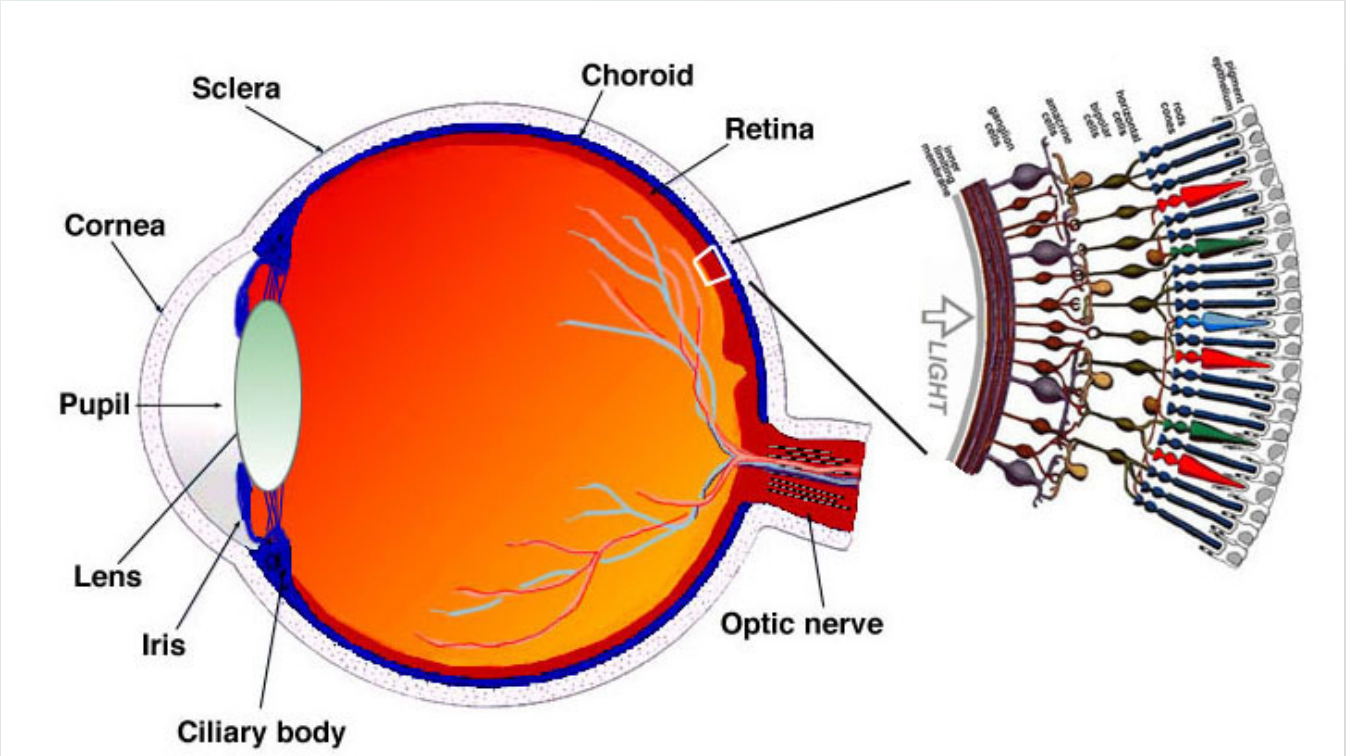
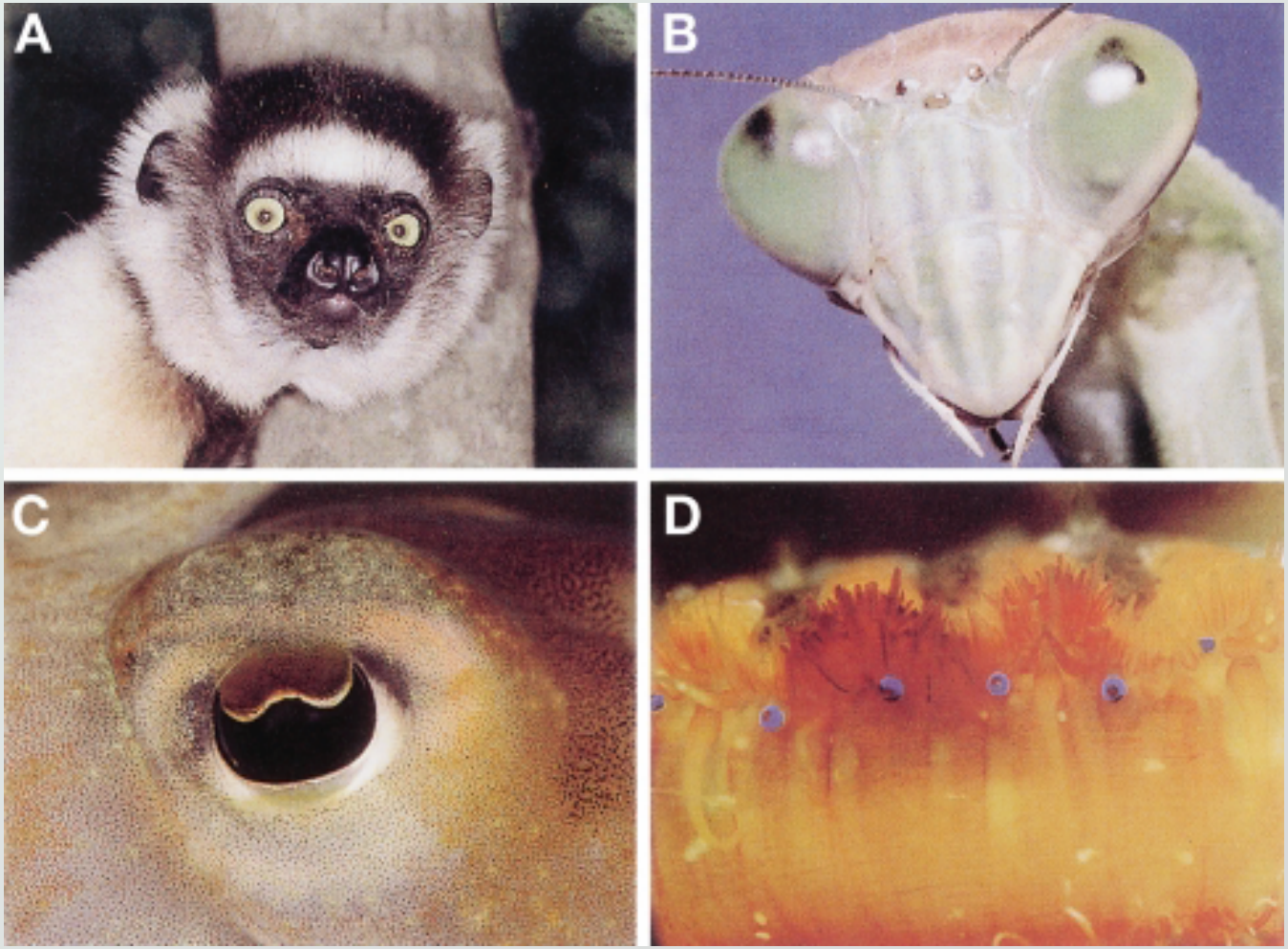
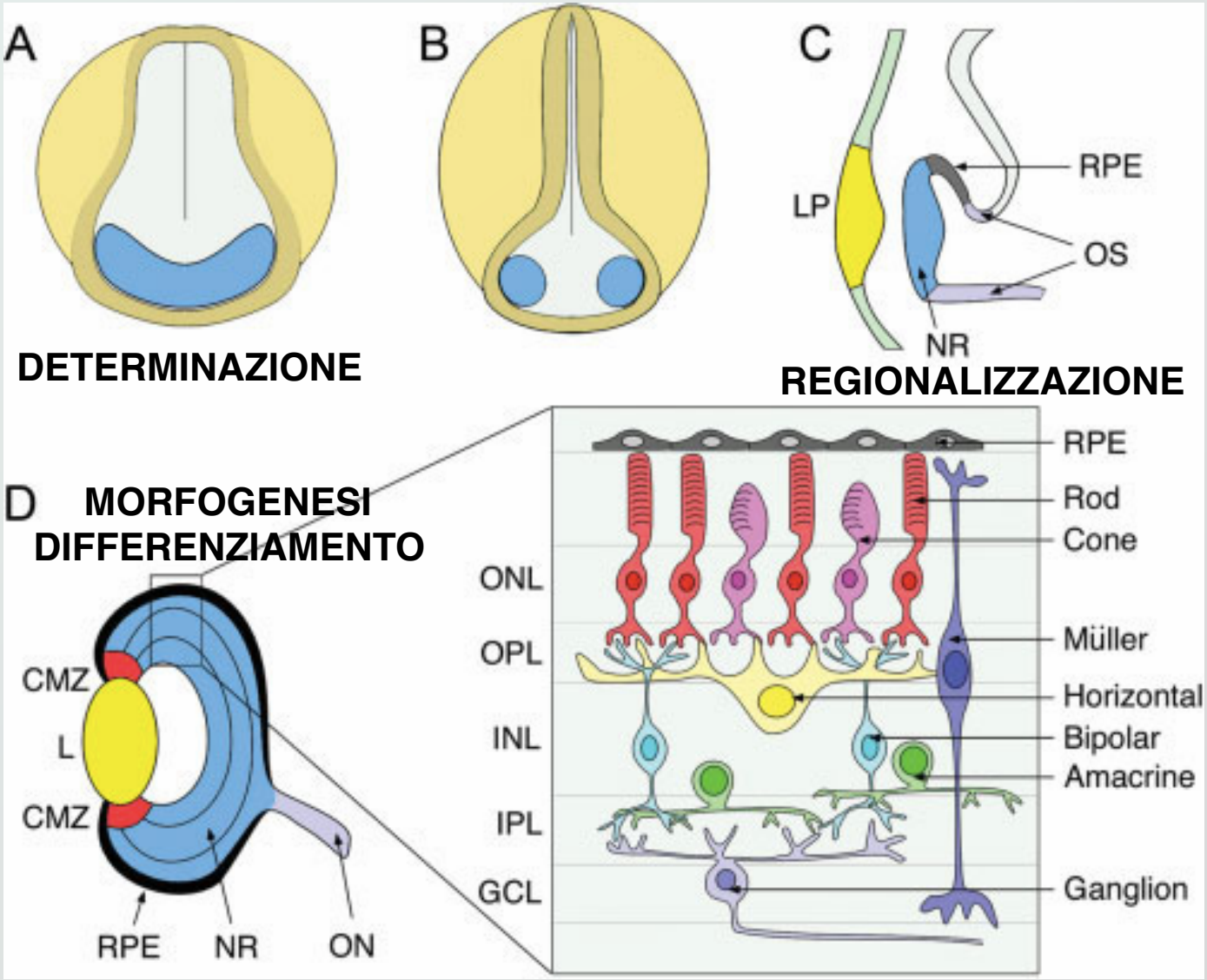
STRUTTURA ANATOMICA DELL'OCCHIO UMANO



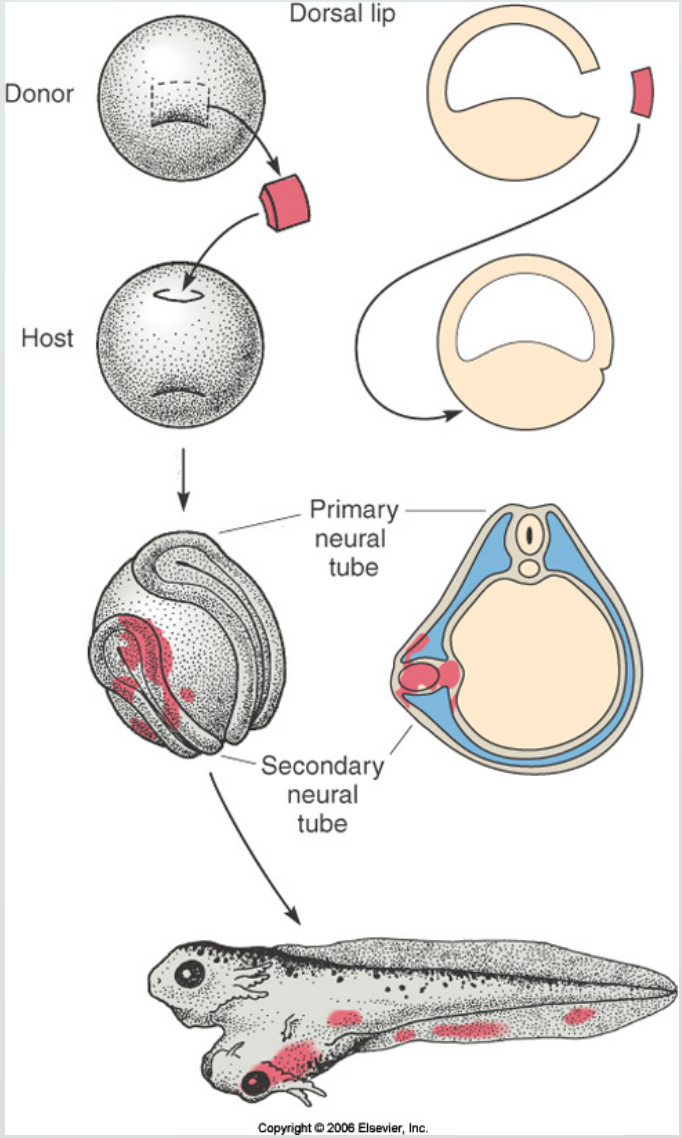
NEL REGNO ANIMALE E' PRESENTE
UNA GRANDE VARIETA' DI STRUTTURE OCULARI



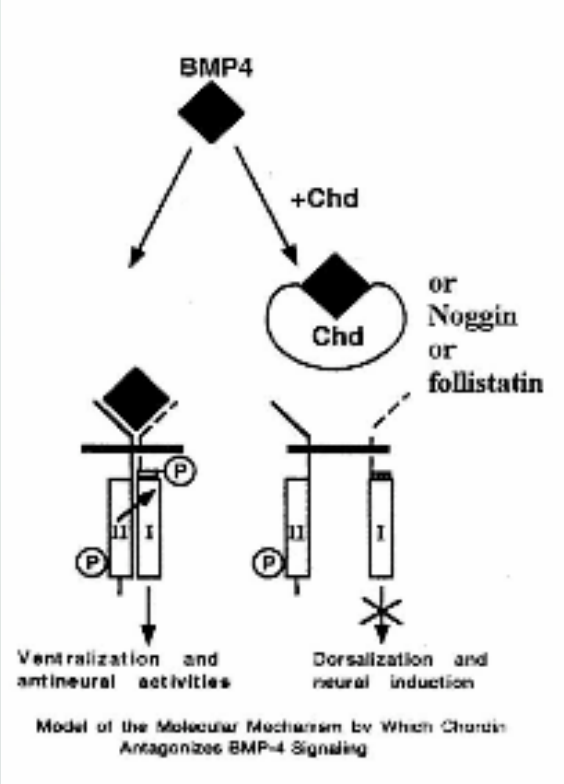
TAPPE FONDAMENTALI NELLO SVILUPPO DELL'OCCHIO

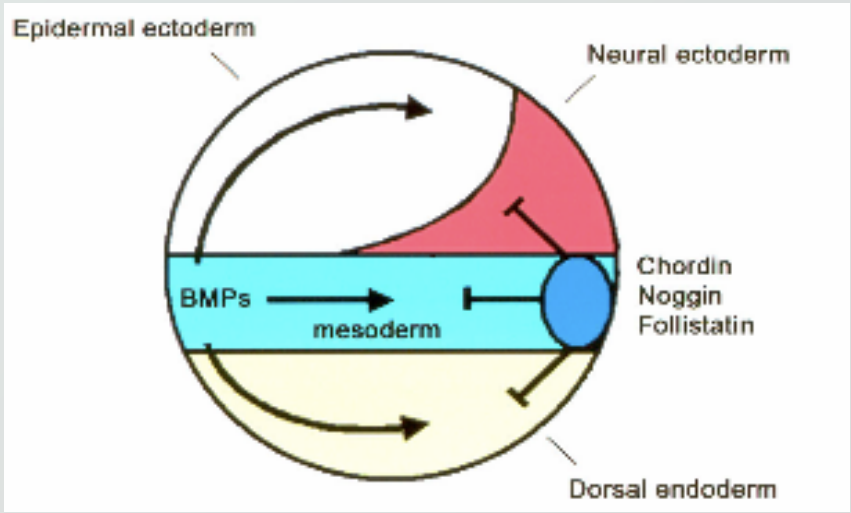


L'INDUZIONE NEURALE E' MEDIATA DA SEGNALI PRODOTTI DAL MESODERMA DORSALE

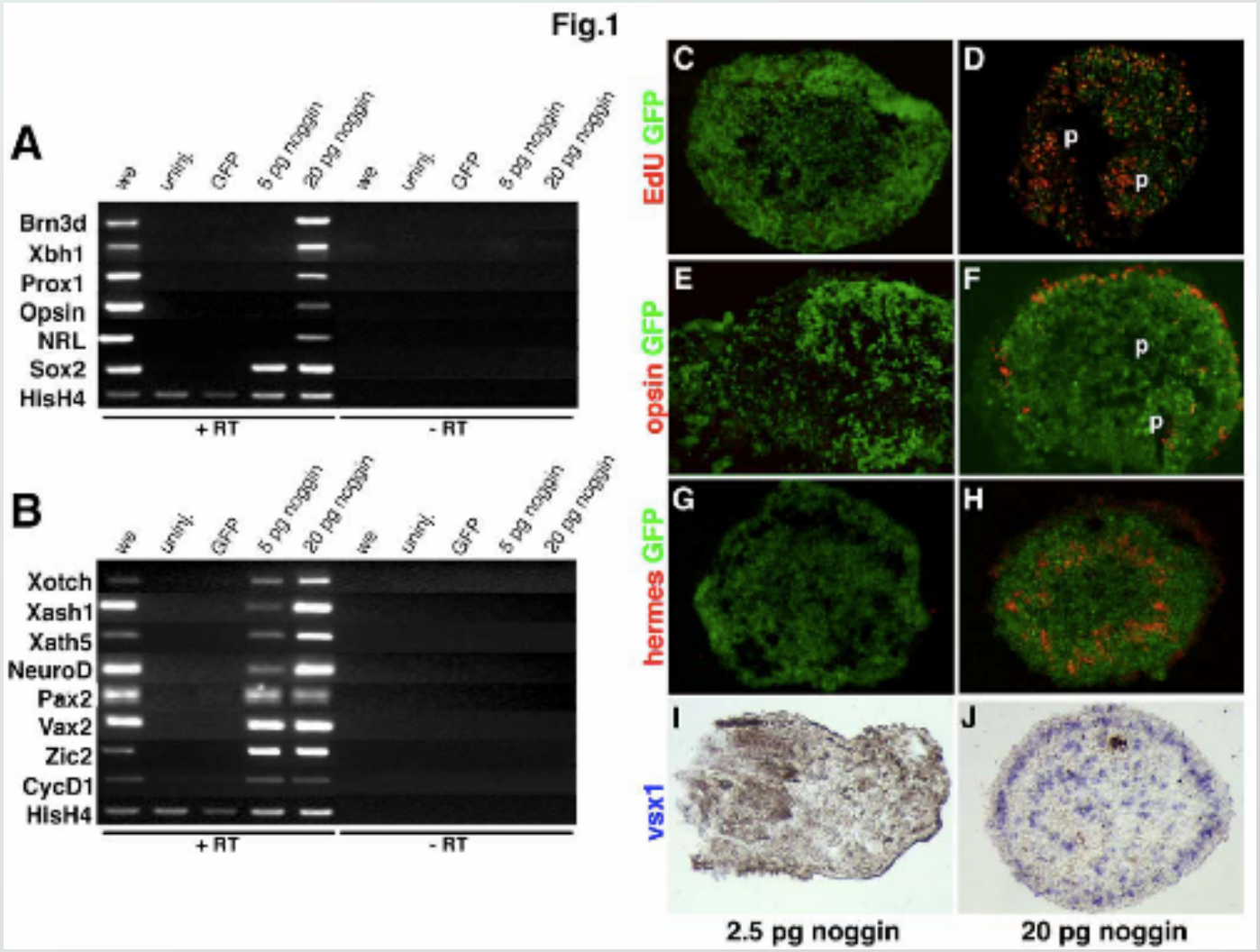


IL MESODERMA DORSALE E' UNA SORGENTE DI ANTAGONISTI DI FATTORI BMP

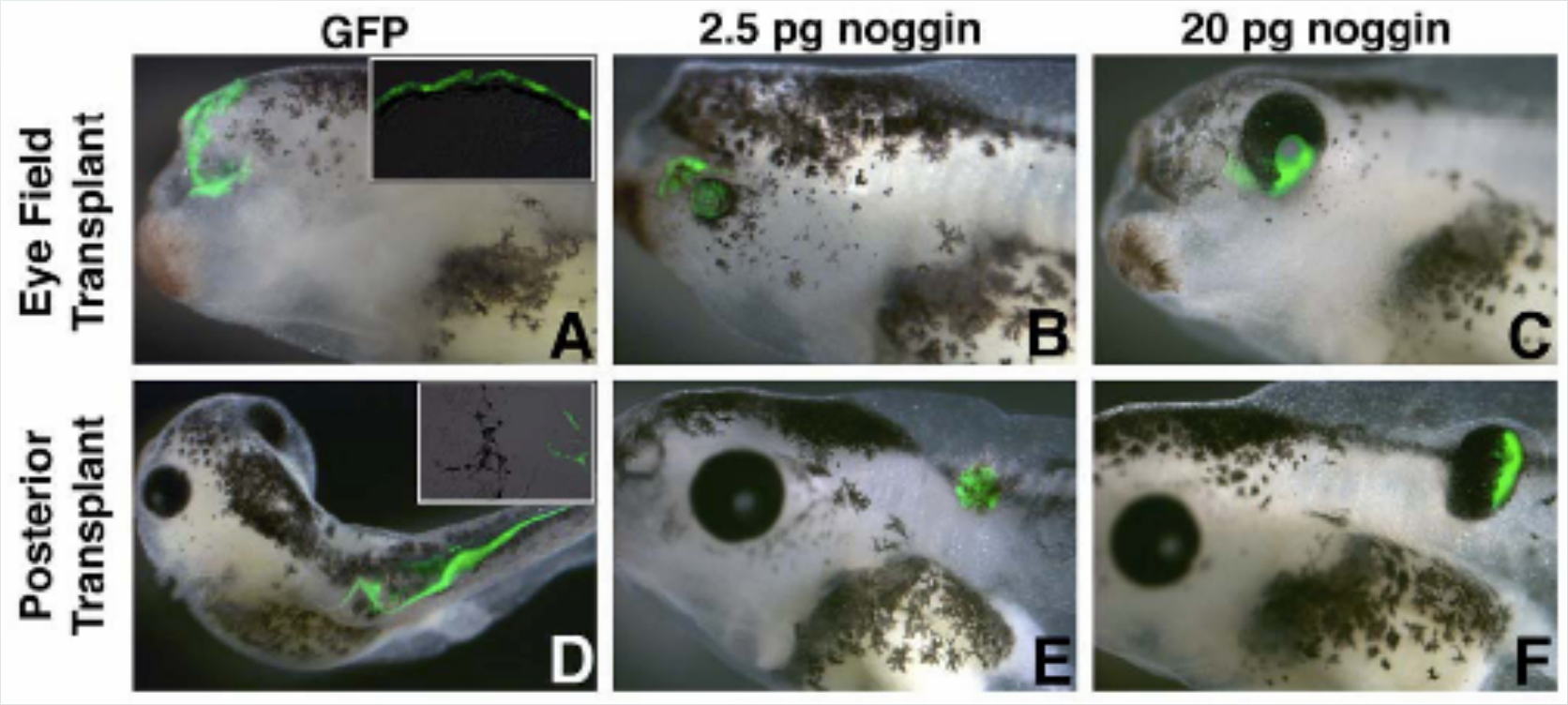




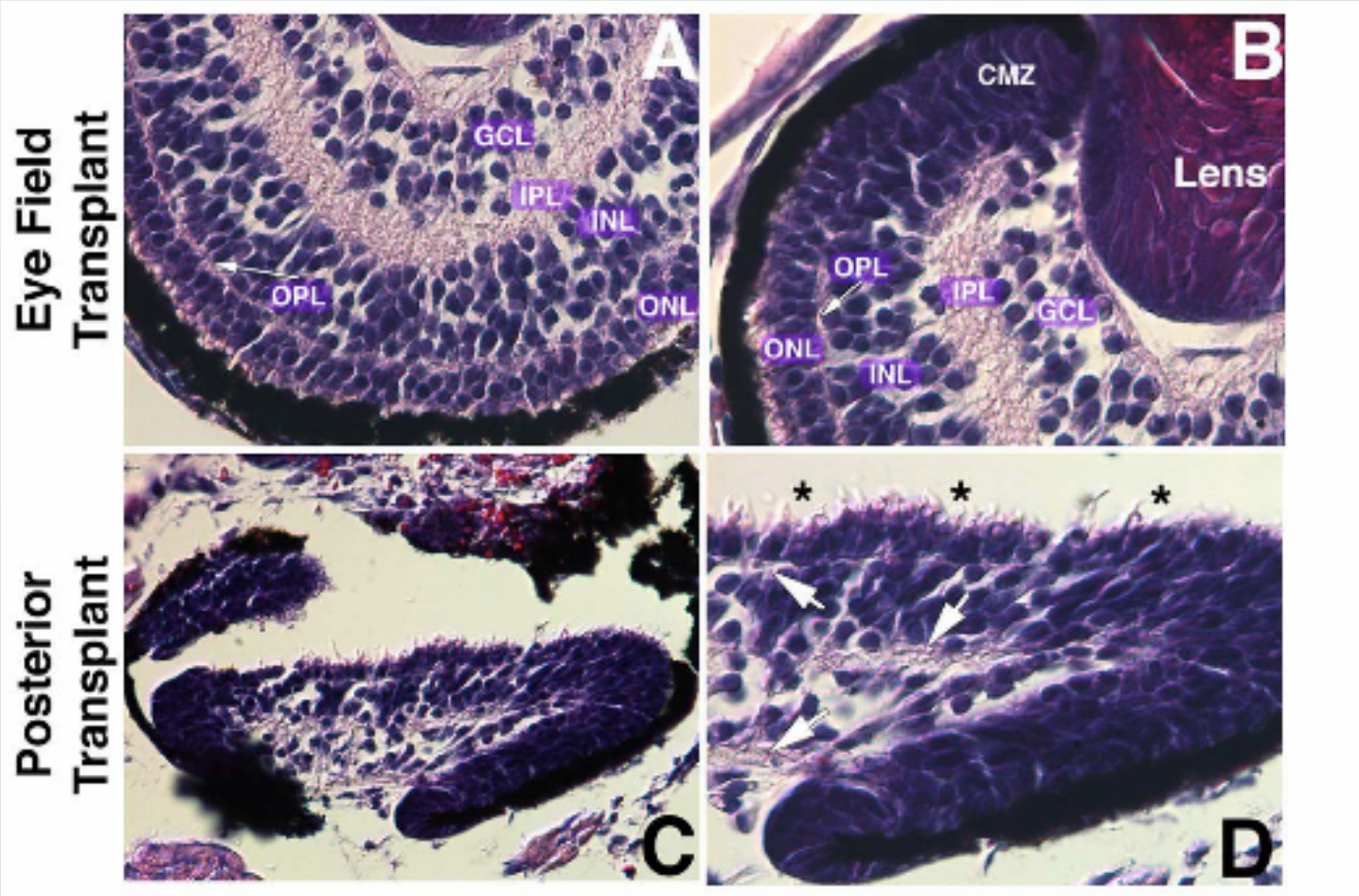
ALTI LIVELLI DEL FATTORE NOGGIN INDUCONO FORMAZIONE DI RETINA IN ESPIANTI ECTODERMICI DI EMBRIONI DI XENOPUS



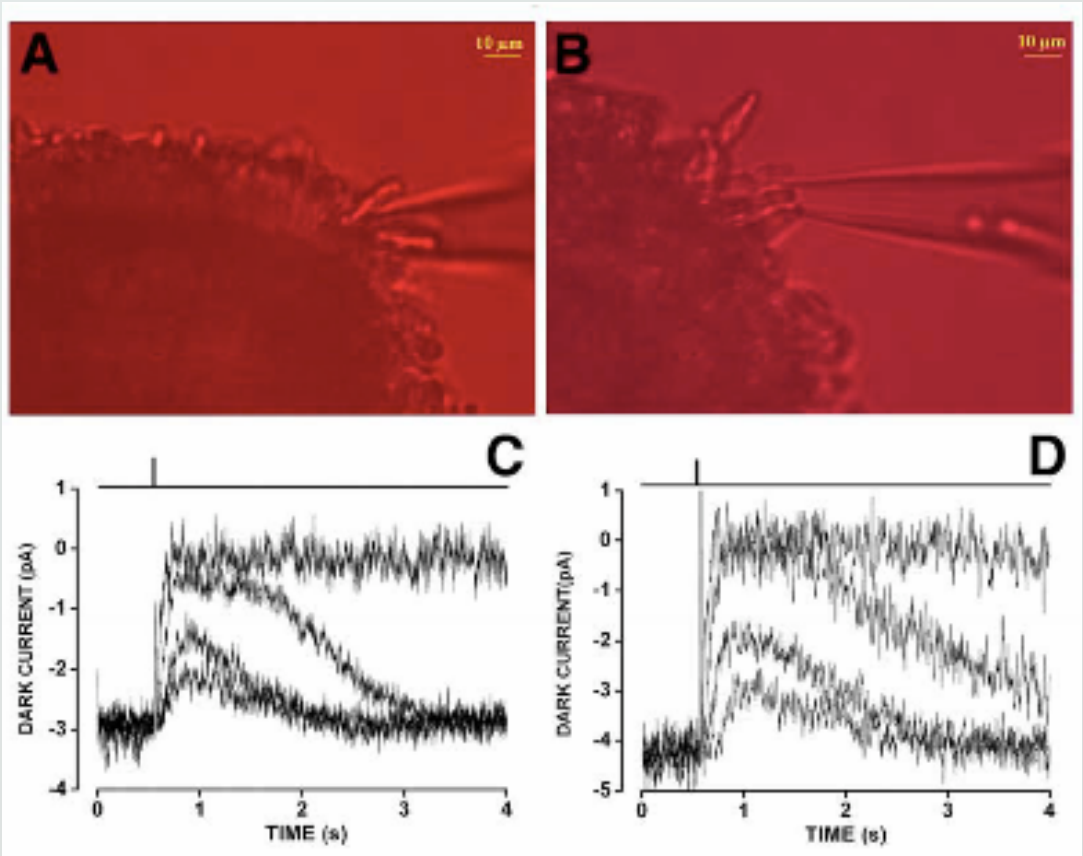
IL TESSUTO RETINICO INDOTTO DA NOGGIN E' IN GRADO DI FORMARE STRUTTURE OCULARI



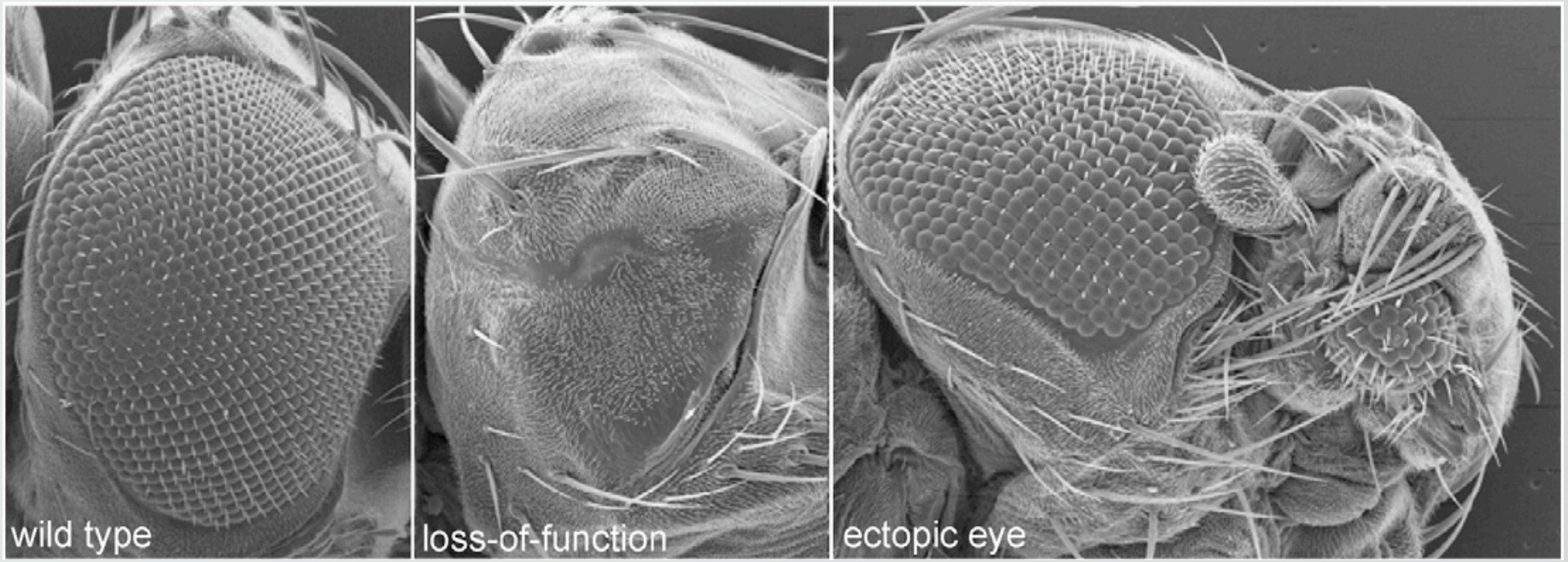
IL TESSUTO RETINICO INDOTTO DA NOGGIN E' IN GRADO DI FORMARE OCCHI MORFOLOGICAMENTE DIFFERENZIATI



IL TESSUTO RETINICO INDOTTO DA NOGGIN E' IN GRADO DI FORMARE OCCHI FUNZIONALMENTE ATTIVI

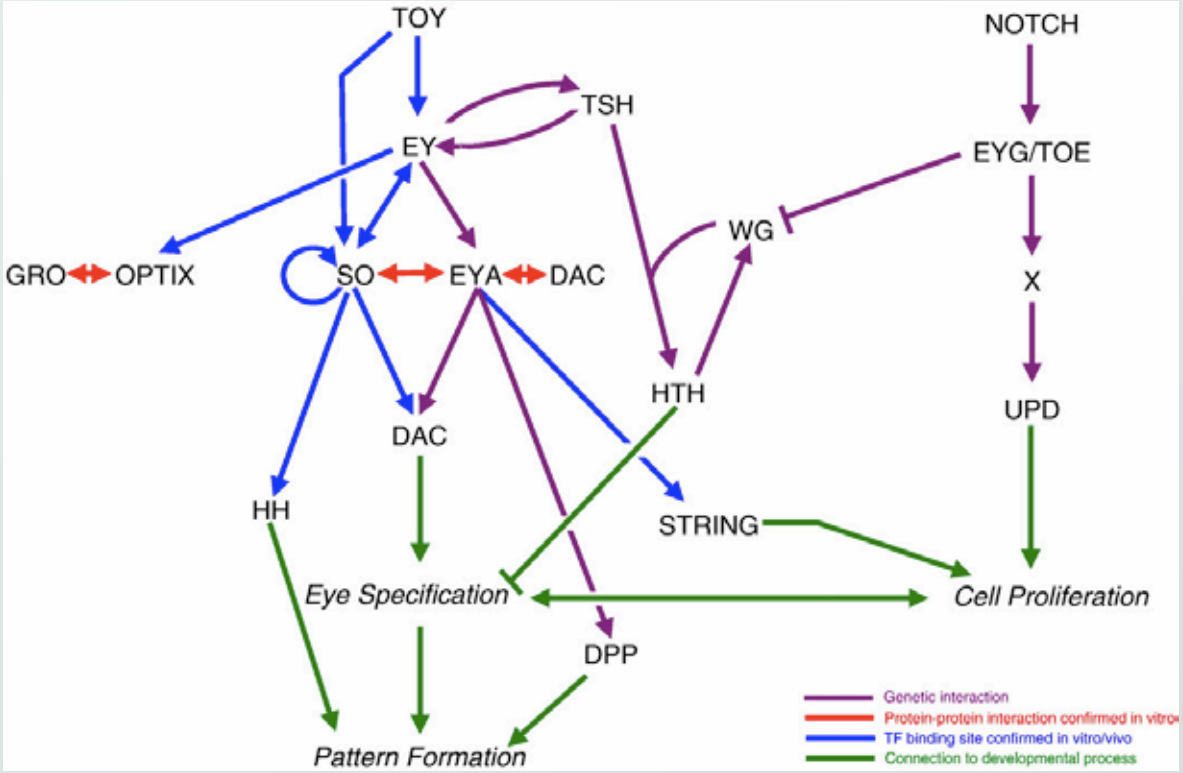


DROSOPHILA COME MODELLO DI STUDIO PER LA GENETICA DELLO SVILUPPO DELL'OCCHIO



INDUZIONE DI OCCHI ECTOPICI TRAMITE SOVRA-ESPRESSIONE DEL GENE EYELESS IN DROSOPHILA

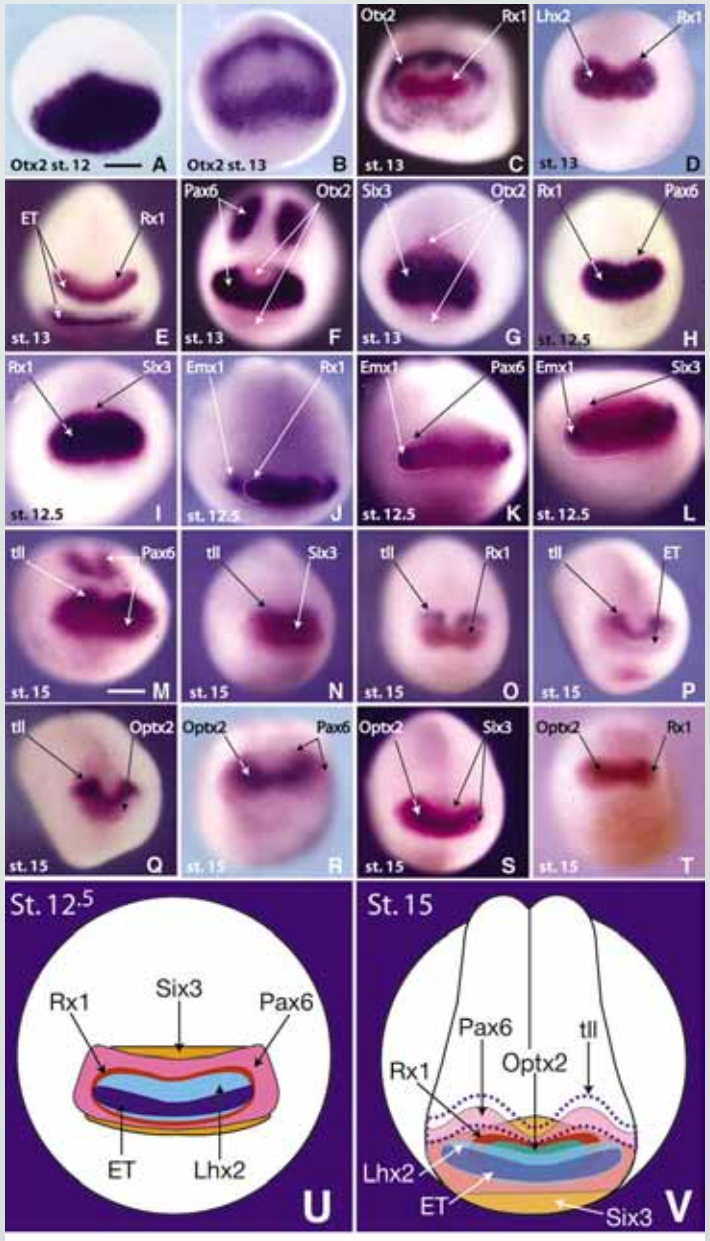
LO SVILUPPO DELL'OCCHIO IN DROSOPHILA E' REGOLATO DA UN NETWORK DI FATTORI DI TRASCRIZIONE CONSERVATO NEI VERTEBRATI



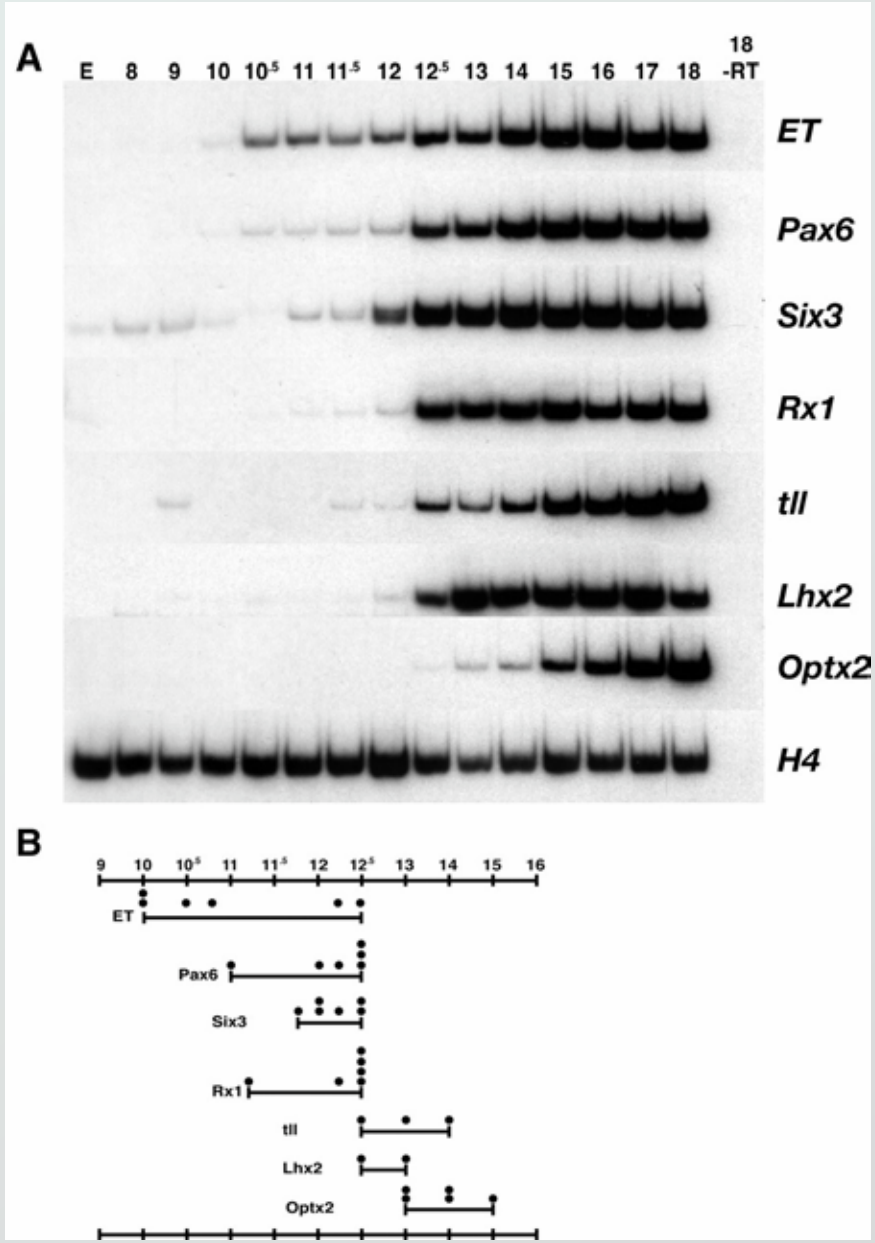
Drosophila Gene(s)	Molecular Function	Domain(s)	Vertebrate Gene(s)
eyeless, twin of eyeless	transcription factor	paired/homeodomain	Pax6
eyegone, twin of eyegone	transcription factor	paired (truncated)/homeodain	Pax6(5a)
eyes absent	co-activator/phosphatase	P/S/T	Eya1-4
dachshund	transcription factor	winged helix turn helix	Dach1-2
sine oculis/optix/DSix4	transcription factor	homedomain	Six1-6
teashirt	transcription factor	zinc finger	Tsh1-4
homothorax	transcription factor	homeodomain	Meis1

UN NETWORK DI FATTORI DI TRASCRIZIONE EFTF E' ESPRESSO PRECOCEMENTE NEL CAMPO DELL'OCCHIO DEI VERTEBRATI

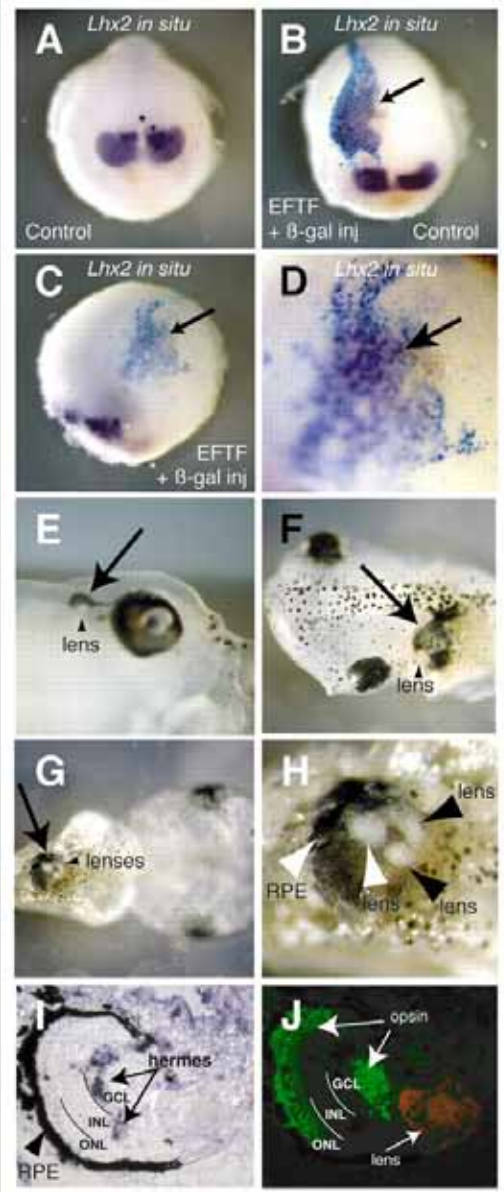
EFTFs = Eye Field Transcription Factors



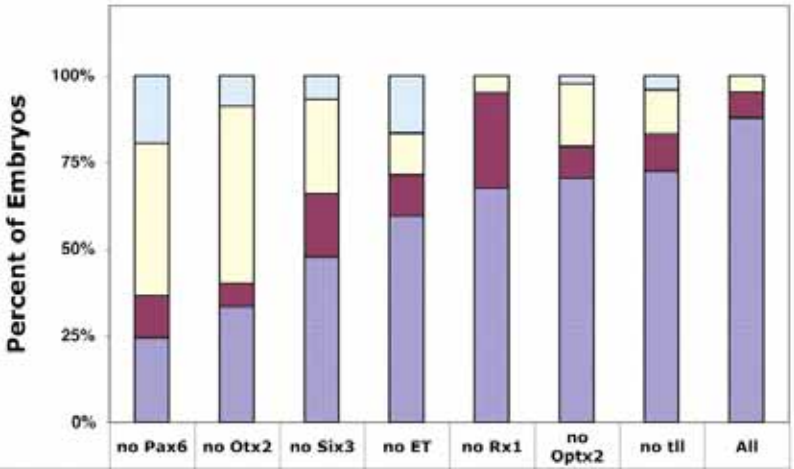
IL NETWORK DI FATTORI DI TRASCRIZIONE EFTF SI ATTIVA ALLA FINE DELLA GASTRULAZIONE



LA SOVRA-ESPRESSIONE DI UN COCKTAIL DI EFTFs INDUCE LA FORMAZIONE DI OCCHI ECTOPICI NEI VERTEBRATI

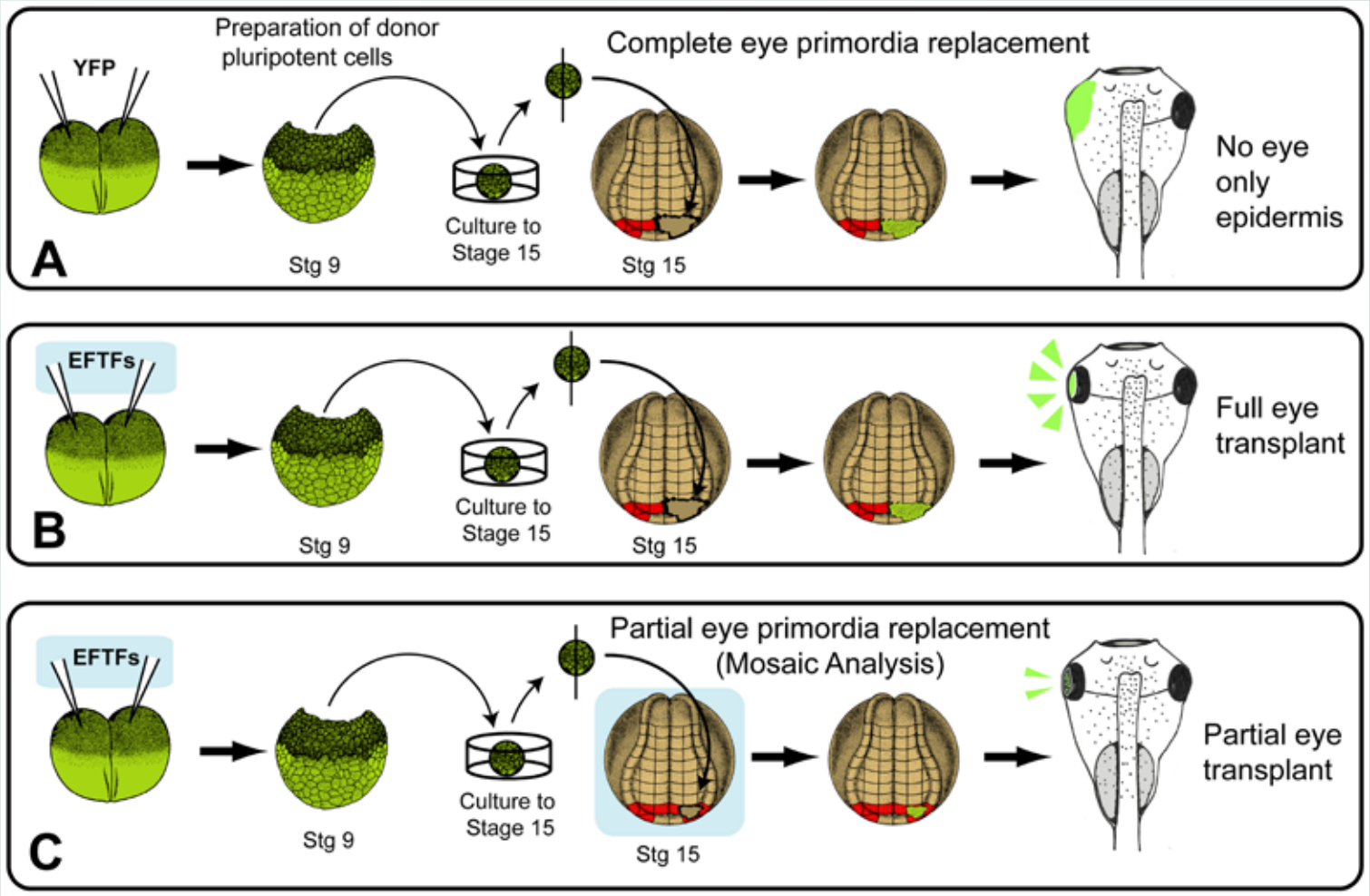


K

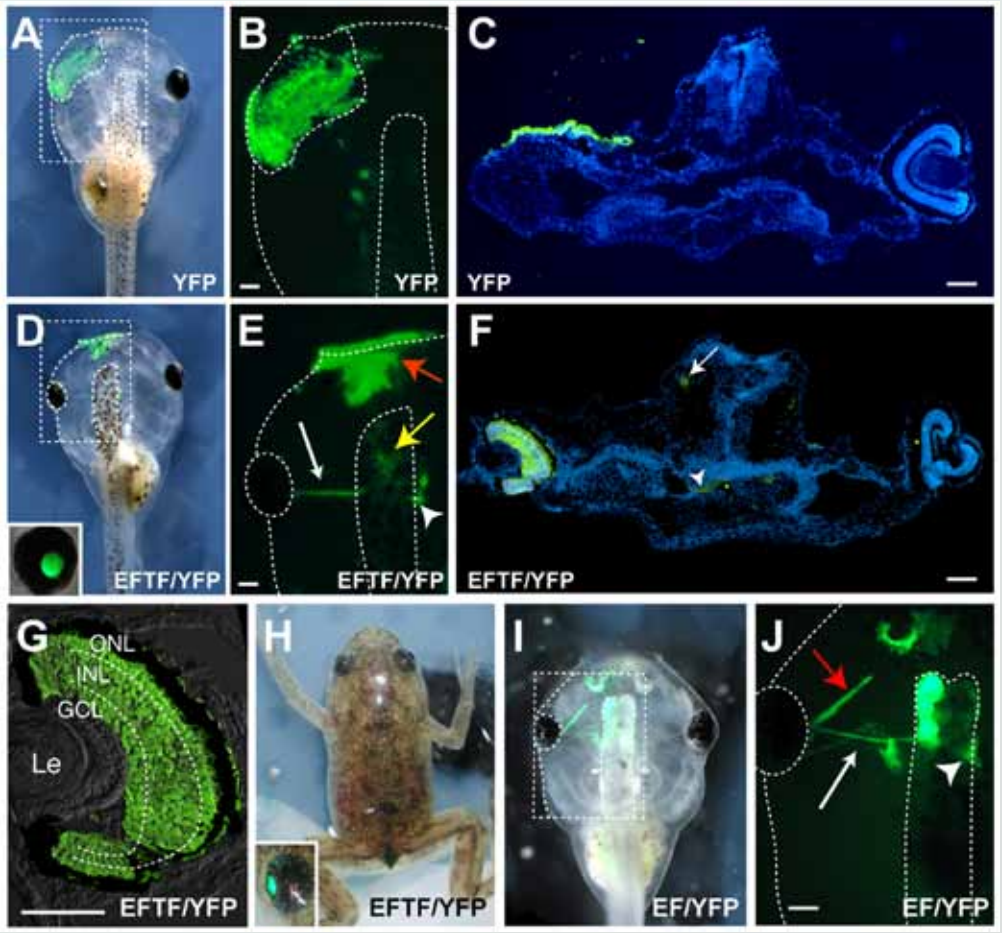


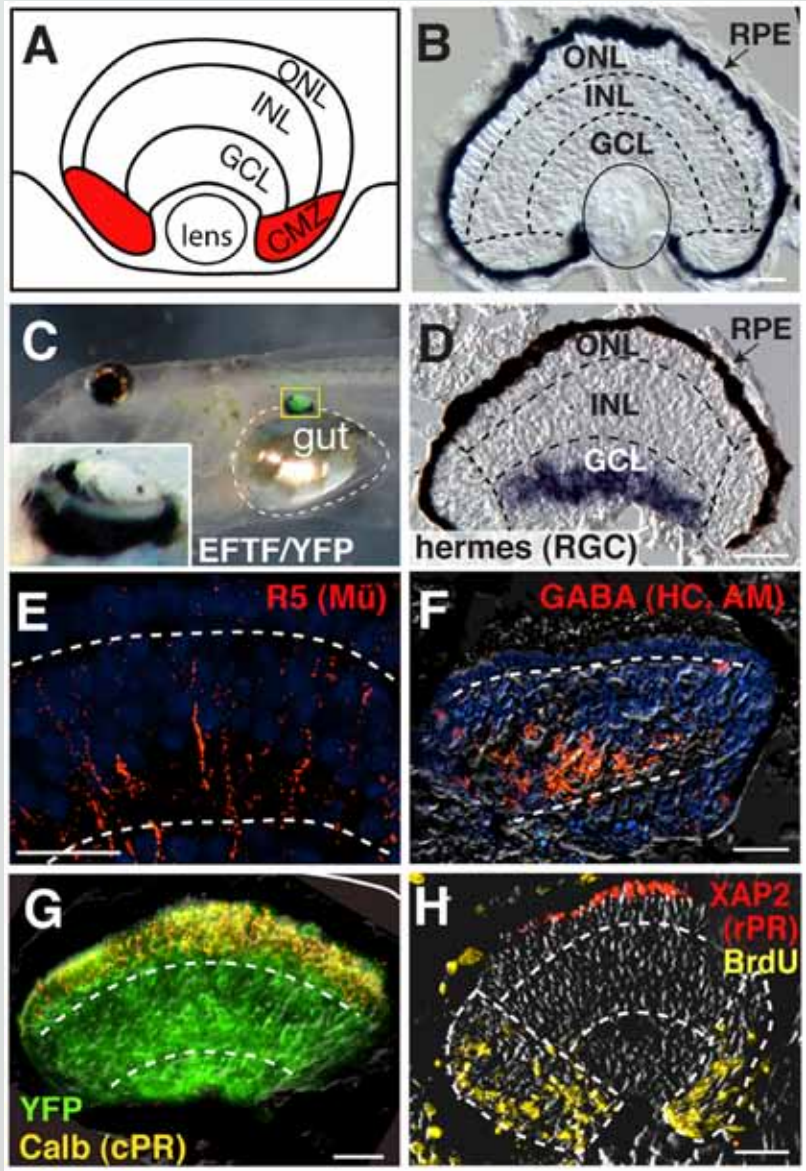
	no Pax6	no Otx2	no Six3	no ET	no Rx1	no Optx2	no tll	All
Normal	20%	9%	7%	17%	0%	2%	4%	0%
Malformed Eye	44%	51%	27%	12%	5%	18%	13%	5%
Streaming Pigment	12%	7%	18%	12%	28%	9%	11%	7%
Ect. Pig./Eye Tissue	24%	33%	48%	60%	68%	70%	72%	88%

ESPERIMENTI DI TRAPIANTO DI CELLULE STAMINALI PLURIPOTENTI CHE ESPRIMONO IL NETWORK DI FATTORI EFTF

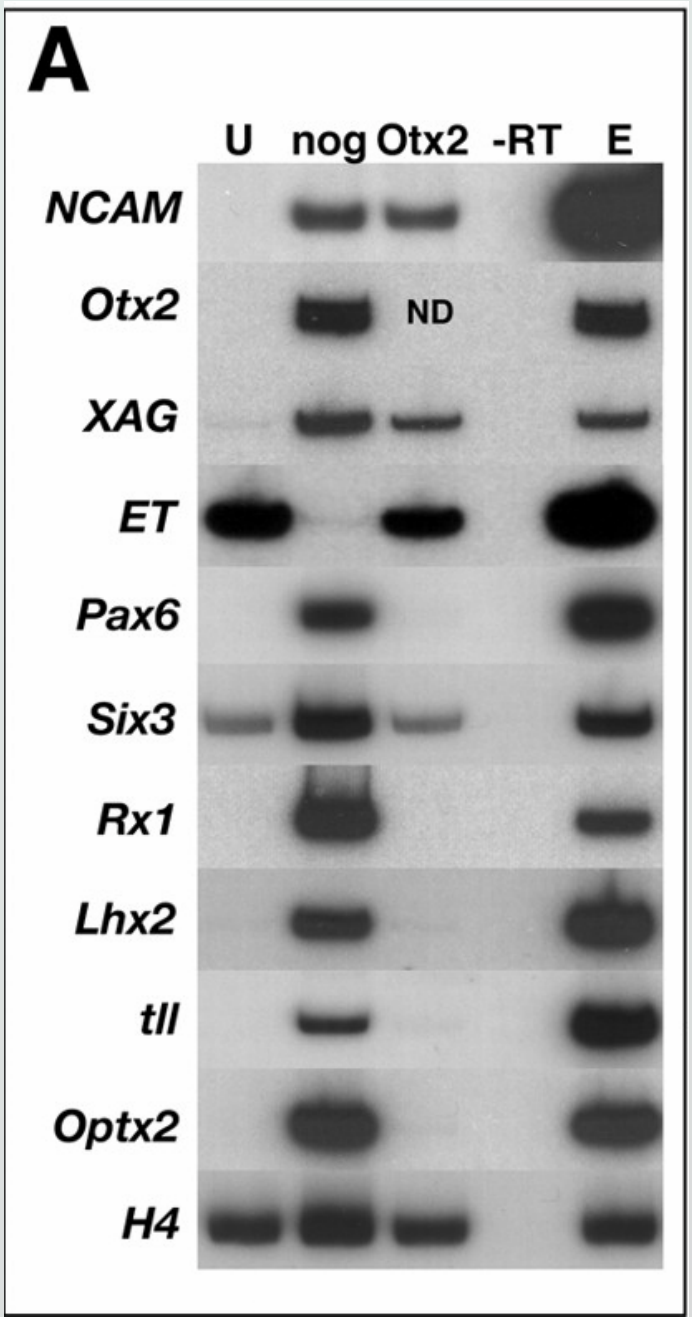


IL NETWORK DI FATTORI EFTF E' IN GRADO DI SPECIFICARE CELLULE STAMINALI PLURIPOTENTI A UN DESTINO RETINICO

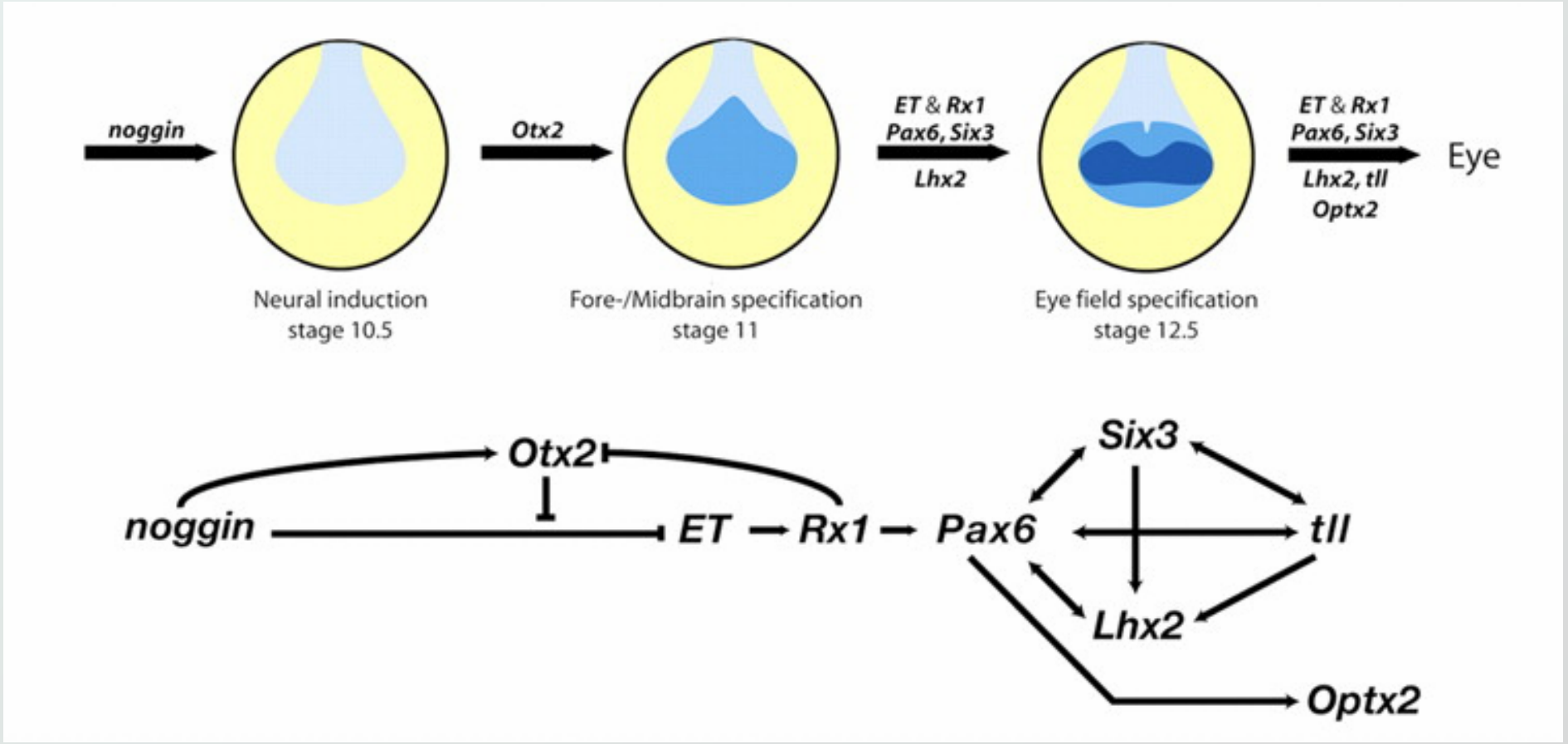




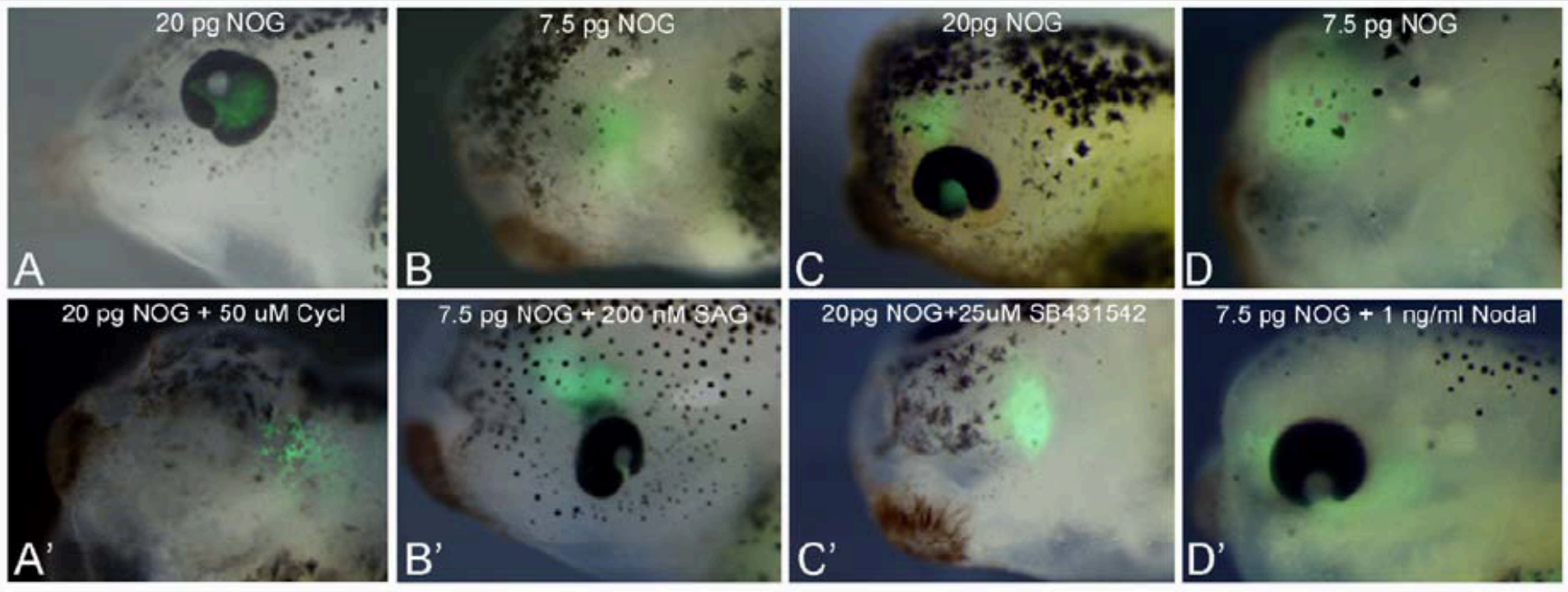
NOGGIN PROMUOVE L'ESPRESSIONE DEI FATTORI EFTF

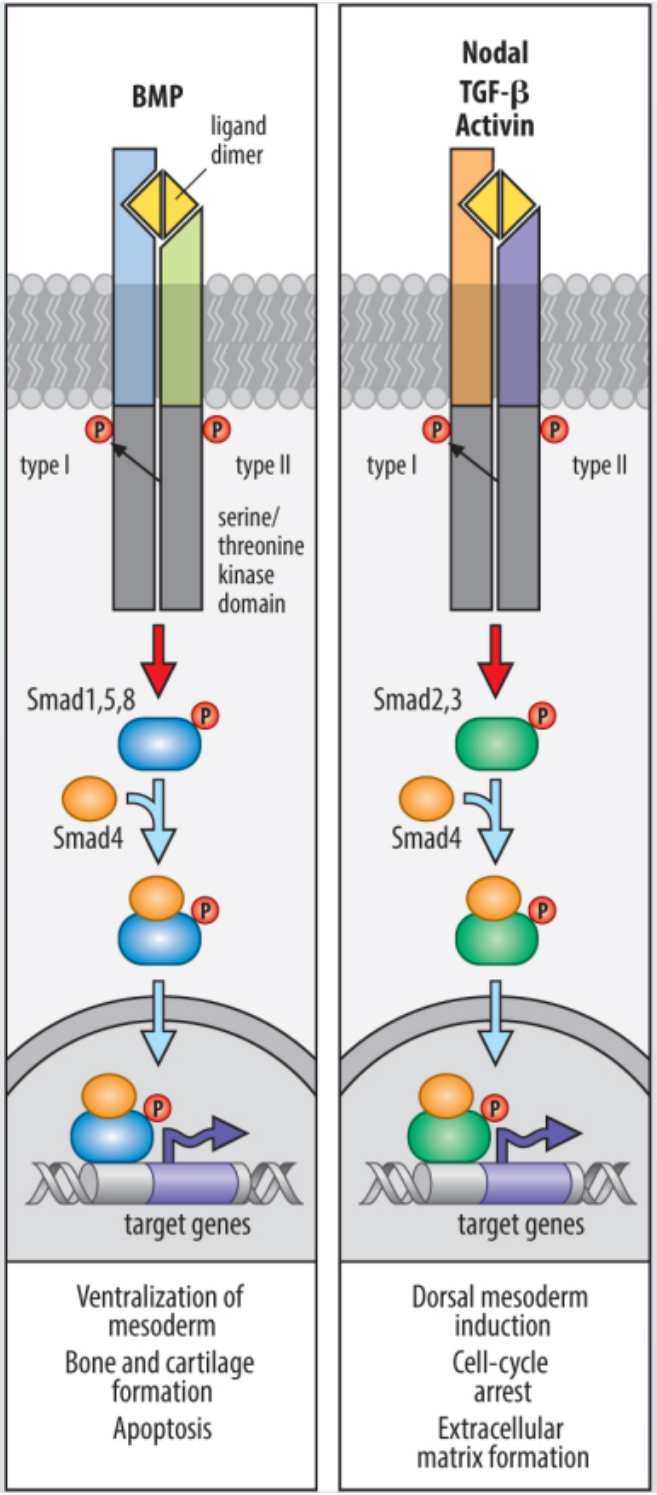


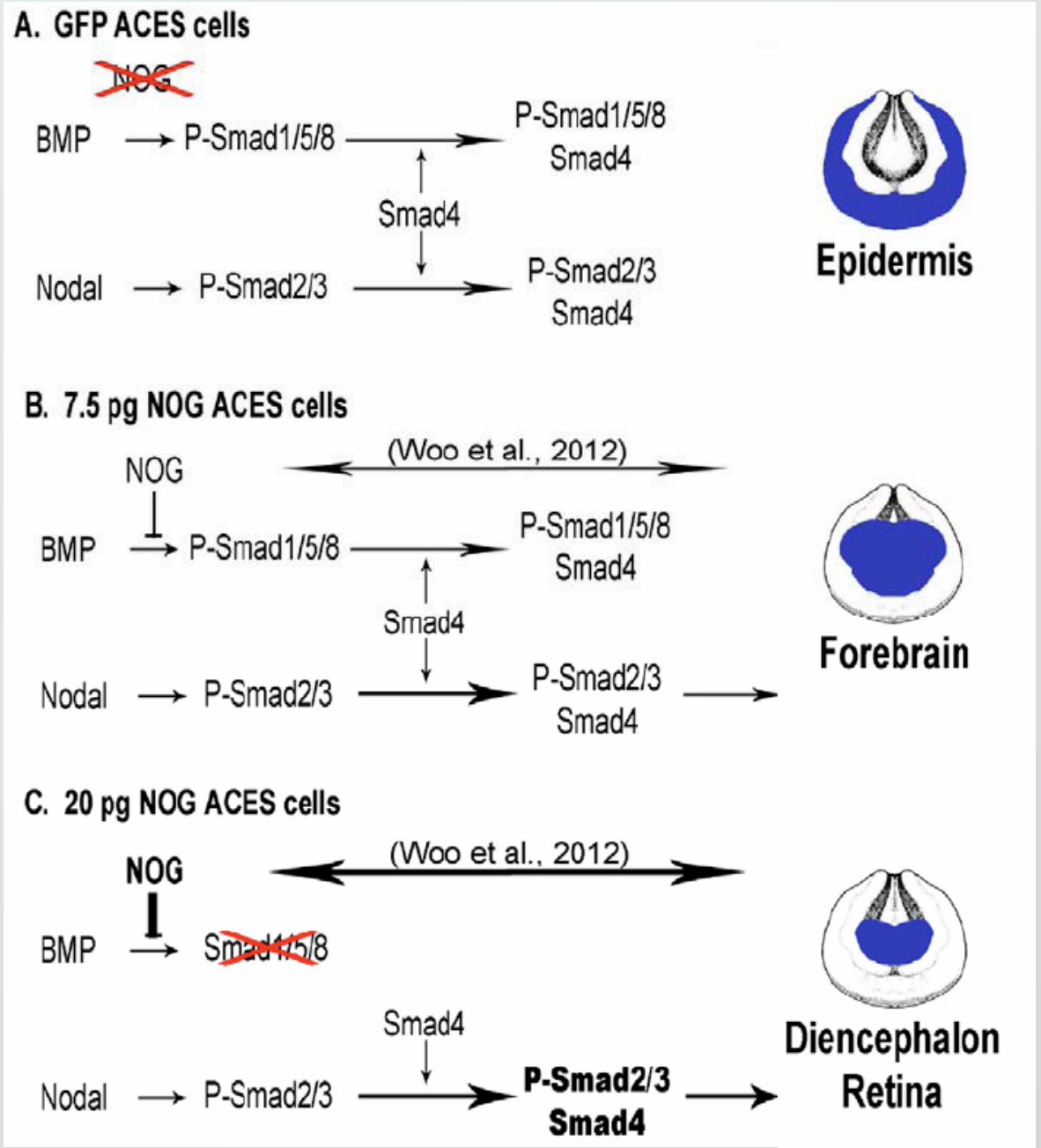
IL NETWORK DI FATTORI EFTF AGISCE NELLA DETERMINAZIONE PRECOCE DELLA RETINA A VALLE DI NOGGIN



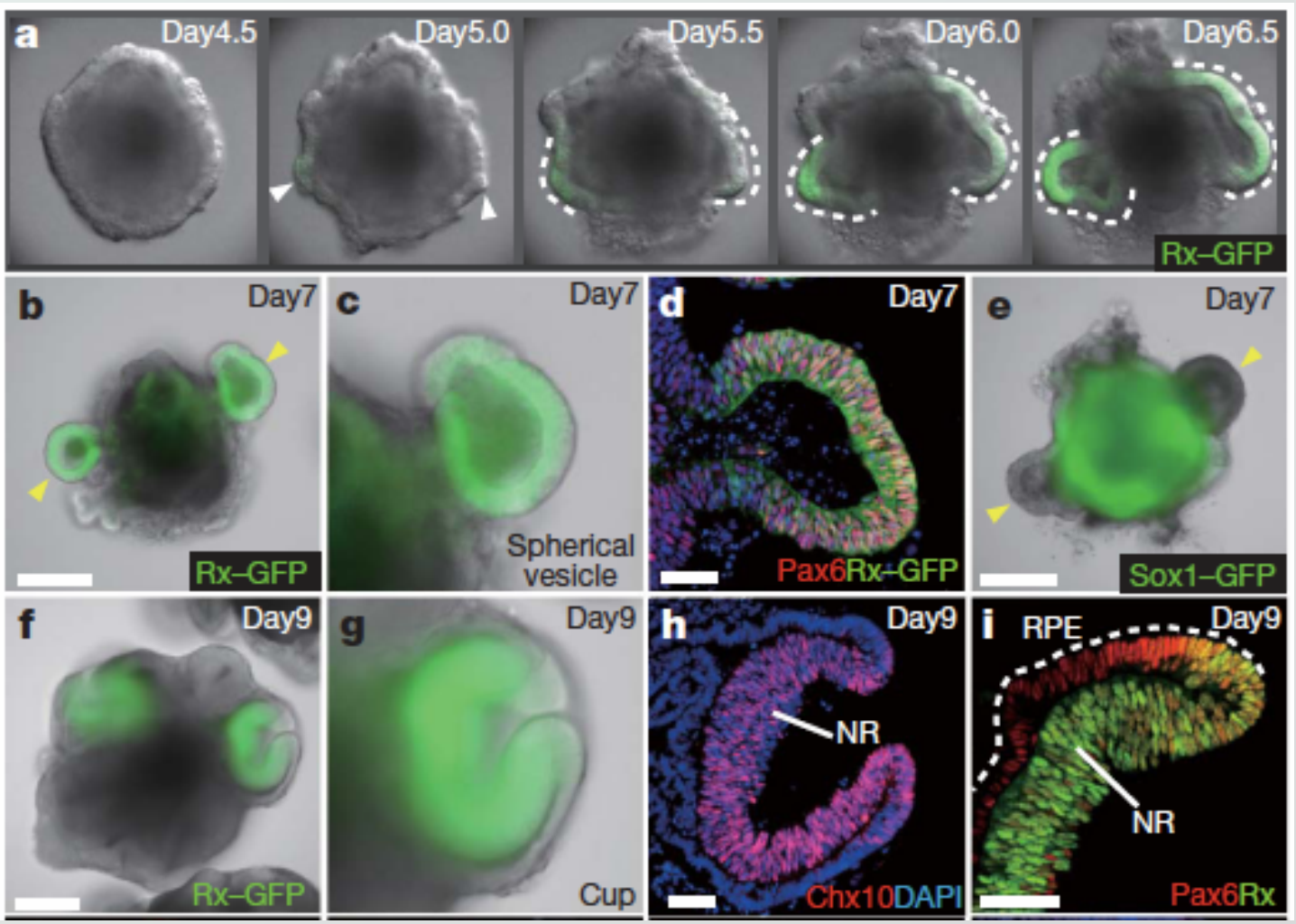
Noggin-mediated Retinal Induction Reveals a Novel Interplay between BMP Inhibition, TGFβ and SHH Signaling



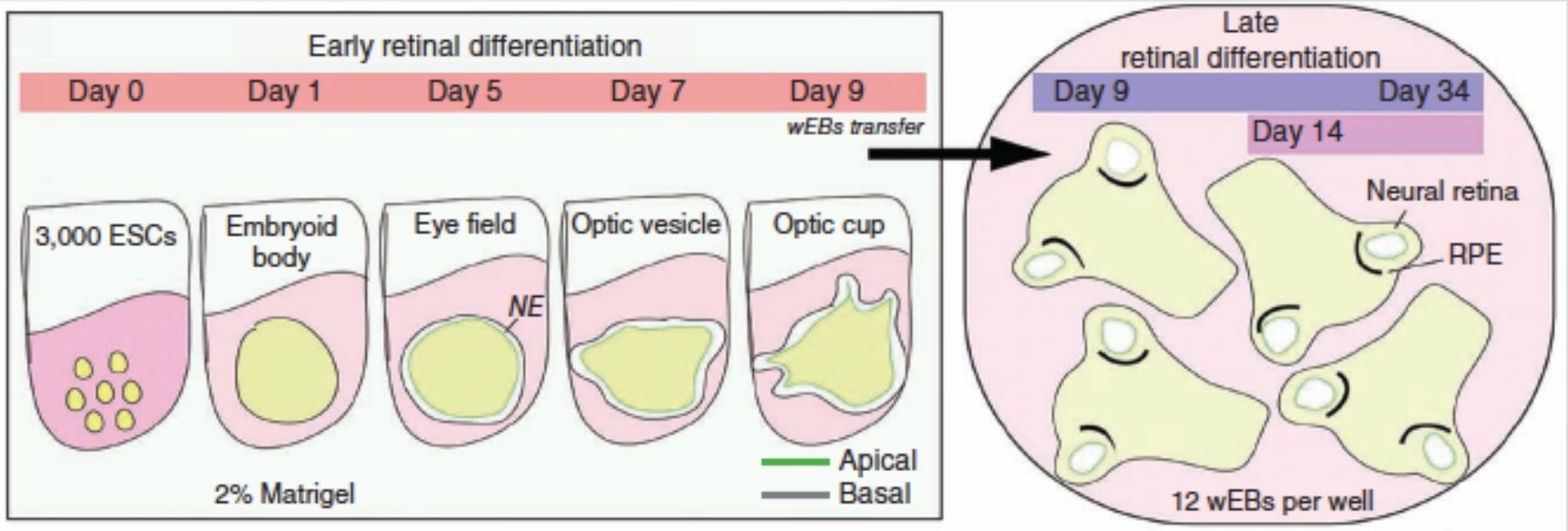

BMP
ligand dimer
type I
type II
serine/ threonine kinase domain
Smad1,5,8
Smad4
target genes
Ventralization of mesoderm
Bone and cartilage formation
Apoptosis
Nodal
TGF-β
Activin
type I
type II
Smad2,3
Smad4
target genes
Dorsal mesoderm induction
Cell-cycle arrest
Extracellular matrix formation

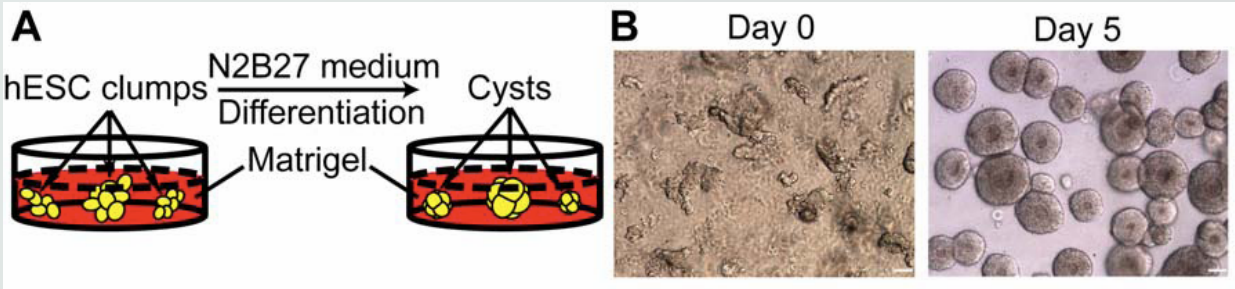

A. GFP ACES cells
NOG
BMP → P-Smad1/5/8 → P-Smad1/5/8 Smad4
Smad4
Nodal → P-Smad2/3 → P-Smad2/3 Smad4
Epidermis
B. 7.5 pg NOG ACES cells
(Woo et al., 2012)
NOG
BMP → P-Smad1/5/8 → P-Smad1/5/8 Smad4
Smad4
Nodal → P-Smad2/3 → P-Smad2/3 Smad4
Forebrain
C. 20 pg NOG ACES cells
(Woo et al., 2012)
NOG
BMP → Smad1/5/8
Smad4
Nodal → P-Smad2/3 → P-Smad2/3 Smad4
Diencephalon
Retina

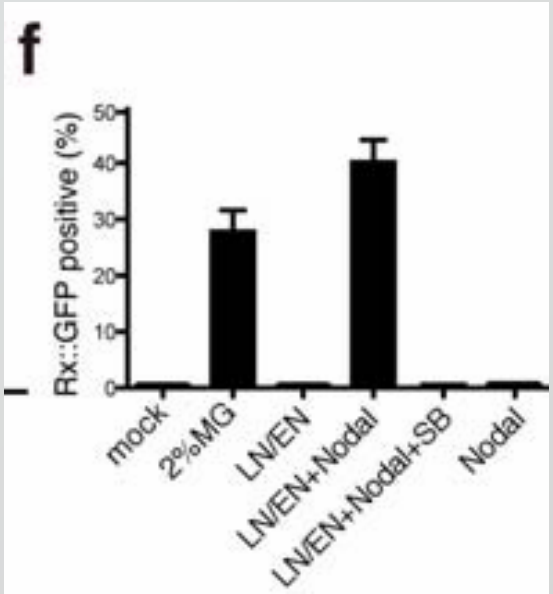
Self-organizing optic-cup morphogenesis in three-dimensional culture



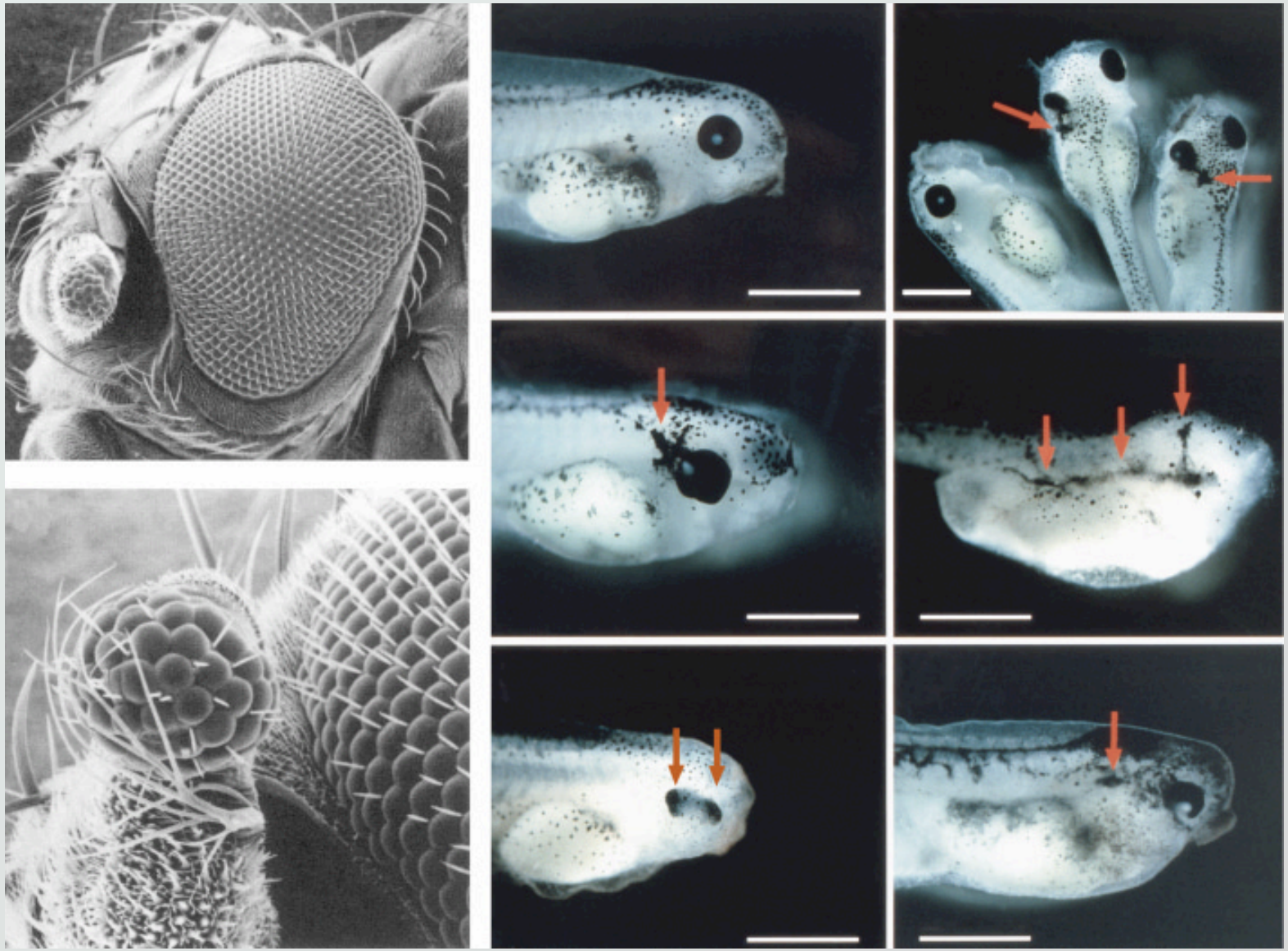
INDUZIONE DI TESSUTO RETINICO IN CELLULE STAMINALI EMBRIONALI COLTIVATE IN PRESENZA DI MATRIGEL



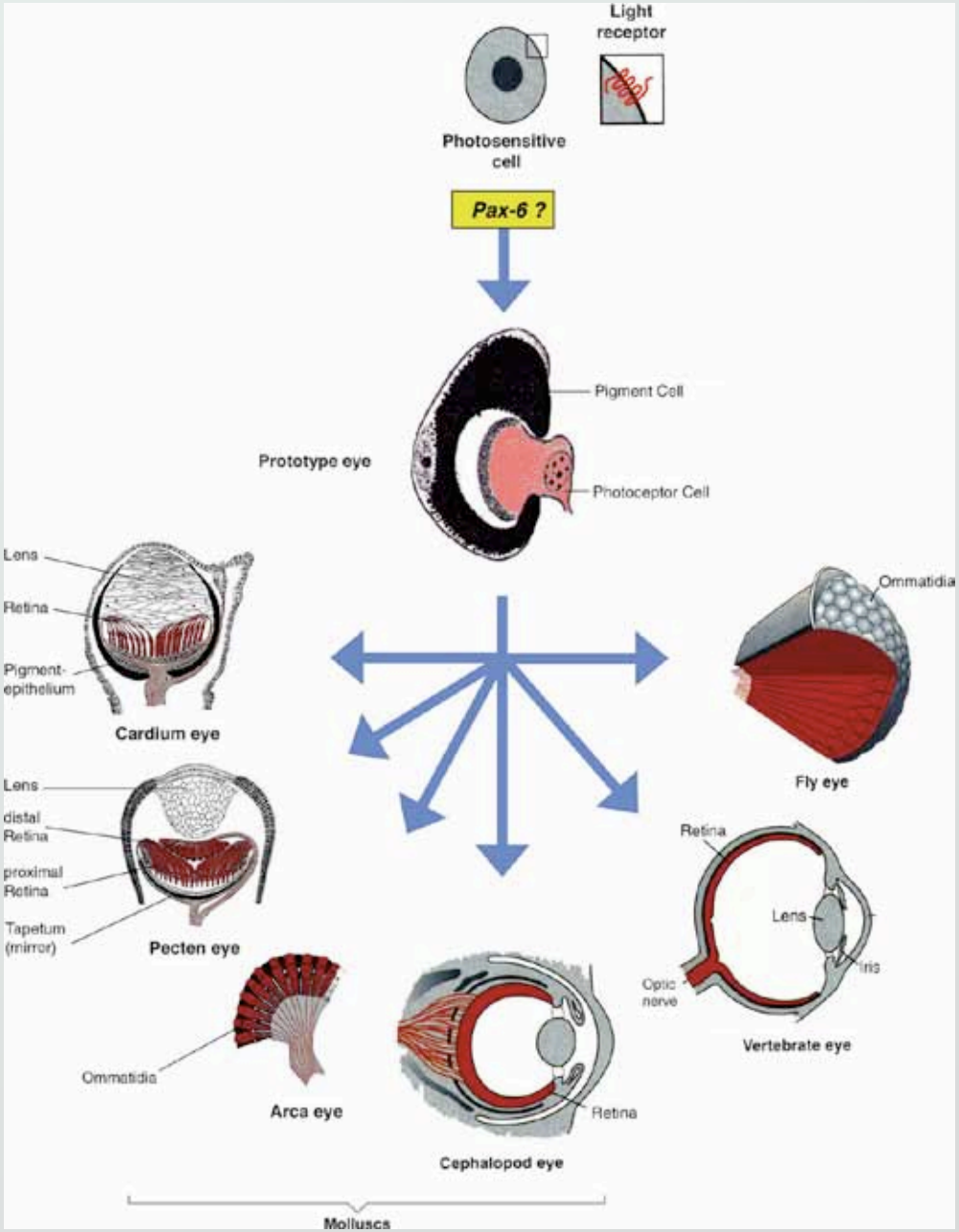




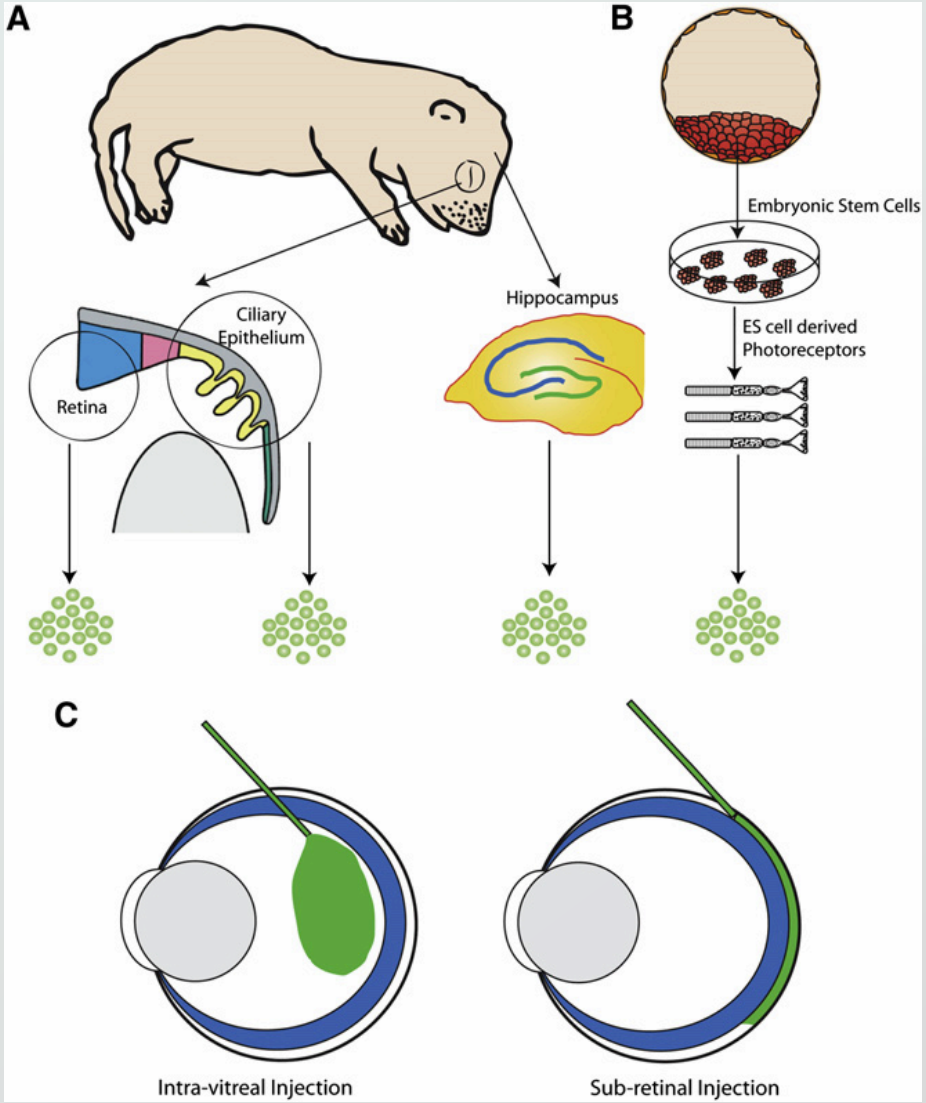
I GENI EYELESS/PAX6 SONO FUNZIONALMENTE INTERCAMBIABILI



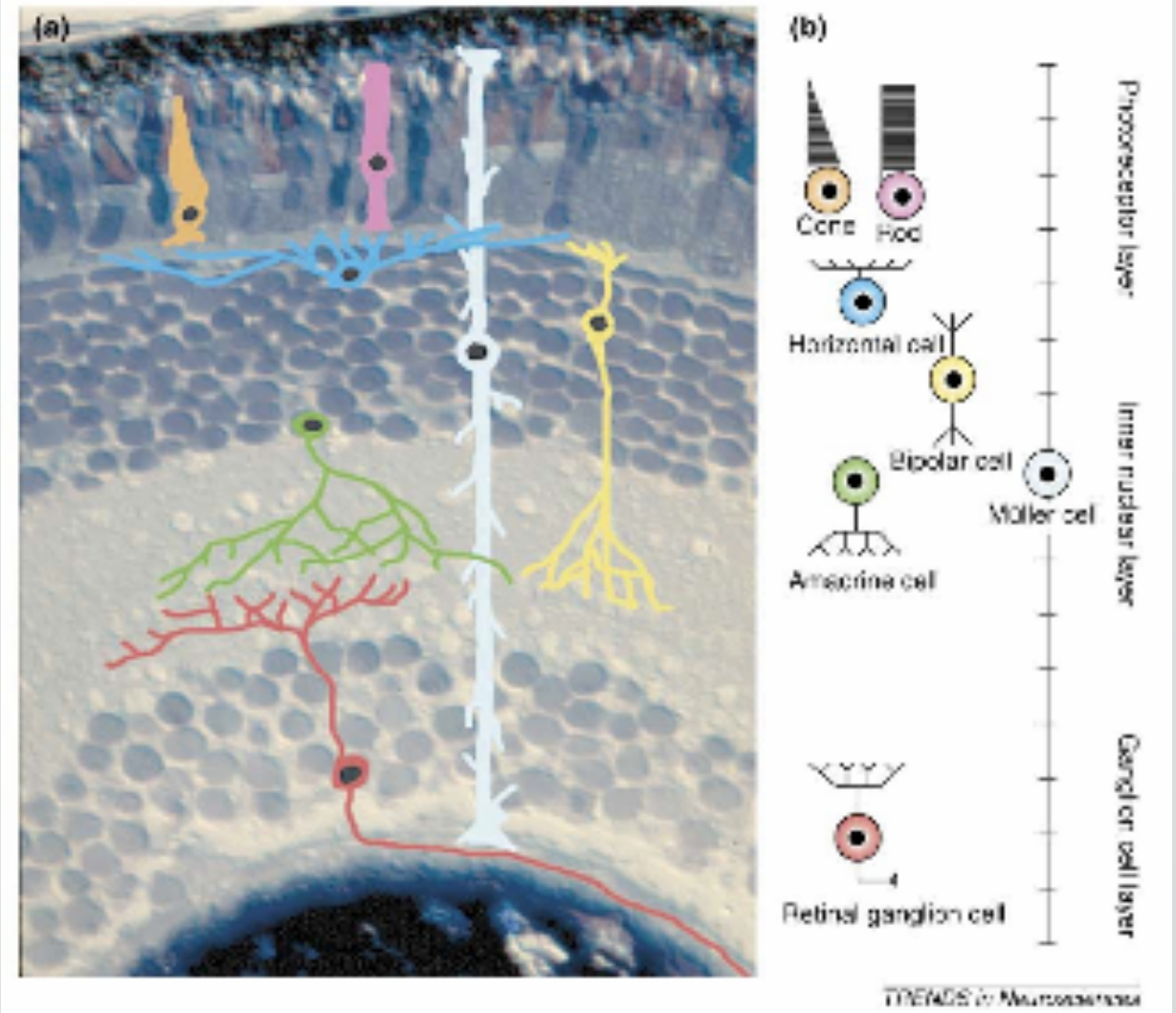
ORIGINE MONOFILETICA DELL'OCCHIO DURANTE L'EVOLUZIONE DEI METAZOI



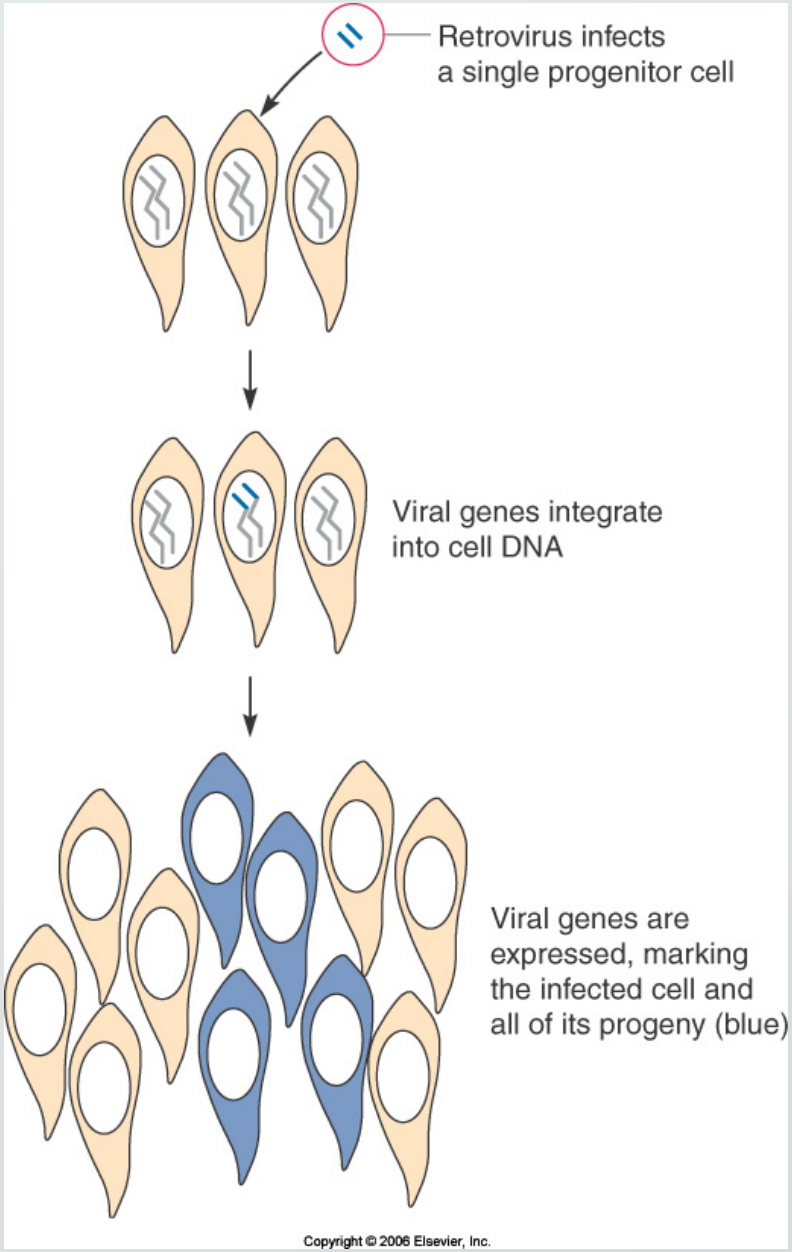
POSSIBILI STRATEGIE PER L'USO DI CELLULE STAMINALI NELLA TERAPIA DI PATOLOGIE RETINICHE



STRUTTURA DELLA RETINA DEI VERTEBRATI

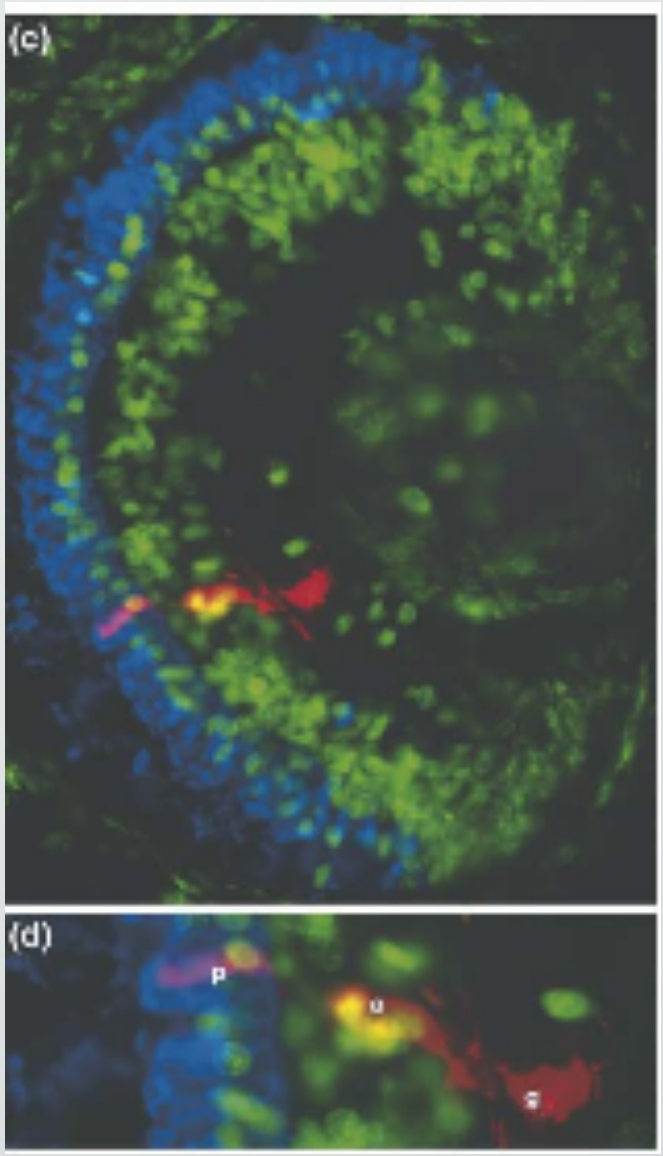


SAGGI DI ANALISI CLONALE IN PRECURSORI NEURALI

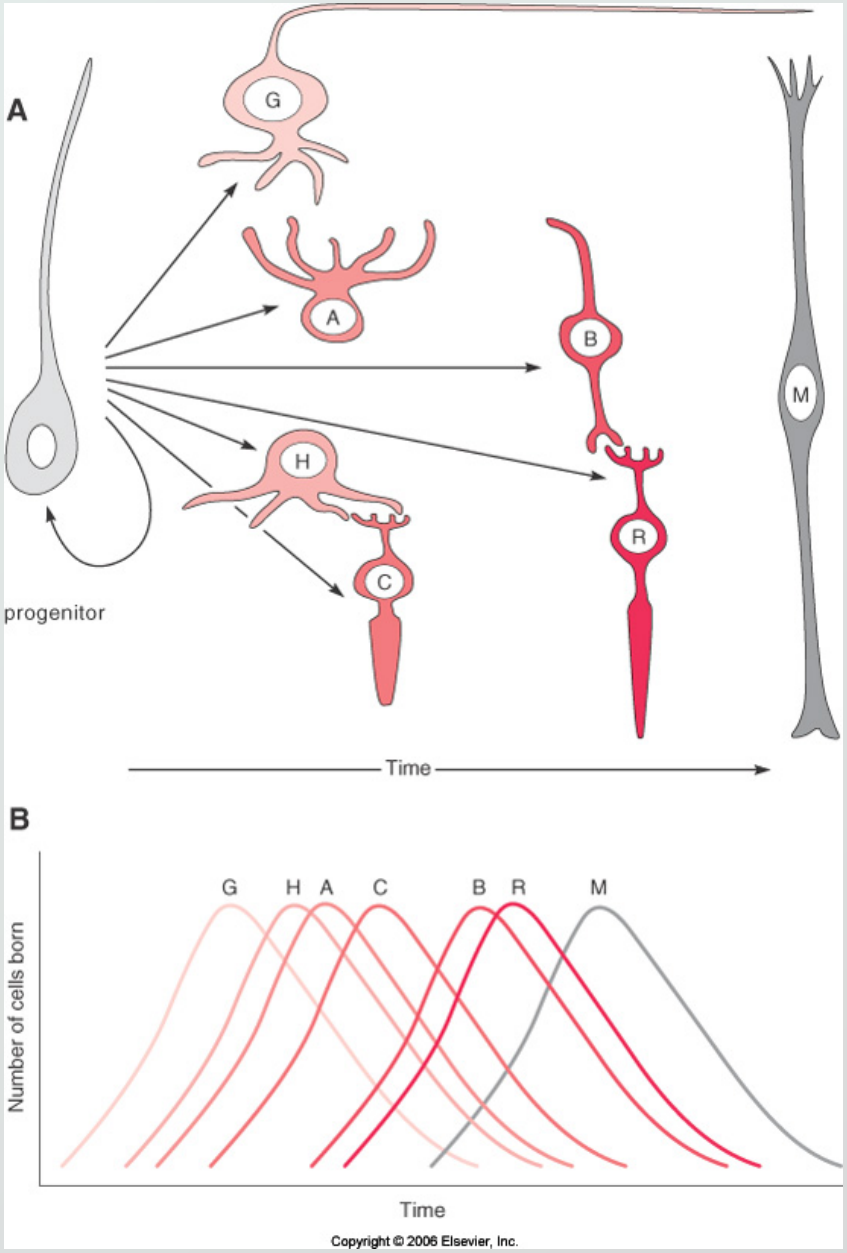


SAGGI DI ANALISI CLONALE IN PRECURSORI RETINICI

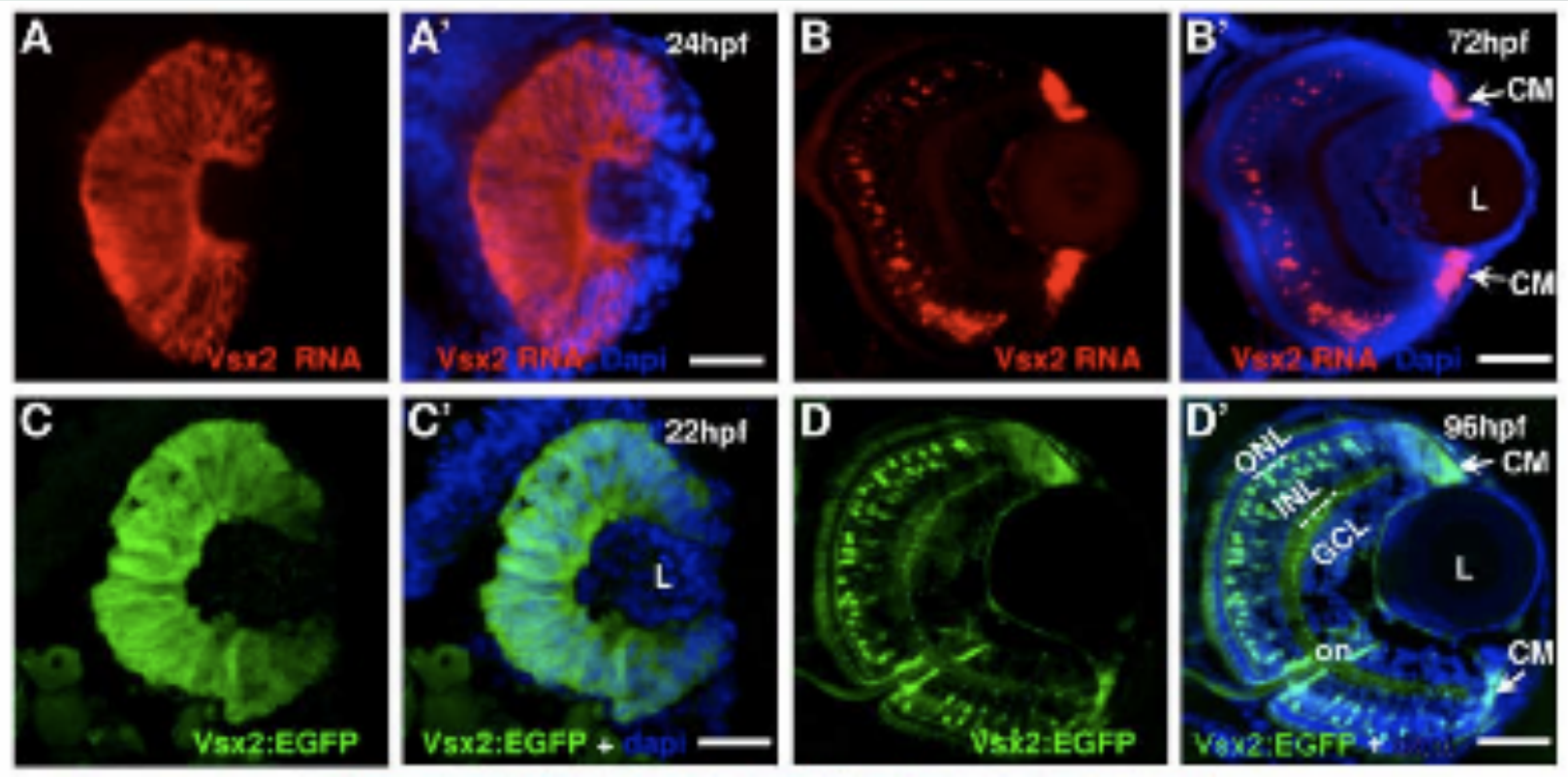
SAGGI DI “BIRTH-DATING” IN PRECURSORI RETINICI



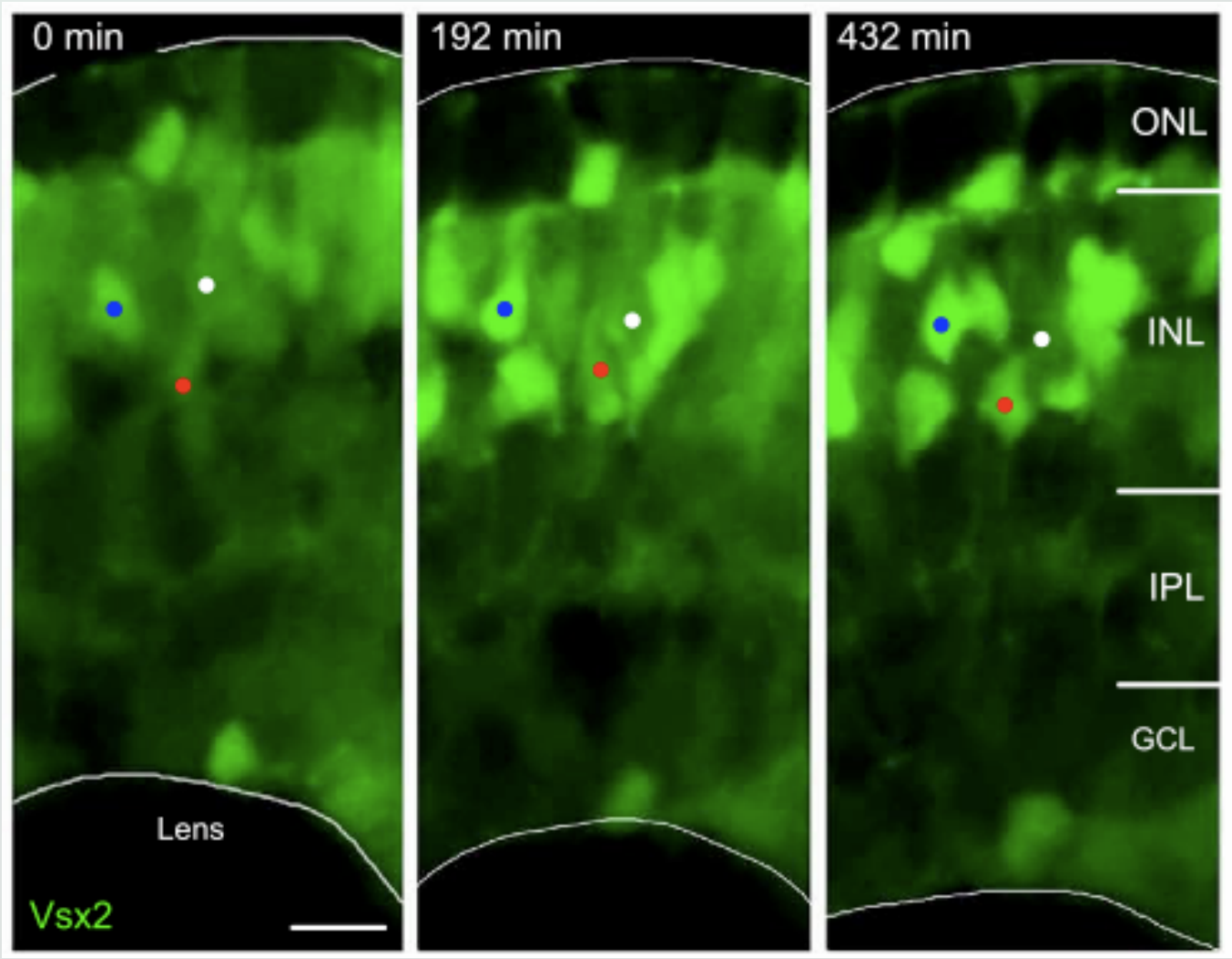
IL DIFFERENZIAMENTO DELLA RETINA AVVIENE SECONDO UNA PRECISA SEQUENZA TEMPORALE



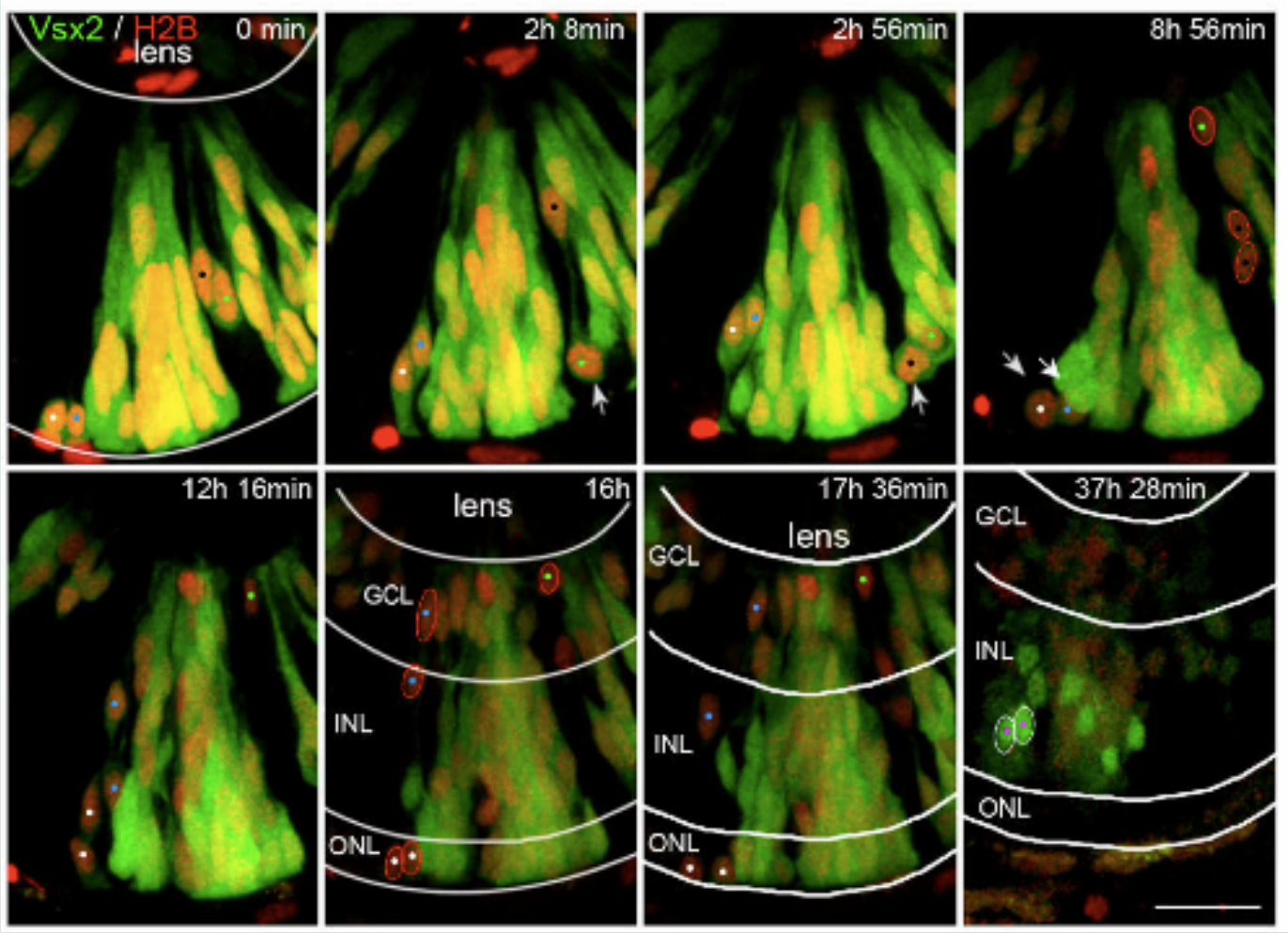
ESPRESSIONE DEL GENE VSX2 DURANTE IL DIFFERENZIAMENTO RETINICO



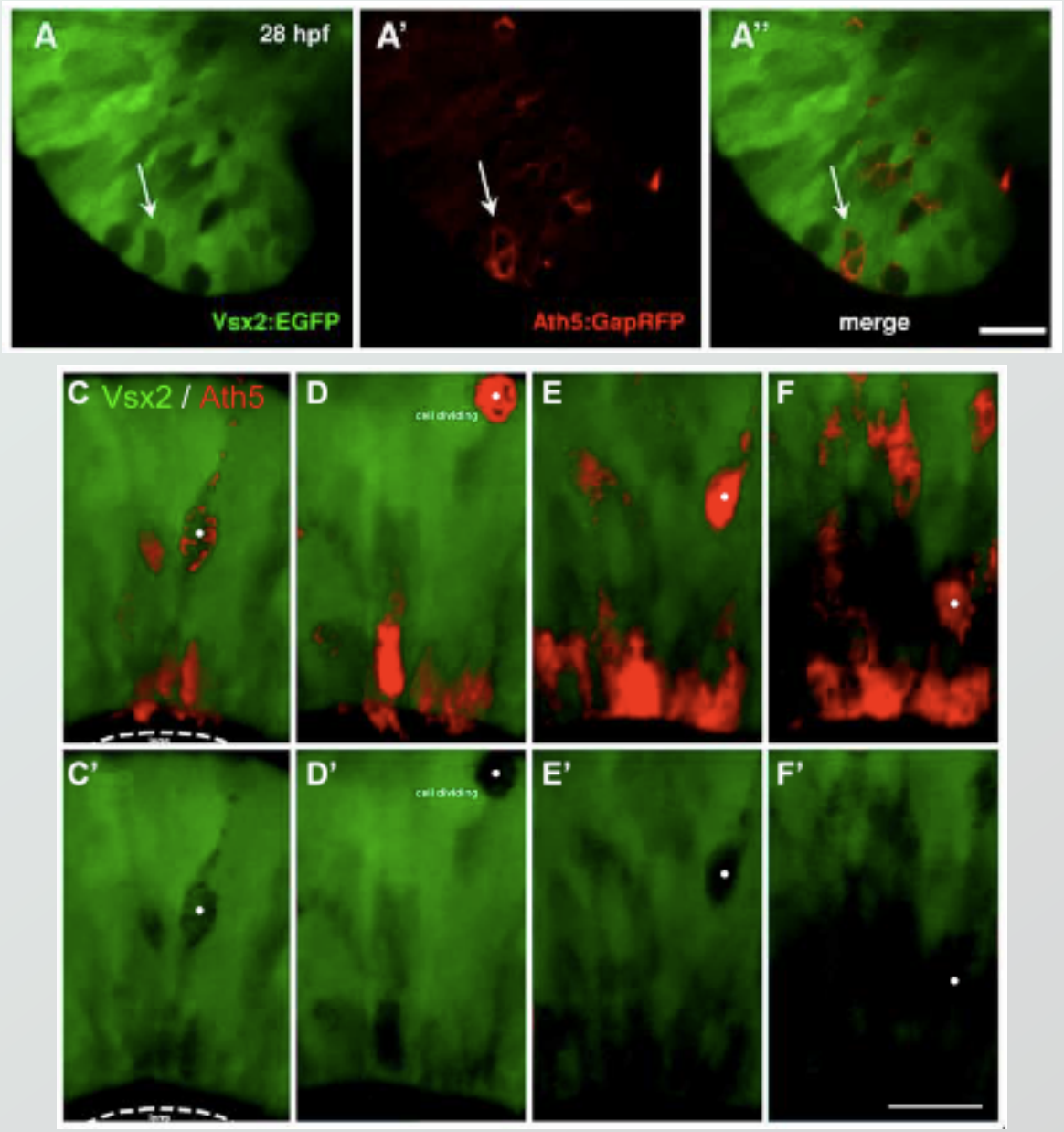
L'ESPRESSIONE DEL GENE VSX2 E' MANTENUTA IN UNA SOTTOPOPOLAZIONE DI CELLULE RETINICHE



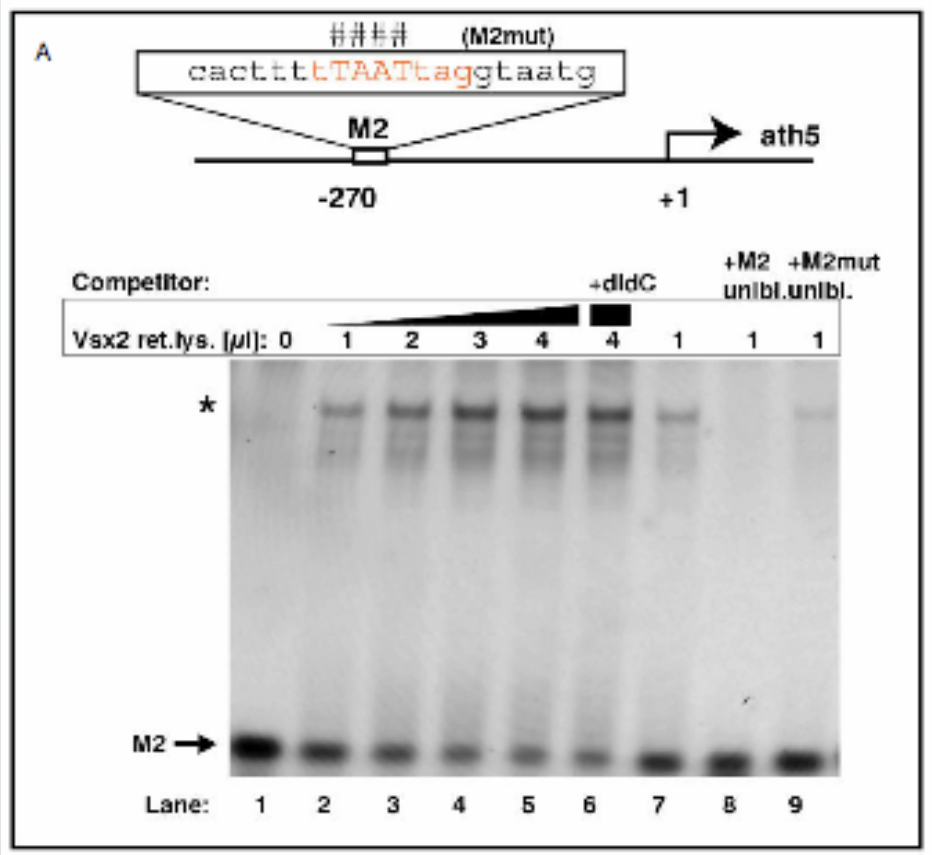
L'ESPRESSIONE DEL GENE VSX2 E' MANTENUTA IN UNA SOTTOPOPOLAZIONE DI CELLULE RETINICHE CHE SI DIFFERENZIANO IN CELLULE BIPOLARI



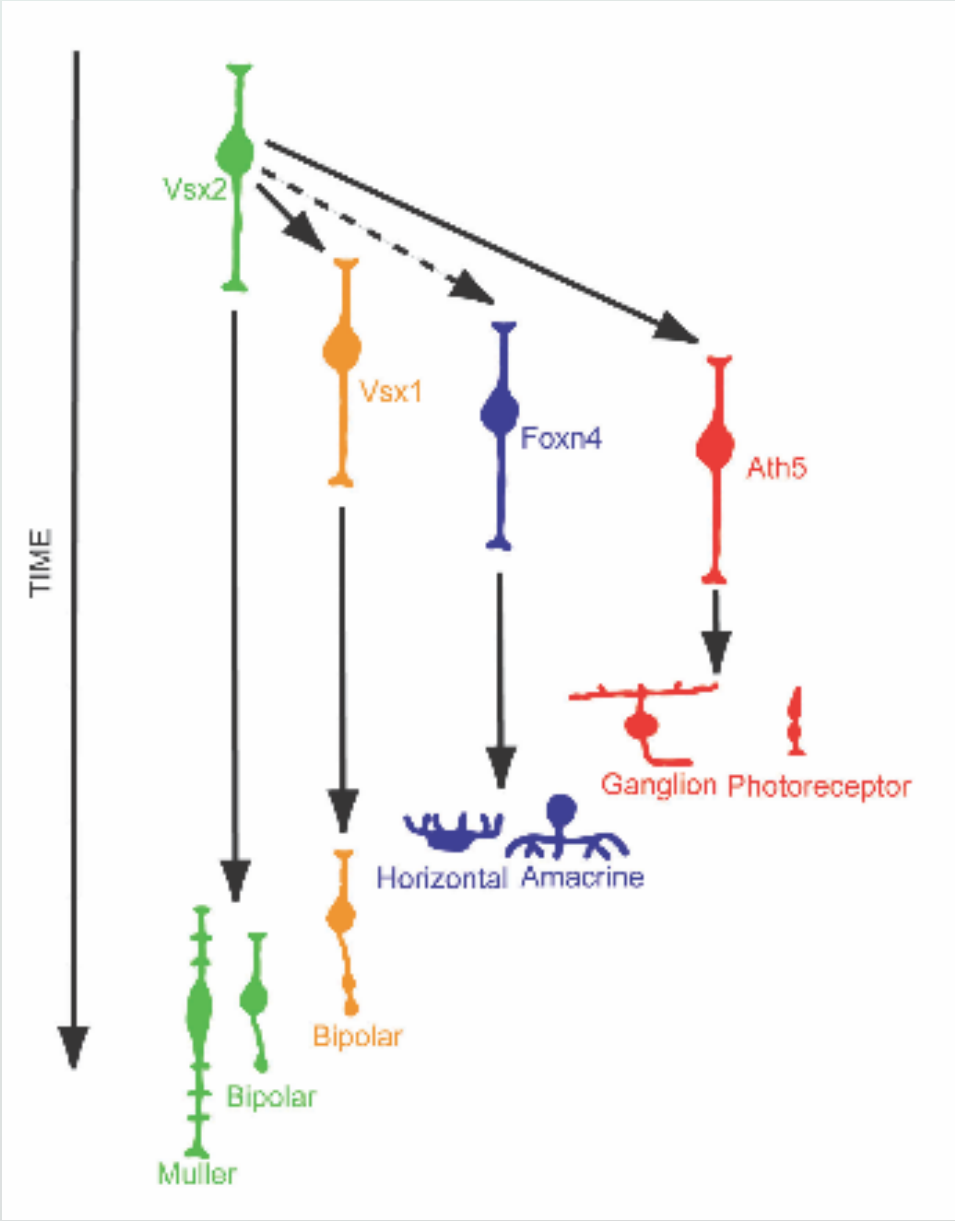
L'ESPRESSIONE DEL GENE VSX2 E' COMPLEMENTARE A QUELLA DEL GENE ATH5



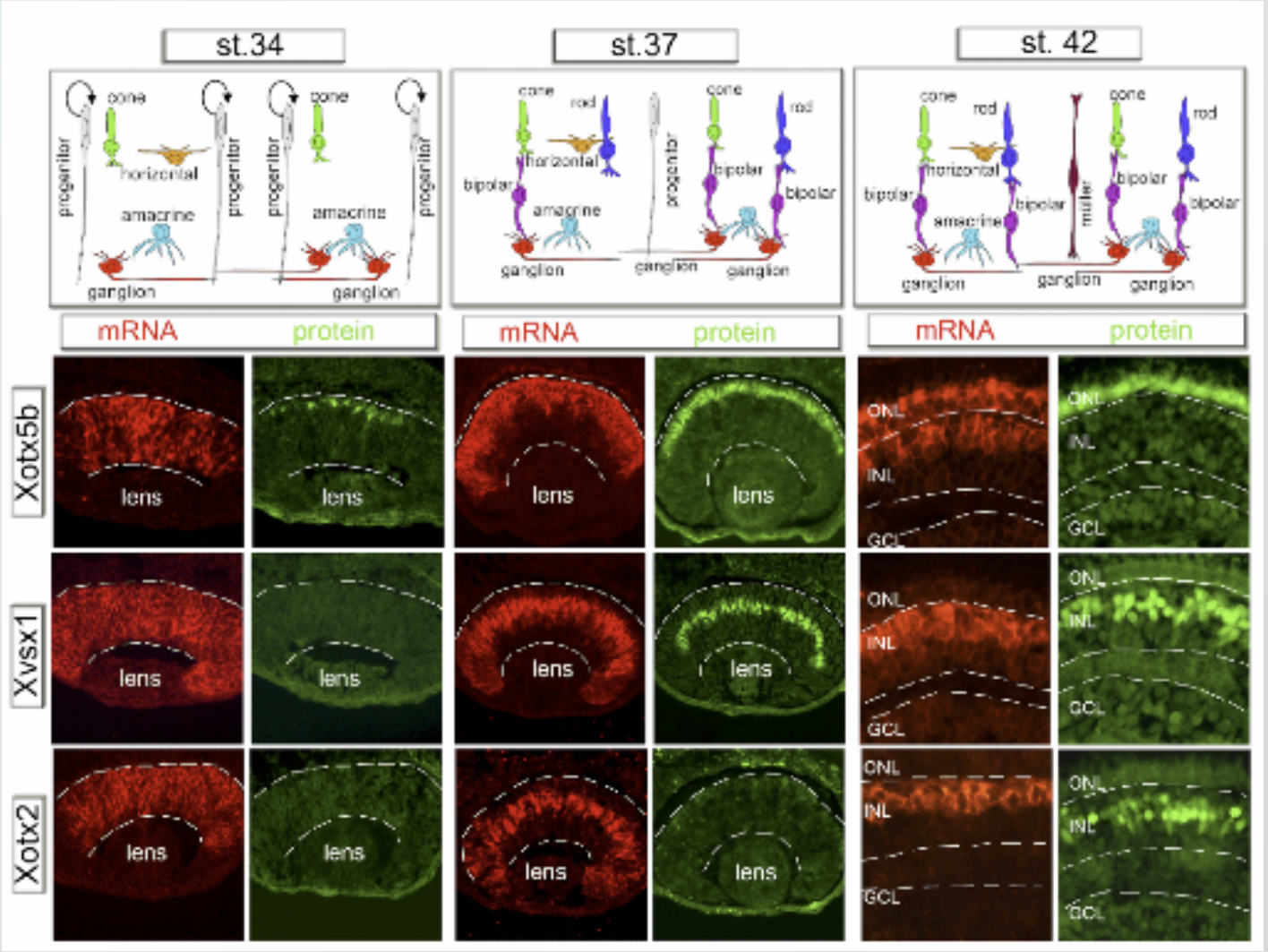
IL FATTORE DI TRASCRIZIONE VSX2 LEGA IL PROMOTORE DEL GENE ATH5



IL GENE VSX2 REGOLA IL TIMING DEL DIFFERENZIAMENTO RETINICO



L'ESPRESSIONE DI FATTORI CHE REGOLANO IL DIFFERENZIAMENTO RETINICO E' REGOLATA A LIVELLO TRADUZIONALE



REGOLAZIONE TEMPORALE DEL DIFFERENZIAMENTO RETINICO IN BASE A SEGNALI INTRINSECI ED ESTRINSECI