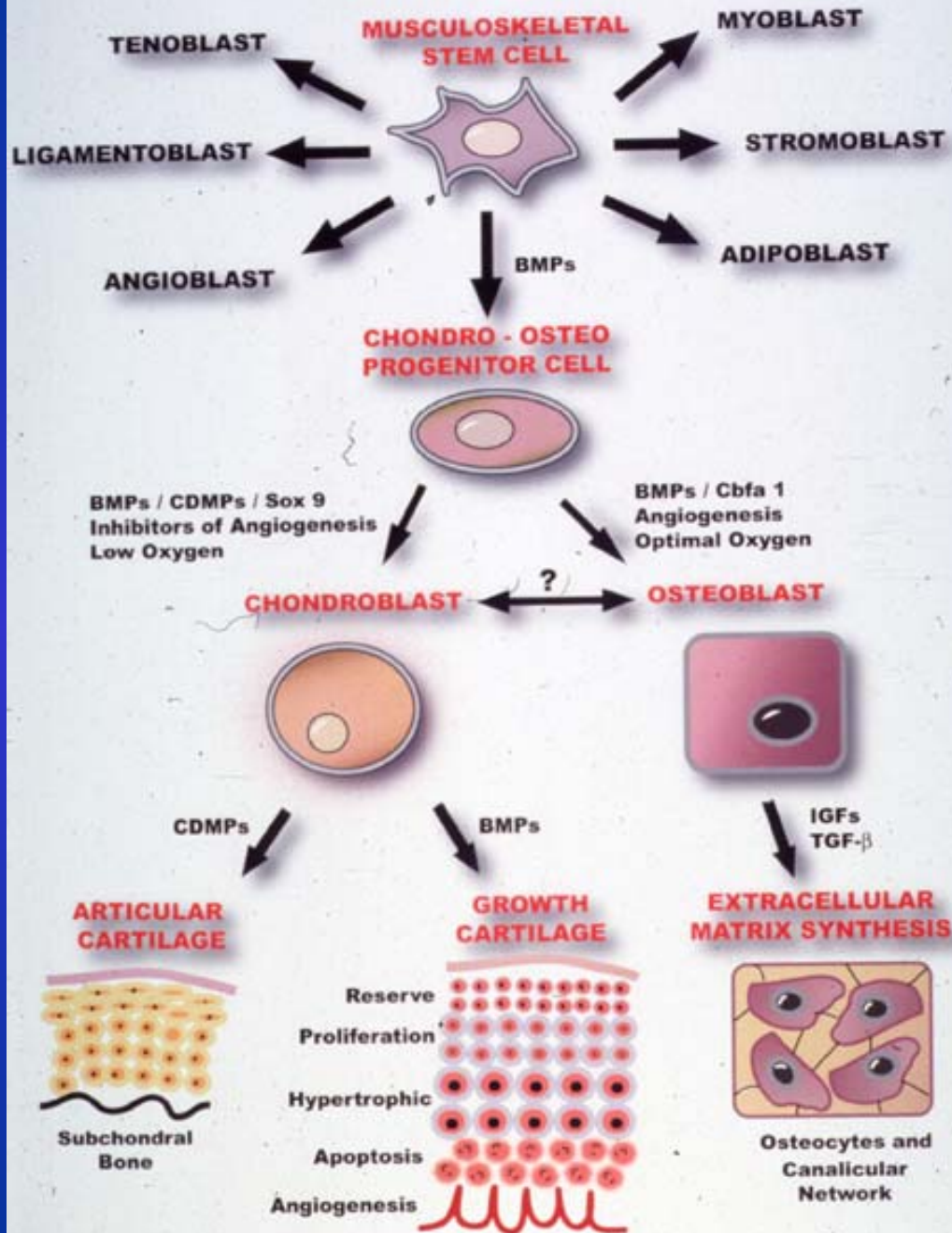
- DEVELOPMENT OF FORM
- MORPHOGENS INDUCE MORPHOGENESIS
- MORPHOGENS INDUCE A HIERARCHY OF GENE CASCADE
- BMPs ARE MORPHOGENS

TISSUE ENGINEERING

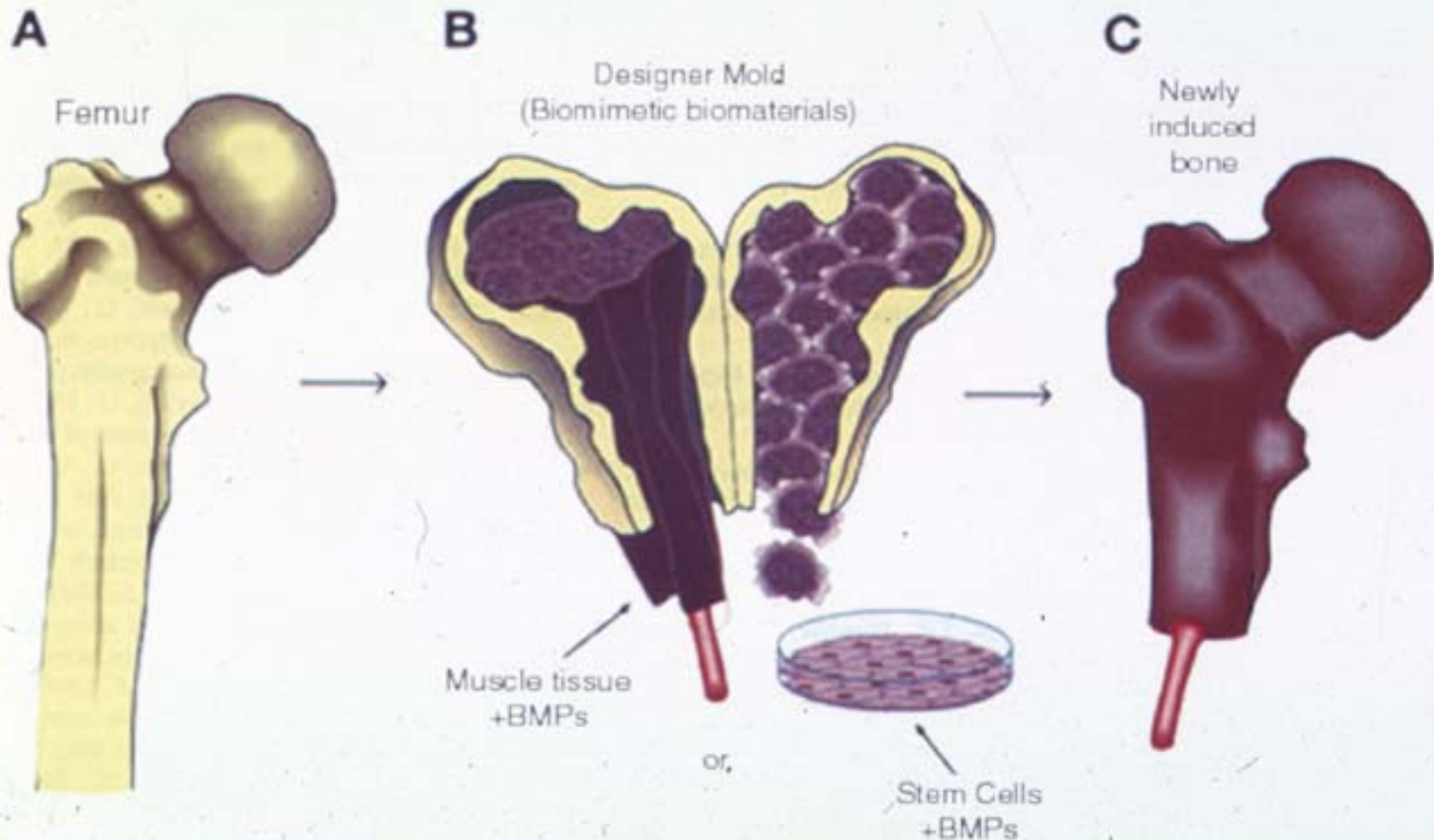
IS THE SCIENCE OF DESIGN AND MANUFACTURE OF NEW TISSUES FOR THE FUNCTIONAL RESTORATION OF IMPAIRED ORGANS AND REPLACEMENT OF LOST PARTS DUE TO CANCER DISEASE OR TRAUMA .

KEY INGREDIENTS FOR TISSUE ENGINEERING AND MORPHOGENESIS

- **Induction Signals/Morphogens**
- **Stem Cells**
- **Biomimetic Biomaterials /
Scaffolding / ECM**



Tissue Engineering: Proof of Concept



**TISSUE ENGINEERING IS THE
SYMBIOSIS OF
BIOTECHNOLOGY
BIOMATERIALS AND
BIOMECHANICS**

Cartilage Repair : Current Strategy

- **GROWTH & MORPHOGENETIC FACTORS**
- **CELL THERAPY**
- **GENE THERAPY**
- **NEW BIOMATERIALS**
- **INHIBITORS OF METALLOPROTEINASES**

