

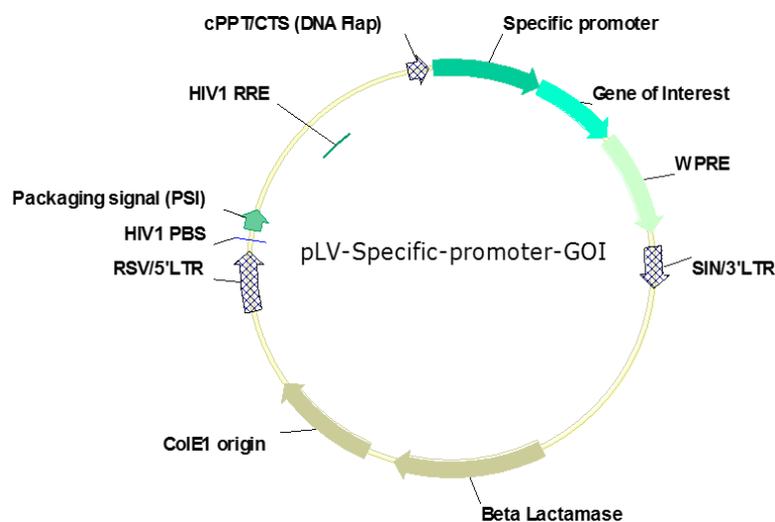
LENTIVIRAL VECTORS WITH TISSUE OR CELL SPECIFIC PROMOTERS

The use of specific promoters allows the expression of your gene of interest under specific conditions. This document describes all cell-type specific promoters already designed by Vectalys for your lentiviral vector batch.

Tissue or cell-specific promoters

Tissue or cell-specific promoters allow:

- ▶ The expression of genes of interest into targeted organs or tissues such as liver, brain, lung...
- ▶ The discrimination or selection of a population of cells within a tissue using fluorescent proteins (i.e. oligodendrocytes vs neurons)
- ▶ To follow the differentiation process of living cells in a tissue



Vectalys has designed and optimized all specific promoters available below, in order to make the construction compatible with the lentiviral particle encapsidation capability. If your specific promoter is not in our list, do not hesitate to [contact our experts](#).

NB: All designed promoters come from bibliographic data and bio-informatics analysis. If you would like more information about the design of promoters and specificity, please contact us.

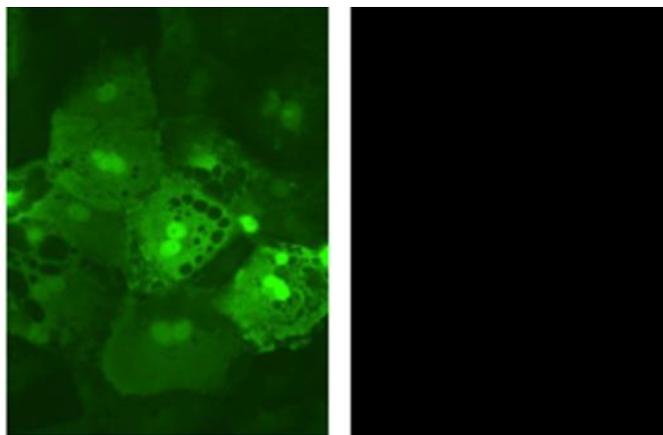
- ▶ Vectalys also offers a growing list of [standard products](#) using specific promoters, ideal for testing your applications with small quantities.

List of specific promoters available for your gene transfer projects:

1. Liver-specific promoters

Liver-specific promoters		
Promoter	Gene Description	Gene Specificity
APOA2	Apolipoprotein A-II	Hepatocytes (from hepatocyte progenitors)
SERPINA1 (hAAT)	Serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1 (also named alpha 1 anti-trypsin)	Hepatocytes (from definitive endoderm stage)
CYP3A4	Cytochrome P450, family 3, subfamily A, polypeptide 4	Mature Hepatocytes
MIR122	MicroRNA 122	Hepatocytes (from early stage embryonic liver cells) and endoderm

► *In vitro* application with the liver specific promoter APOA2



Liver cells

Pancreatic cells

Figure 1: Transduction of liver (Hepatocytes) and pancreatic B cells using specific promoter ApoA2 (apolipoprotein A-II) + GFP



Yang G, Si-Tayeb K, Corbineau S, Vernet R, Gayon R, Dianat N, Martinet C, Clay D, Goulinet-Mainot S, Tachdjian G, Tachdjian G, Burks D, Vallier L, Bouillé P, Dubart-Kupferschmitt A, Weber A. Integration-deficient lentivectors: an effective strategy to purify and differentiate human embryonic stem cell-derived hepatic progenitors. BMC Biol. 2013 Jul 19;11:86.

- *In vivo* application with the liver specific promoter APOA2

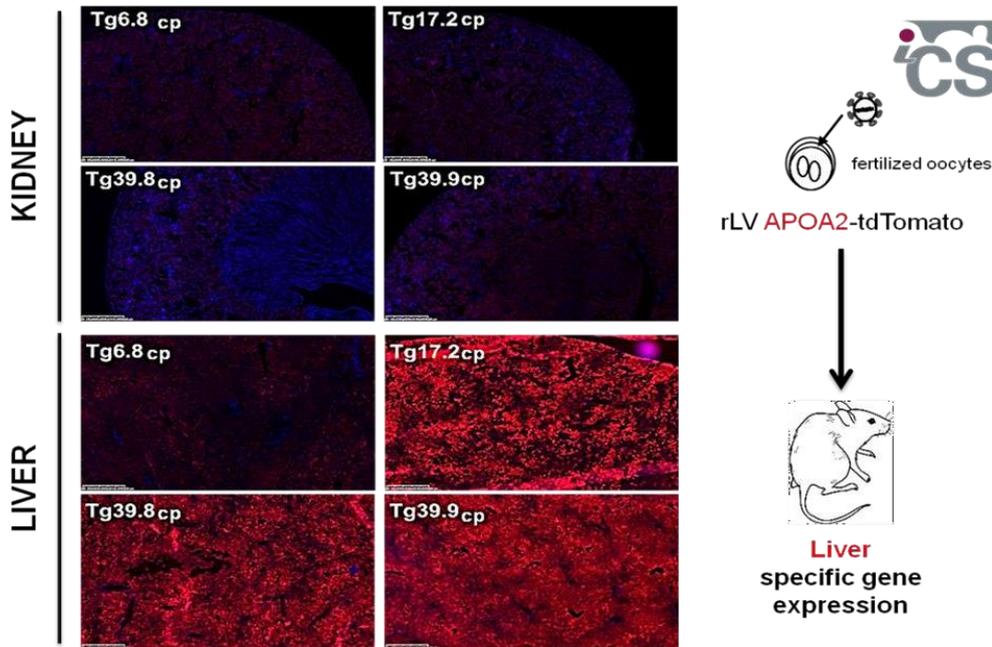
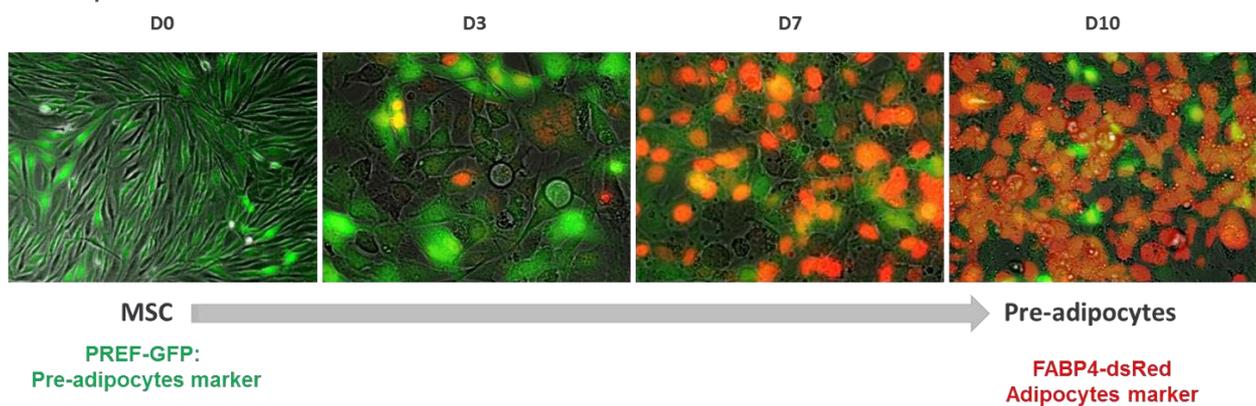


Figure 2: *in vivo* screening by lentigenesis using the specific promoter ApoA2 (apolipoprotein A-II) + GFP

- Application: *in vitro* monitoring of stem cell differentiation using specific promoters

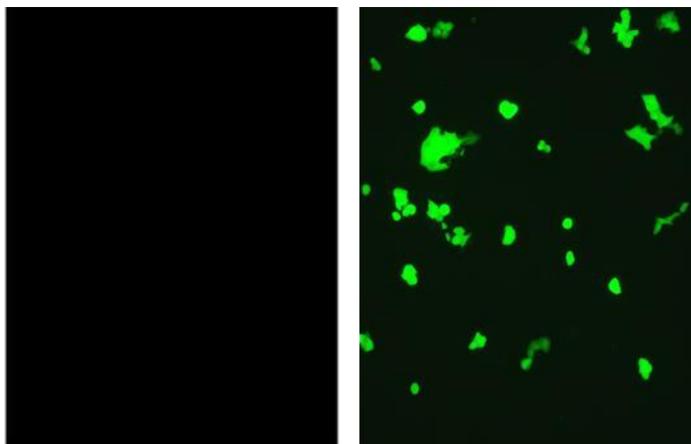


These data show that it is possible to follow the cell differentiation process in living cells by using a pre-adipocyte specific promoter and an adipocyte specific promoter.

2. Specific promoters for pancreatic cells

Pancreas-specific promoters		
Promoter	Gene Description	Gene Specificity
INS	Insulin	Pancreatic beta cells (from definitive endoderm stage)
IRS2	Insulin receptor substrate 2	Pancreatic beta cells
Pdx1	Pancreatic and duodenal homeobox 1	Pancreas (from definitive endoderm stage)
Alx3	Aristaless-like homeobox 3	Pancreatic beta cells (from definitive endoderm stage)
Ppy	Pancreatic polypeptide	PP pancreatic cells (gamma cells)

► *In vitro* application with pancreas specific promoter INS



Liver cells

Pancreatic cells

Figure 3: Transduction of liver and pancreatic cells using specific promoter INS (Insuline) + GFP



Yang G, Si-Tayeb K, Corbineau S, Vernet R, Gayon R, Dianat N, Martinet C, Clay D, Goulinet-Mainot S, Tachdjian G, Tachdjian G, Burks D, Vallier L, Bouillé P, Dubart-Kupperschmitt A, Weber A. Integration-deficient lentivectors: an effective strategy to purify and differentiate human embryonic stem cell-derived hepatic progenitors. BMC Biol. 2013 Jul 19;11:86.

3. Cardiac specific promoters

Cardiac-specific promoters		
Promoter	Gene Description	Gene Specificity
Myh6 (αMHC)	Myosin, heavy chain 6, cardiac muscle, alpha	Late differentiation marker of cardiac muscle cells (atrial specificity)
MYL2 (MLC-2v)	Myosin, light chain 2, regulatory, cardiac, slow	Late differentiation marker of cardiac muscle cells (ventricular specificity)
TNNI3 (cTnl)	Troponin I type 3 (cardiac)	Cardiomyocytes (from immature state)
NPPA (ANF)	Natriuretic peptide precursor A (also named Atrial Natriuretic Factor)	Atrial specificity in adult cells
Slc8a1 (Ncx1)	Solute carrier family 8 (sodium/calcium exchanger), member 1	Cardiomyocytes from early developmental stages

Chakraborty S, Christoforou N, Fattahi A, Herzog RW, Leong KW. A robust strategy for negative selection of Cre-loxP recombination-based excision of transgenes in induced pluripotent stem cells. PLoS One. 2013 May 22;8(5)



► *In vitro* application with cardiac specific promoter MYL2

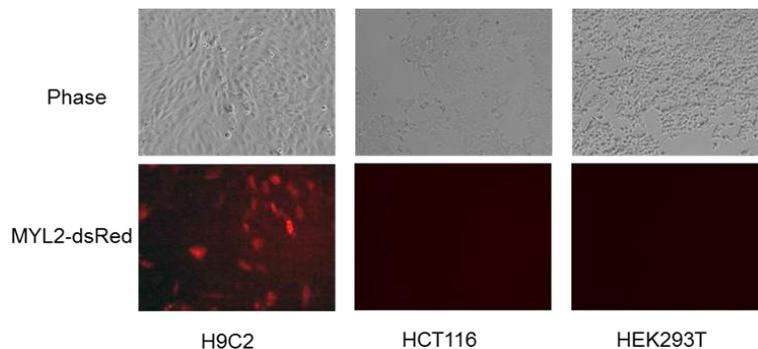


Figure 4: Transduction of cardiac cells (H9C2) using specific promoter MYL2 + dsRed

4. Specific promoters for the Central Nervous System (CNS) cells

CNS-specific promoters		
Promoter	Gene Description	Gene Specificity
SYN1 (hSyn)	Synapsin I	Neurons
GFAP	Glial fibrillary acidic protein	Astrocytes
INA	Internexin neuronal intermediate filament protein, alpha (α -internexin)	Neuroprogenitors
NES	Nestin	Neuroprogenitors and ectoderm
MOBP	Myelin-associated oligodendrocyte basic protein	Oligodendrocytes
MBP	Myelin basic protein	Oligodendrocytes
TH	Tyrosine hydroxylase	Dopaminergic neurons
FOXA2 (HNF3 beta)	Forkhead box A2	Dopaminergic neurons (also used as a marker of endoderm)

- *In vitro* application with 2 CNS specific promoters: GFAP (astrocytes specific) and Syn (neurons specific)

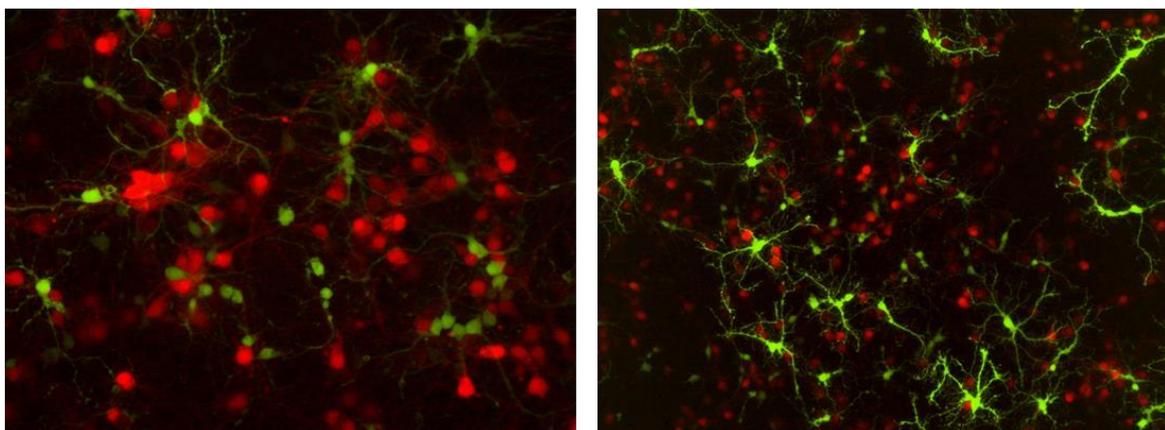


Figure 5: Transduction of CNS cells using promoters specific to astrocytes (GFAP + GFP) and neurons (Syn + DsRed)

- ▶ *In vivo* application with two CNS specific promoters: GFAP (astrocytes specific) and Syn (neurons specific)

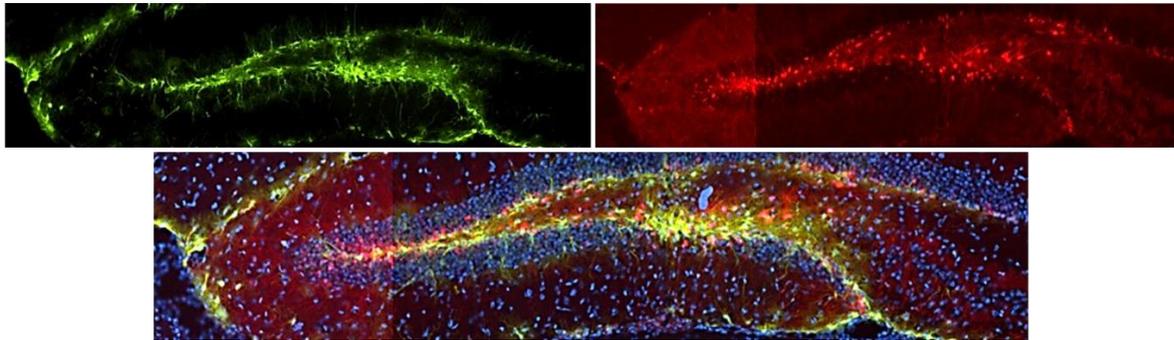


Figure 6: Direct co-injection of 2 lentiviral vectors into dentate gyrus with 2 fluorescent reporters driven by 2 specific promoters (hSynapsin and GFAP)

5. Specific promoters for skin cells

Skin-specific promoters		
Promoter	Gene Description	Gene Specificity
FLG	Filaggrin	Keratinocytes from granular layer
K14	Keratin 14	Keratinocytes from granular and basal layers
TGM3	Transglutaminase 3	Keratinocytes from granular layer

- ▶ Application with skin cells specific promoter K14

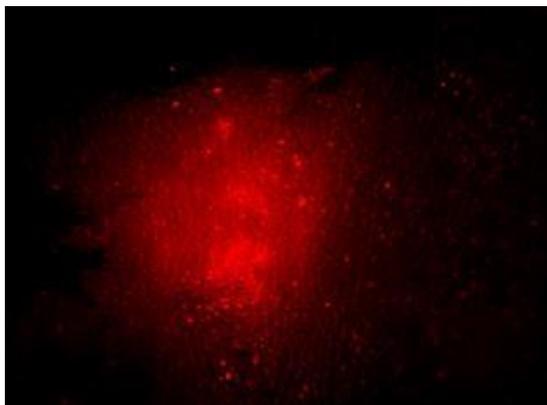


Figure 7: Transduction of skin cells *in vivo* using promoter K14 + RFP

6. Specific promoter for immune system cells

Specific promoter for immune system cells		
Promoter	Gene Description	Gene Specificity
ITGAM (CD11B)	Integrin, alpha M (complement component 3 receptor 3 subunit)	Monocytes, macrophages, granulocytes, natural killer cells

7. Specific promoters for urogenital cells

Specific promoters for urogenital cells		
Promoter	Gene Description	Gene Specificity
Pbsn	Probasin	Prostatic epithelium
Upk2	Uroplakin 2	Bladder
Sbp	Spermine binding protein	Prostate
Fer1L4	Fer-1-like 4	Bladder

8. Specific promoter for endothelial cells

Specific promoter endothelial cells		
Promoter	Gene Description	Gene Specificity
ENG	Endoglin	Endothelial cells

Germ line and pluripotency specific promoters

9. Specific promoters for pluripotent and embryonic germ layers

Pluripotency & embryonic germ layers		
Promoter	Gene Description	Gene Specificity
Oct4 (POU5F1)	POU class 5 homeobox 1	Pluripotent cells (germ cells, ES cells, iPS cells)
NANOG	Nanog homeobox	Pluripotent cells (ES cells, iPS cells)
Synthetic Oct4	Synthetic promoter based on a Oct-4 core enhancer element	Pluripotent cells (ES cells, iPS cells)
T brachyury	Brachyury	Mesoderm
NES	Nestin	Neuroprogenitors and Ectoderm
SOX17	SRY (sex determining region Y)-box 17	Endoderm
FOXA2 (HNF3 beta)	Forkhead box A2	Endoderm (also used as a marker of dopaminergic neurons)
MIR122	MicroRNA 122	Endoderm and hepatocytes (from early stage embryonic liver cells)

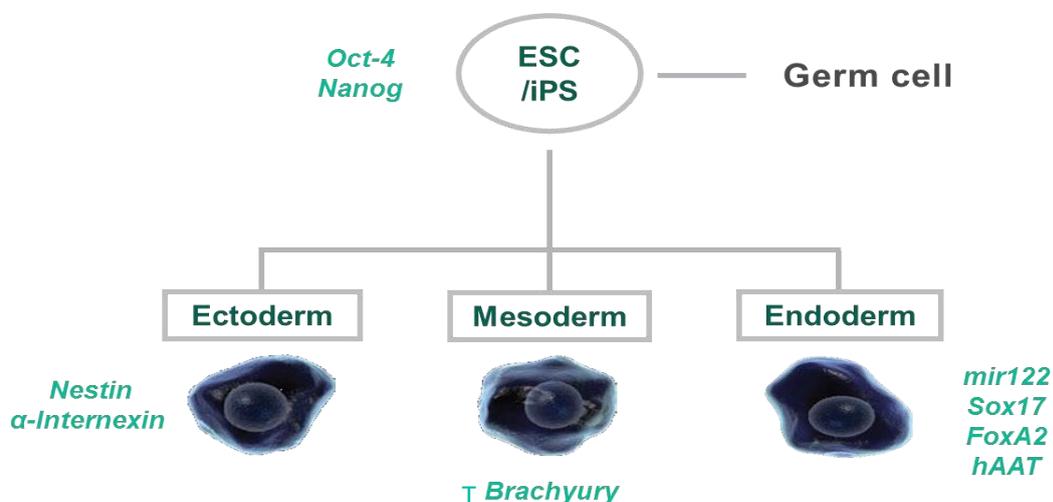


Figure 8: Differentiation monitoring from pluripotent stages

- ▶ Application in neurosphere with ectoderm specific promoters:

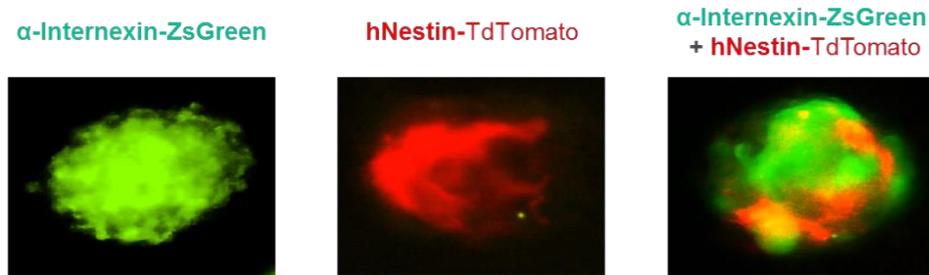


Figure 9: Specific neural stem cells expression of nestin or α -Internexin promoters. 9 weeks old C57Bl/6 mice were injected stereotactically with both lentiviral vectors into the subventricular zone of the brain. At day 7, the brains were sectioned and the corresponding sections were dissociated for subsequent neural stem cells culture.

Each specific promoters above are available for custom lentiviral vector projects. [Premade lentiviral particles](#) with fluorescent proteins are also available for testing.