

.

Noggin:
Activin/Nodal Wnt .

– 03.01.03 –

, 2012

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«16» 2012 10

.002.019.01

16/10.

: 117997, -7, , -437, - ,

«13» 2012 .

Noggin (Noggin1)

1992 . *Xenopus*

. Noggin1

TGF- , Bone Morphogenetic Proteins (BMP) (Smith and Harland, 1992).

, BMP

I II

Smad1/5/8,

Smad4

(Shi and Massague, 2003).

Noggin

BMP

(Groppe et al., 2002),

Smad1/5/8.

, Noggin1,

Xenopus,

Noggin1

(Smith and

Harland, 1992),

(Botchkarev et al., 1999)

(Brunet et al., 1998; Botchkarev et al., 1999; Shi and Massague, 2003).

, Noggin1

BMP-

Noggin1

TGF- ,

Activin/Nodal/TGFbeta,

Smad2/3 (Branford and Yost, 2002).

(Piccolo et al., 1999),

(Meno et al., 2001)

(Grande and

Patel, 2009).

“ ” Noggin1,

2006). Noggin, Noggin2 Noggin4 (Furthauer et al., 1999; Fletcher et al., 2004; Eroshkin et al.,

Noggin2,

Xenopus Danio,

BMP-

, Noggin2 ,
Noggin1 (Furthauer et al., 1999).

,
Noggin,

(Eroshkin et al., 2006),

Xenopus.

in vivo.

Noggin

1.

Noggin.

2.

Noggin

3.

Noggin1 Noggin2

4.

Noggin1 Noggin2

Noggin1 Noggin2

Noggin.

Noggin2 Noggin4

Xenopus

vitro,

BMP,

Noggin2,
Activin/Nodal- Wnt
in vivo.

Noggin *in*
– ActivinB, Xnr2, Xnr4 Wnt8 –

BMP.

Noggin1

Noggin2.

Noggin2

Wnt-

BMP-, Activin-

Noggin2.

Noggin

BMP-, Activin/Nodal- Wnt-

16th International Society of Developmental Biologists Congress (, 2009) " " (, 2011).

8

, . . . 6

4

Noggin

Noggin (

Noggin1).

Noggin (*Noggin1*, -2, -3),

Xanf1,
(Eroshkin et al., 2006).

Xenopus
Xanf1

19

Noggin1.

Noggin2,

Noggin2.

Danio rerio (67%

30%

Noggin1 *Noggin2*

Noggin4,

Danio *Noggin3*.

, *Noggin3* *Danio*

Noggin1 (62%

), . . .

Danio.

Noggin2 *Noggin4*

(GenBank).

Noggin4 *Danio*

Noggin5.

, *Noggin1*.

Noggin4

22

3

Noggin4, . .

Noggin4 (35-43%), *Noggin* (20-28%) (.1).
Noggin4 *Noggin*,

BMP (Groppe et al., 2002).

BMP

Noggin4 (Paine-Saunders S et al., 2002). *Noggin*

Noggin4 (.1). *Noggin*

Noggin (.1).

Noggin

Suberites domuncula, *Trichoplax adhaerens*, *Hydra magnipapillata*,
Ciona intestinalis,

Noggin

Noggin, *Smed-nog1* and *Smed-nog2*, *Schmidtea mediterranea* 2
Noggin-Like Gene, 8 *Noggin*- , *Smed-nlg1* – *Smed-nlg8* ()
(Molina et al., 2009). *Nematostella vectensis*

Noggin, *NvNoggin1* *NvNoggin2* (Matus et al., 2006).

Noggin

Noggin2 *Noggin4*

(-) ,

Noggin1, -2 -4.

(*ODC*). ,

Noggin2 (.12.5).

(.2).

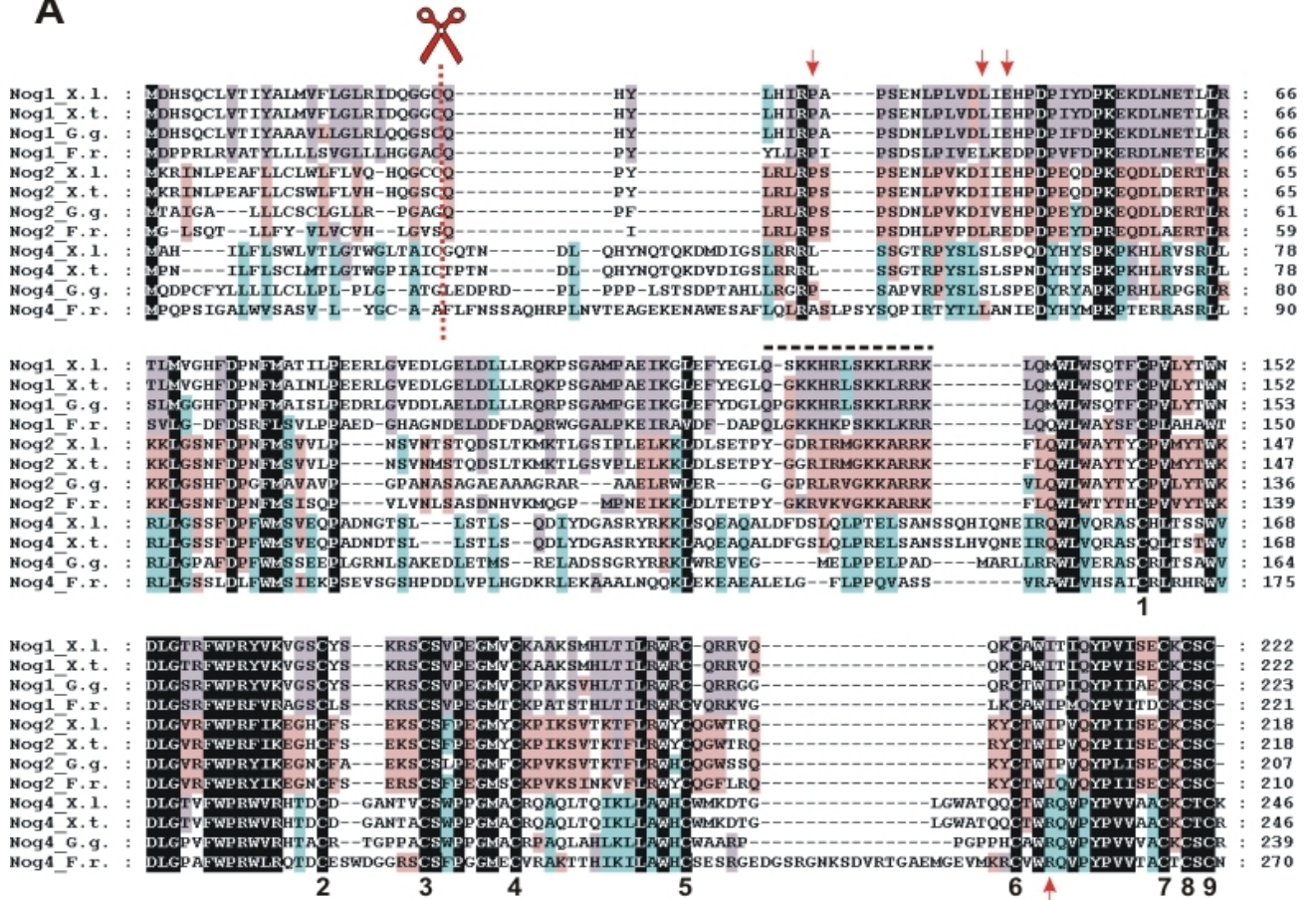
Noggin2, *Noggin4*

(.8). (.10.5)

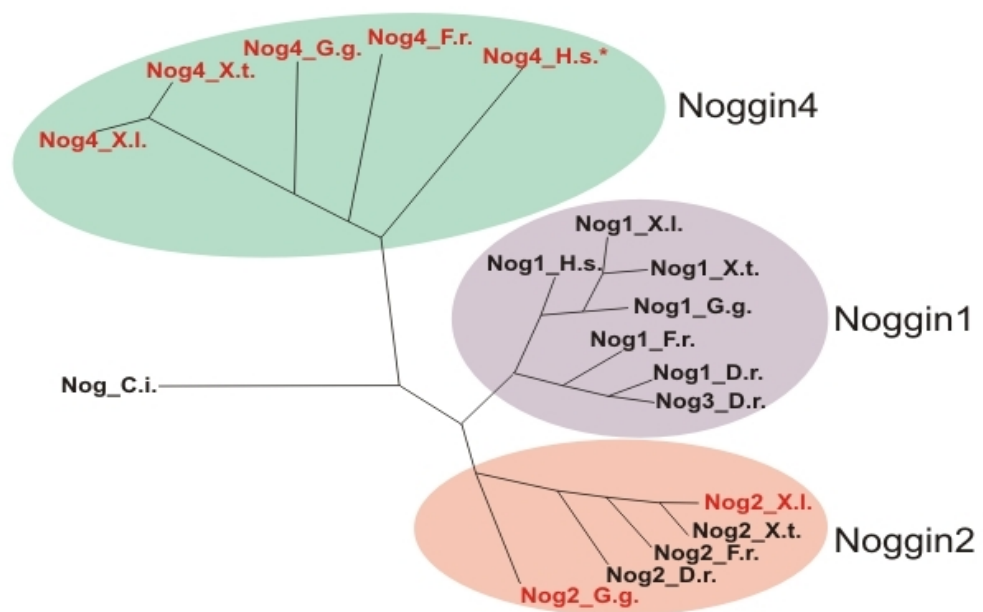
Noggin1 (Smith and Harland, 1992) (.2).

in situ

A



B



.1 () *Noggin Xenopus laevis, Xenopus tropicalis (X.t.), Fugu rubripes (F.r.) and Gallus gallus (G.g.), Danio rerio (D.r.).*

BMP. *()* *Noggin C.i., Ciona intestinalis, D.r., Danio rerio, F.r., Fugu rubripes, G.g., Gallus gallus, H.s., Homo sapiens. X.l., Xenopus laevis, X.t., Xenopus tropicalis.*

14) *Noggin2*, *Noggin2* (.
Noggin1 (.2 -).
(Fletcher et al., 2004).

15 () *Noggin1*, *Noggin2* in situ.
(. 24) *Noggin2* 26

(.3 -). *Noggin1, Noggin2*
(.3 -).
Noggin4 (.2 ,).
Noggin4 (.2).

Noggin4, *Noggin1*,
Noggin4 (.2).

Noggin4, *Noggin1*,
Noggin4

Noggin4 (.2). 24, *Noggin4*
(.3 -). *Noggin4*

Noggin4,
(.3 -).
Noggin - *Noggin1* *Noggin2* -
- *Noggin4* -

Noggin,

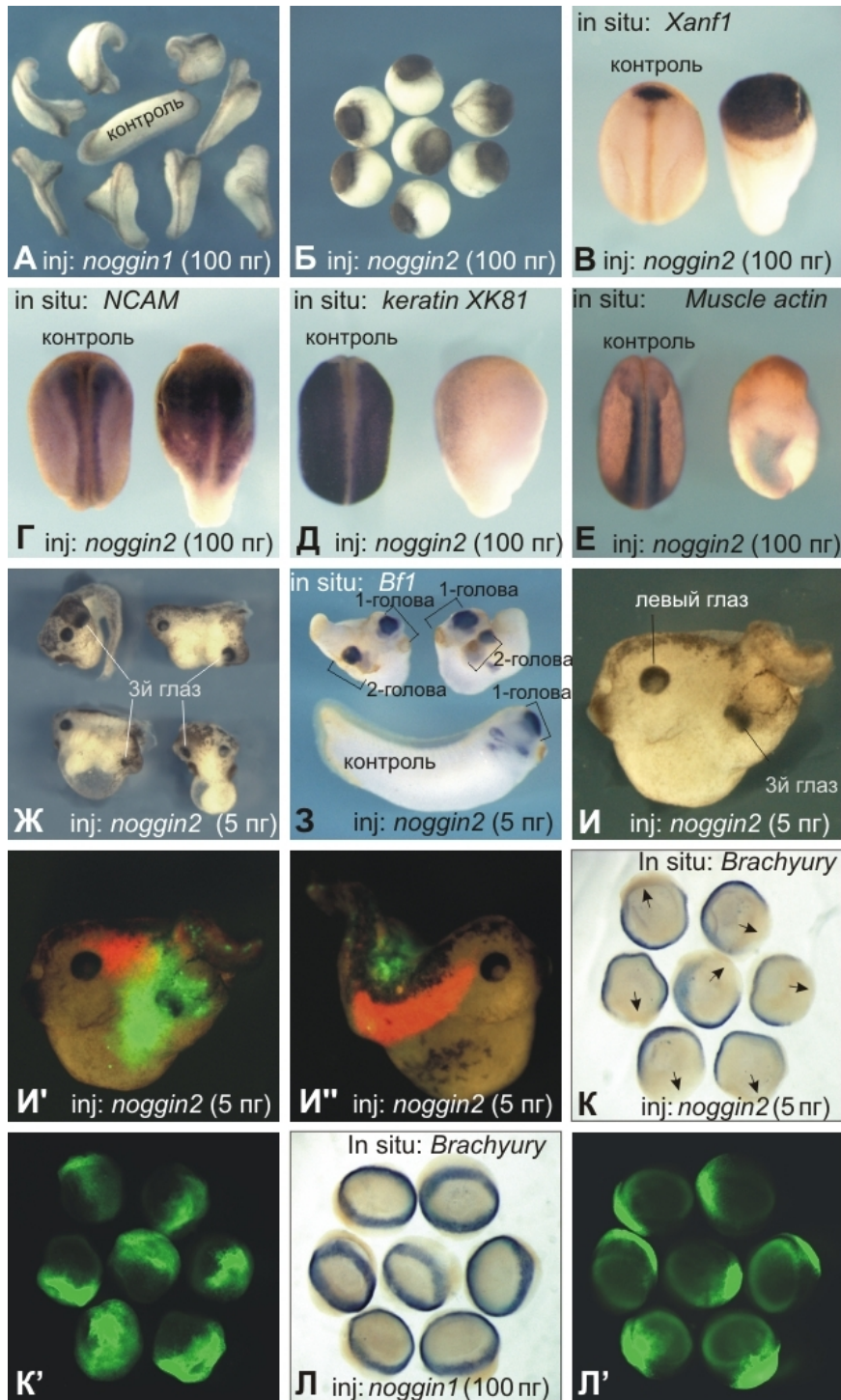
Noggin1 -2.

Noggin1 -2

Noggin1
Noggin1
BMP-
Noggin1 *Noggin2*,
Noggin
 4-8
 5, 5' - (*Noggin1*)
 (Smith and Harland, 1992) 20 400 (/).
 (.4).
Noggin2,
 5 *Noggin1*, 5' - (.4)
in situ
NCAM,
Xanf1 (.4 ,).
 (keratin) (muscle actin) (.4 ,).
Noggin2
Noggin2
 3-5 / .
 35%
 (.4 -).
Noggin2
 (Shcherbo et al., 2007).
 3-5 / *Noggin1*,
 , *Noggin2*

Noggin1 -2

Noggin2
 -
BMP-, *Nodal-* *Wnt-*
 Cerberus,



4. *Noggin2*, *Noggin1*

in situ: *Xanf1* контроль

in situ: *NCAM* контроль

in situ: *keratin XK81* контроль

in situ: *Muscle actin* контроль

in situ: *Bf1* 1-голова, 2-голова, контроль

In situ: *Brachyury* контроль, inj: *noggin2* (5 нг)

fluorescence: inj: *noggin2* (5 нг) (I', I'')

fluorescence: inj: *noggin1* (100 нг) (L')

in situ: *Brachyury* inj: *noggin1* (100 нг) (L)

in situ: *Brachyury* inj: *noggin2* (5 нг) (K)

(Piccolo et al., 1999).

Noggin2

Noggin1 (Smith and Harland, 1992),

Noggin1 *Noggin2*,

5'-

Noggin1

Noggin2,

myc N-

(.5

).

-myc

Noggin1,

5'-

5,

5'-

200

Noggin2,

5'-

(.5)..

Noggin2

5'-

5'-

Kozak (.5).

Noggin1

Noggin2

(.5).

Noggin2

Noggin1.

Noggin1 *Noggin2*

Noggin1,

Noggin2 (.5).

(.5),

myc-

Noggin2

Noggin1.

myc-

Noggin1 -2,

5'-

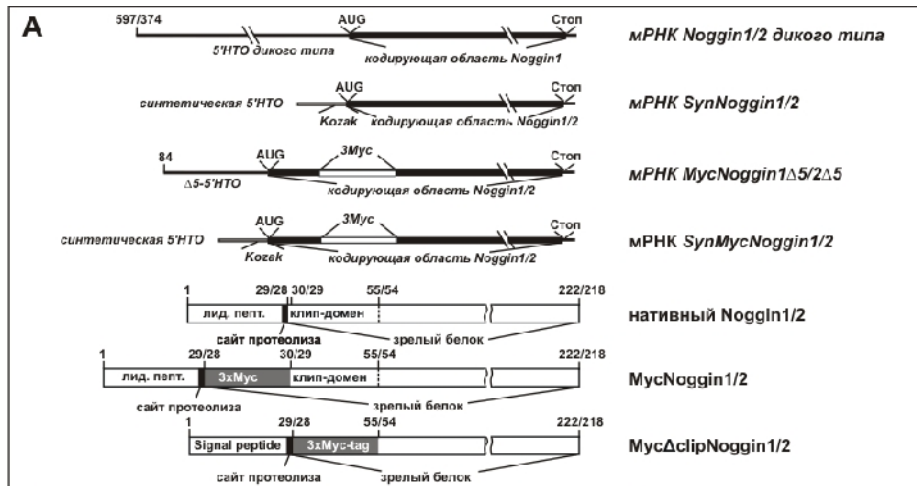
Kozak.

myc-

Noggin1 -2

Noggin1 -2

myc-



Б РНК

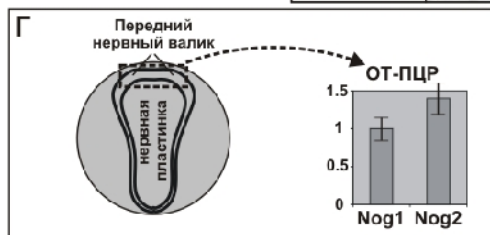
MycNog1Δ5 400 пг/эмбр	+		
MycNog2Δ5 2 пг/эмбр		+	
Myc Western			
MycNog2	→		-30kD
MycNog1	→		-20kD
Tubulin Western			
Tubulin	→		-50kD

В РНК

MycNog2Δ5 100 пг/эмбр	+		
SynMycNog2 100 пг/эмбр		+	
SynMycNog1 100 пг/эмбр			+
Myc Western			
MycNog2	→		-30kD
MycNog1	→		-20kD
Tubulin Western			
Tubulin	→		-50kD

Ж Myc ко-ИП + Flag-Western

MycNog1	+		
MycNog2		+	
wtMycNog1			+
Flag-BMP4			-30kD
Flag-ADMP			-20kD



З Myc ко-ИП + Flag-Western

MycNog1	+		
MycNog2		+	
wtMycNog1			+
Flag-activinB			-16kD
Flag-Xnr2			-30kD
Flag-Xnr4			-20kD
Flag-Wnt8			-60kD
Flag-Zyxin			-45kD

Д

	эндотенный Noggin1	эндотенный Noggin2	
Noggin Western			
Nog2	→		-30kD
Nog1	→		-20kD
Tubulin Western			
Tubulin	→		-50kD

Е РНК

SynNoggin1 50 pg/embryo	+	
SynNoggin2 50 pg/embryo		+
Noggin Western		
Nog2	→	-30kD
Nog1	→	-20kD
Tubulin Western		
Tubulin	→	-50kD

И Myc ко-ИП + Flag-Western

MycNog1	+		
MycΔclipNog1		+	
MycΔclipNog2			+
Flag-BMP4			-30kD
Flag-ActivinB			-16kD
Flag-Xnr2			-30kD
Flag-Xnr4			-20kD
Flag-Wnt8			-60kD

5. Noggin1, Noggin2, TGF- β , Wnt-1, MycNoggin1, MycNoggin2, myc-Noggin1, myc-Noggin2, ADMP, BMP, ActivinB, Wnt8, Xnr2, Xnr4, Zyxin, Wnt8.

Noggin1 -2.

Noggin1 -2 BMP-, Activin/Nodal- Wnt-

Noggin1 -2

flag N- C-

ADMP, BMP4 (BMP-); Activin B, Xnr2, Xnr4 (*Activin/Nodal*) *Wnt8* (*Wnt*).

, -myc, -G, -flag

, *Noggin1* *Noggin2*, BMP4, (.5 -).

Zyxin.

Noggin1 5'- BMP4 (.5,).

Noggin1, - BMP-

, TGF- - *Wnt*- , BMP.

Noggin1 , *Noggin1* *Noggin2* BMP

, 20 . TGF- - *Wnt*- *Noggin*

, N- , . . - *Noggin1* BMP (Groppe et al., 2002).

Noggin1 TGF- - *Wnt8*, *Noggin1* *Noggin2*, 28 N- /

(- *Noggin1* -2).

, *Noggin1* *Noggin2* BMP4 (.5) . - *Noggin1* -2 TGF- - ,

, *Noggin* (*Wnt8* (.5)).

Noggin TGF- - (BMP) *Wnt*- .

Noggin1 *Noggin2* *Activin/Nodal* *Wnt*

Noggin

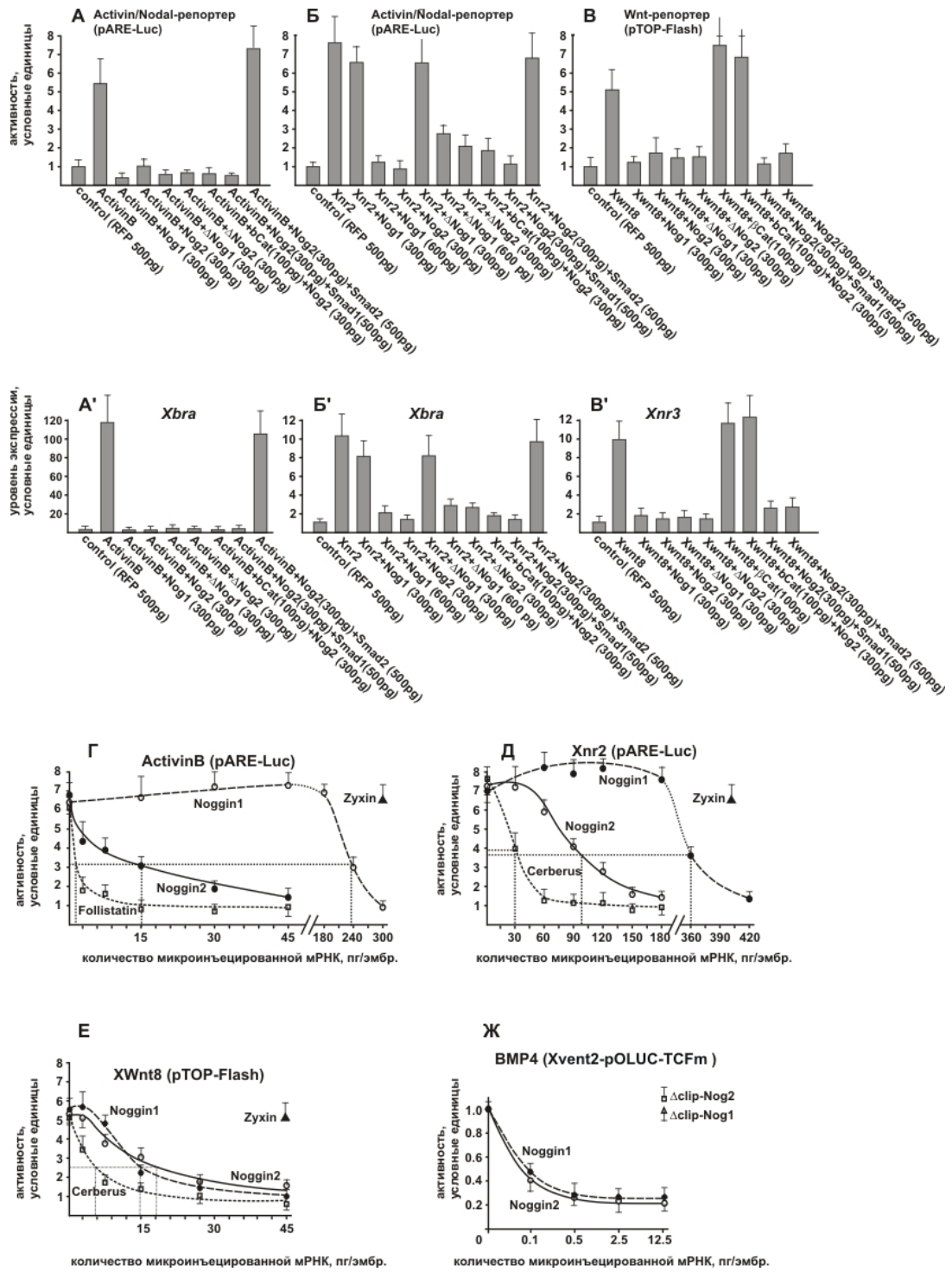
TGF- - *Wnt*- , *Xenopus*.

(pARE-Luc) (*Activin/Nodal*-) -Catenin (pTOPflash) (*Wnt*-) - Smad2-

, pARE-Luc, *ActivinB* *Xnr2*, pTOPflash, *Wnt8*,

Noggin1 -2, -*clip-Noggin1* -2, ,

ActivinB, *Xnr2* *Wnt8*. , *ActivinB* *Wnt8*, *Xnr2*



.6.	Noggin (SynNoggin)	ActivinB, Xnr2	XWnt8. (-)	Noggin,
	()			
	1;			
(-)		Noggin1	Noggin2	
				2
				Zyxin

Noggin2, *-clip-Noggin2*, *Noggin1* -
clip-Noggin1 (.6 -).
Noggin *ActivinB, Xnr2 Wnt*

Xbra (*Activin/Nodal-*) *Xnr3*
(*Wnt-*) (.6 -).
Noggin

(Smad2 -Catenin) (.6 -),
Noggin.
Smad2, *Smad1*, *Wnt-* *Noggin,*
-Catenin *Smad1* *Noggin.*
Noggin

Noggin1 500 / .
Noggin1 -2,
- Cerberus

(Nodal Wnt) Follistatin (Activin) .
2 .
(*ActivinB, Xnr2 Wnt8*),
flag-
Noggin2 *ActivinB* 10 ,
Follistatin, *Xnr2 Wnt8* - 3 , *Cerberus* (.6 -). , *Noggin1*
Wnt8 , *Noggin2, ActivinB Xnr2* - 4 , *Noggin2*
(.6 -).
BMP *Noggin*
TCFm-Luc, *Smad1-*
Noggin1
Noggin2 *BMP-* (.6).

Noggin1 *Noggin2*
Activin/Nodal Wnt- .

Noggin *TGFβ-* *Wnt-* ,
Noggin, ,
Activin/Nodal- *Wnt-*
Noggin1 *Noggin2* *Smad2-* ,
in situ *Noggin1* -2 ,
XBra and *gooseoid*, *Smad2.*
Noggin1 *Noggin2.* ,

BMP, , , Noggin1,
Smad2- , *goosecoid*,
Xbra. , *Smad1*-
(*Cerberus*) *Xbra*,
goosecoid (Bouwmeester et al., 1996; Eimon and Harland,
1999).
Noggin2 *XBra*
(90%, n=65) (.7), *Noggin2*
Xnr. , *Noggin1*
Xbra (42%, n=70) (.
7), *Xnr*,
-2 , *Smad2*- , *-clip-Noggin1*
goosecoid
(.7 ,).
3-5 / *Noggin2* 4-8
BMP, Nodal *Wnt.* 500 /
Noggin1 ,
BMP. ,
Noggin1 *Noggin1*
Nodal- *Wnt-* , *Noggin1*
(.7).
Noggin2 (15%, n=126 35%, n=120).
Noggin1,
Noggin2,
Noggin2
Nodal/Xnr, *Noggin1*. *Noggin2* *Cerberus*,
Nodal- *Wnt-* .
Noggin2 10 , 3 0.3 / ,
Noggin1 ().
Noggin2 , *Wnt-* *Nodal-*
Noggin2 ,
BMP- ,
BMP, *Wnt* *Nodal.* *Noggin2*
(0.3 /) ,
Noggin1 50 / (35%, n=118 31%, n=117).
200 .
Noggin1 *Noggin2*
2-5 / ,
(.7). , ,
(.7 ,).

Noggin2, *Noggin1* *Noggin2*

BMP- and *Wnt-*, *Noggin2*, *Nodal/Xnr-*
Nodal/Xnr-

(Schier et al., 1996).

Cerberus *CerberusS*, *Nodal/Xnr-* (Bouwmeester et al., 1996; Piccolo et al., 1999).

clipNoggin2, *Noggin1* -2, *BMP*,
Xnr *Wnt*, *Xnr* *Wnt*, *clipNoggin1*

Noggin (. 7 ,).
BMP, - *Noggin1* -2

(100 /) ().

Wnt8

Wnt8, *Wnt-*, *Cerberus* *Dkk*,
Wnt8, *clipNoggin1*

clipNoggin2, (

Wnt

Wnt

Cerberus *Dkk* (Glinka et al., 1997; Glinka et al., 1998; Piccolo et al., 1999).

Noggin *Wnt*

pCSKA-Wnt8, *Wnt8*

- *pCSKA-Wnt8* *clipNoggin1* *clipNoggin2* 8

Noggin *Wnt* ().

clipNoggin *Wnt-*

Nodal/Xnr- () “ ” *BMP*, *Dkk* -

tBR (Glinka et al., 1998; Glinka et al., 1997).

BMP - tBR *Noggin1* 5.

- *BMP* ,

).

- *clipNoggin2*

10% (n=75 64).

clipNoggin1.
Nodal/Xnr-

clipNoggin1 ().

Noggin *Wnt- Nodal/Xnr-* .

Noggin2, *Noggin1,*

Xenopus.

Noggin1 *Noggin2* ,

8

(),

(Kuroda et al., 2004),

Noggin1 ().

Noggin1 ,

Noggin1,

Activin/Nodal *Wnt-* .

Noggin2, ,

(90%,

n=116) (. 8).

(XBf1) *(Pax6)* (. 8 ,).

Noggin2 , (

7).

Noggin2 (. 8 , ,).

Noggin2,

Noggin2 *clipNoggin2,*

Noggin2 , *clipNoggin2* (. 8 -).

Noggin2.

Activin- *Noggin2*

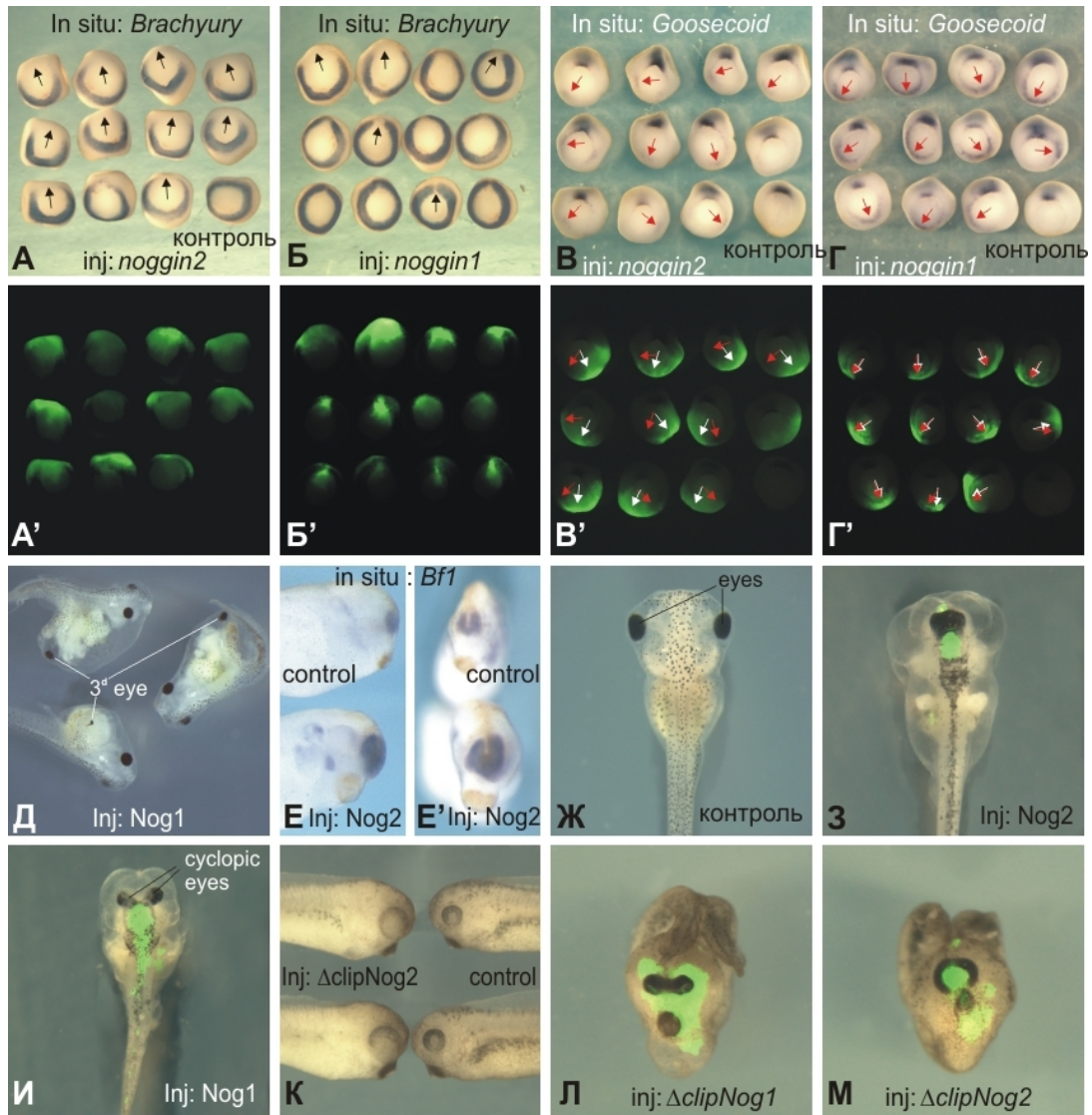
Noggin2 *BMP*

Wnt- *Wnt-*

(Kiecker and Niehrs, 2001; Lagutin et al.,

2003; Onai et al., 2004). , *Noggin2* *Smad2-*

ActivinB (Dohrmann et al., 1993).



7. *Noggin*, *Nodal/Xnr* *Wnt*. (-)
Xbra (,) *goosecoid* (,) () (' - ') *Noggin*
Noggin1 -2, *Noggin1*. (,) FLD,
Noggin1 -2 in situ *XBF1*. (-)
() (, , ,).

Noggin2,
Noggin2 4172 . . (.10).
“ ” , . . . *GFP*
Noggin2 (.10 -). ,
8 -*Noggin2* (4
/) 26,
in situ - *XBF1*.
Noggin2 tALK4- Dkk1- ,
(.10 -). , (P<0.001)
tBR-

($P < 0.001$).

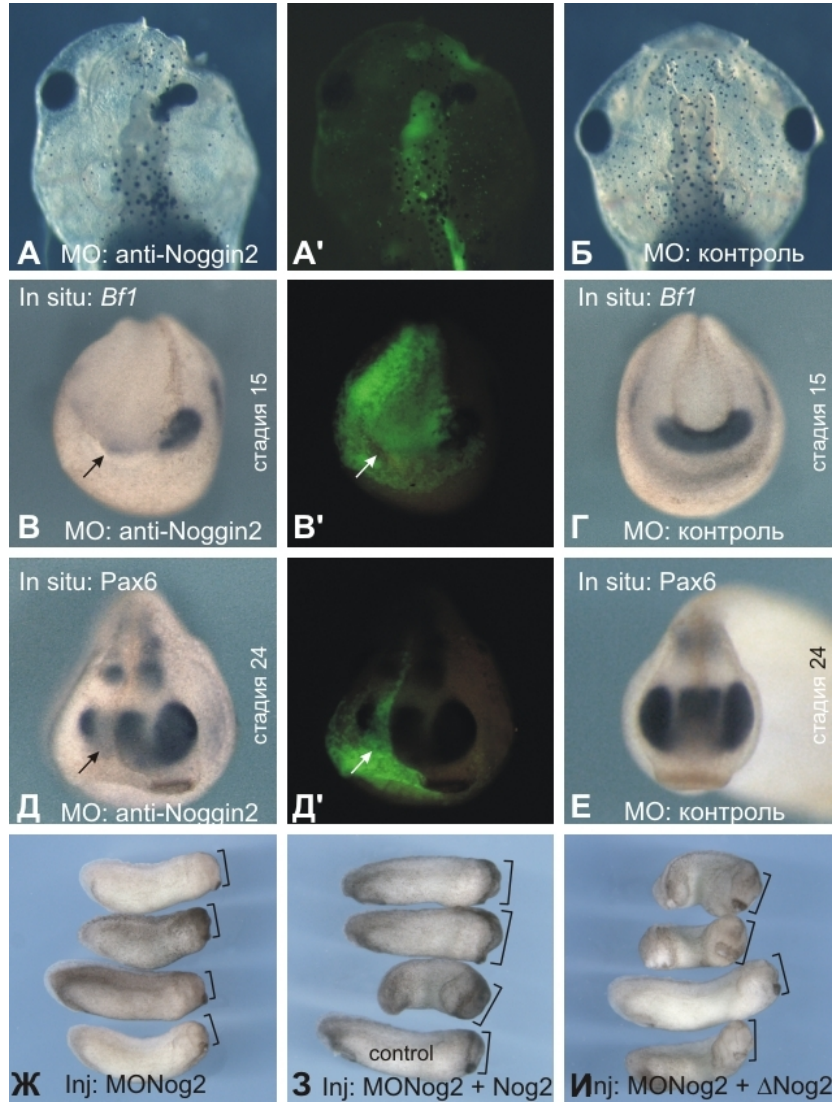
(10^{-10} -).

XBF1

-*Noggin2*

($P < 0.001$)

Noggin2.



.8.	- <i>Noggin2</i>	<i>Noggin2</i>	(,)
	- <i>Noggin2</i>		(-)
(,).(,)		<i>XBF1</i> (,)	<i>Pax6</i>
<i>Noggin2</i> .		-	<i>Noggin2</i> -

TGF-β (*BMP*) *Wnt* *Noggin.*

, *Noggin1* *Noggin2* ,
BMP, *TGF-β,* *Wnt8,*
 , *N-*
 - , *BMP* (*Groppe et al., 2002*),
Noggin ,
BMP, -
Noggin1 *Noggin2*
ActivinB *Xnr,*
 : *Noggin2*
ActivinB *Xnr* , *Noggin1.*
 , *Noggin1* *BMP-*
BMP, (*Groppe et al., 2002*).
BMP, *Noggin1* *Noggin2*
TGF-β *Wnt* ,
Noggin1 , *5'-* ,
Noggin1 ,
 -*BMP* *Noggin1,* ,
 , *Activin/Nodal* *Wnt* *Noggin*
SMAD2- *β-catenin-*
 , *Noggin*
 , *ActivinB/Xnr2* *Wnt8.*
 , *Noggin* -
Activin/Nodal *Wnt:* *Wnt-*
 , “ ” *BMP* ,
 .

Activin-, BMP- Wnt- Noggin2

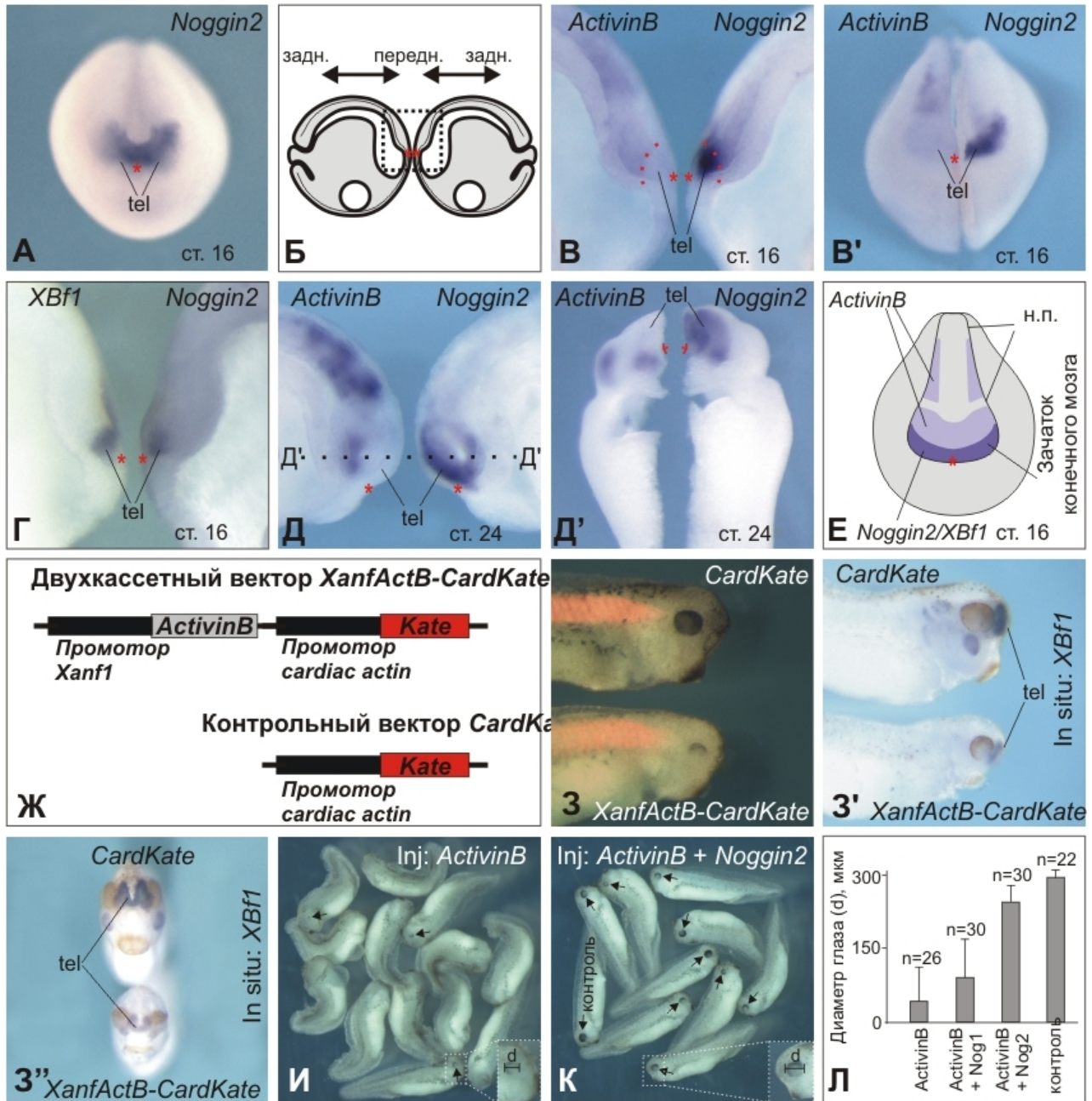
, *Activin, BMP Wnt,*
Noggin2 ,
BMP- Wnt-

(Kiecker and Niehrs, 2001; Lagutin et al., 2003; Onai et al., 2004).

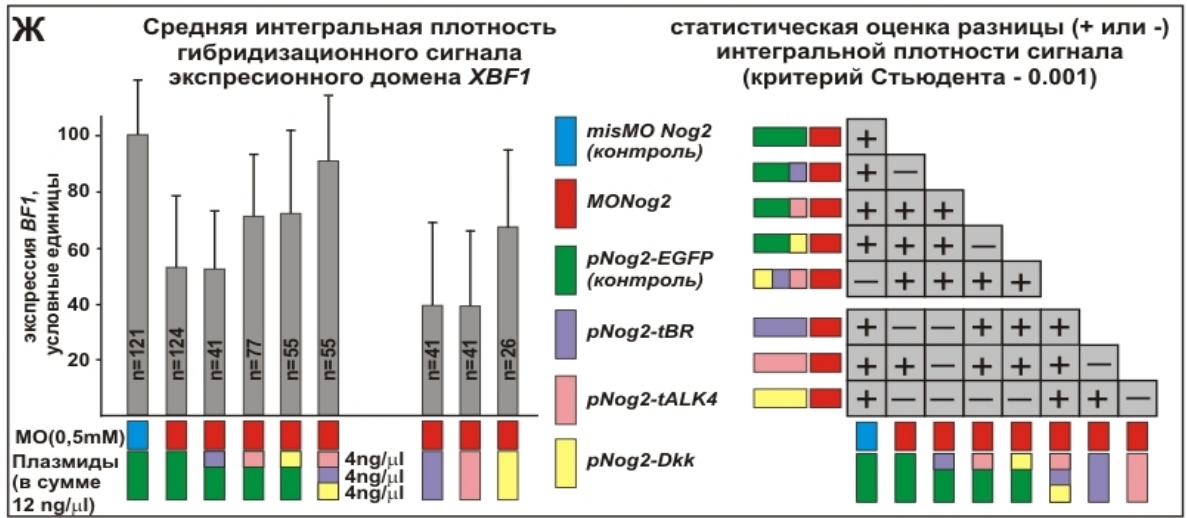
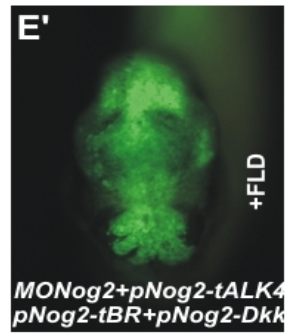
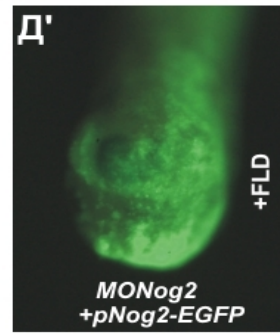
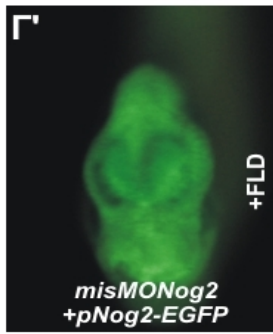
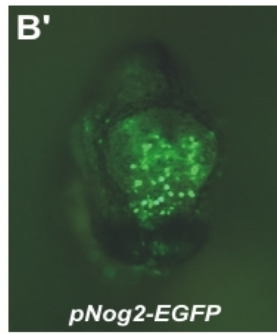
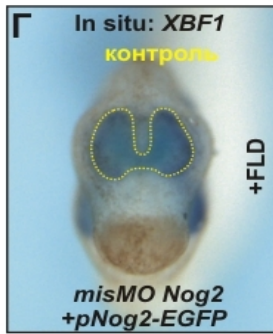
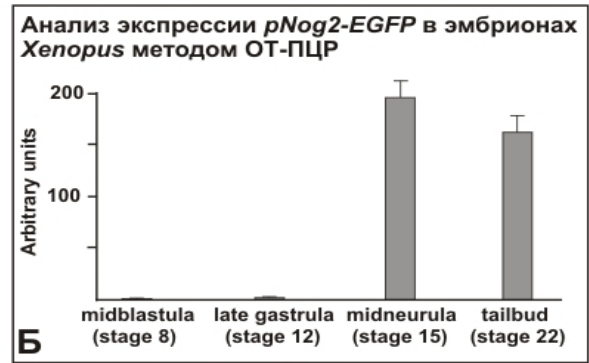
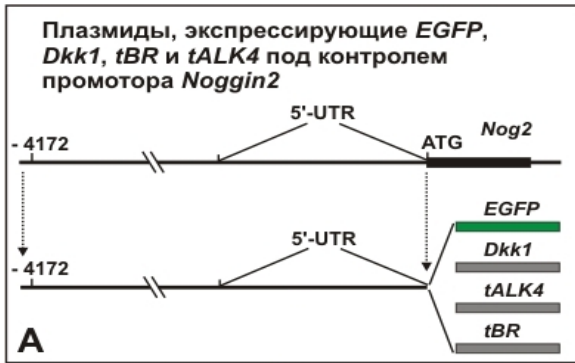
, - *BMP* ,
Noggin2 . ,

BMP-
Activin/Nodal-
BMP- Wnt-
 (Niehrs, 1999; Piccolo et al., 1999).
 ActivinB (*Xenopus*)
 Noggin2.
 Noggin2
 Noggin1, Noggin2.
Noggin1
 (McMahon et al., 1998).
Noggin2
Activin/Nodal-
Wnt-
Noggin1
Activin/Nodal, BMP Wnt)

-
1. 8 *Noggin.*
 2. *Noggin2* *Noggin4 Xenopus.*
Noggin2 *Noggin4*
 3. *Xenopus.*
Noggin1 *Noggin2* *in vitro,* *BMP,*
Activin/Nodal- Wnt- – *ActivinB, Xnr2, Xnr4* *Wnt8.*
Activin/Nodal- Wnt- *BMP.*
 4. *Noggin1* *Noggin2* *BMP-, Activin/Nodal-*
Wnt- *in vivo*
ActivinB, Xnr2 *Wnt8.*
 5. *BMP-, Activin- Wnt-*
Noggin2.



9. Activin
: tel –
Noggin2
(telencephalon); . . –
()
in situ,
()
ActivinB *Noggin2*
Noggin2,
XBF1 *Noggin2*
()
ActivinB
ActivinB, *XBF1*
*XanfActB-
XBF1*. ()
ActivinB (0.5 /) . ()
(telencephalon); . . –
: tel –



.10. *Noggin2* () *pNog2-EGFP* *Noggin2* EGFP, *Dkk1*, *tBR* *tALK4* *Xenopus* -

EGFP. *XBF1* () 26, *EGFP* () 26, ()

Noggin2 ImageJ. () FLD.

t- 0,001.

