Claudin-11 (*CLDN11*) is a new kid to regulate the vascular smooth muscle cell plasticity

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Conflict of interest disclosure

None

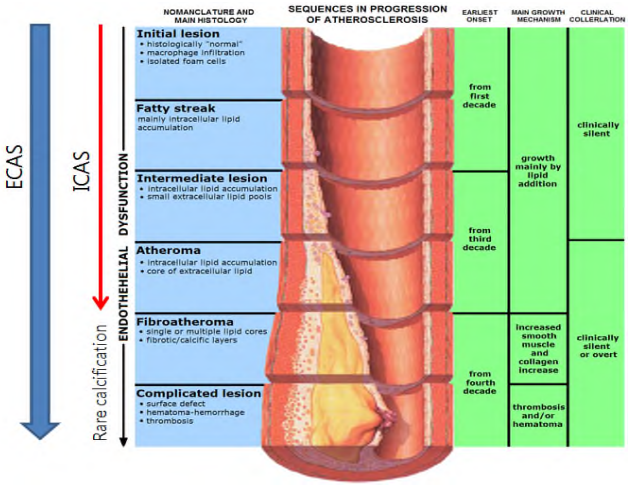
Committee of Scientific Affairs

Part I. Comparison of gene expression profiles of human cerebral and coronary arteries to identify novel genes related to vascular diseases

Part II. CLDN11 Expression in Vascular Smooth Muscle Cell and role for Cardiovascular Disease

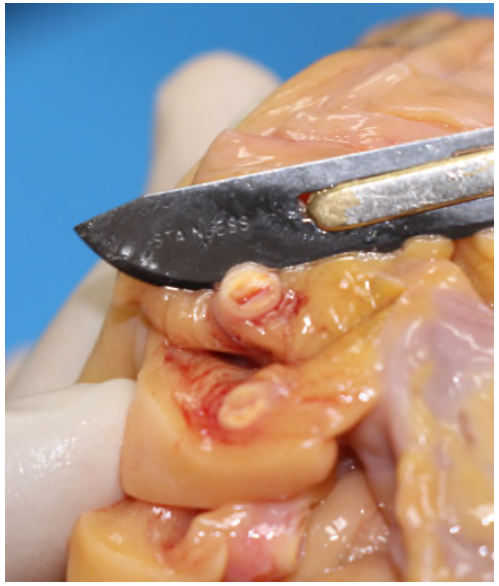
Introduction

- 죽상동맥경화증은 침범하는 혈관에 따라 발생연령, 빈도, 그리고 복합판(complicate plaque) 까지의 진행양상 등이 극명이 다름
- **소위 발병장소에 따른 조절인자 있을 것으로 추정**
- **두개강외 동맥경화증 (extra-cerebral atherosclerosis, ECAS)과 대뇌 동맥경화증 (intra-cerebral atherosclerosis, ICAS)은 병태생리학적으로 많은 차이를 보임**

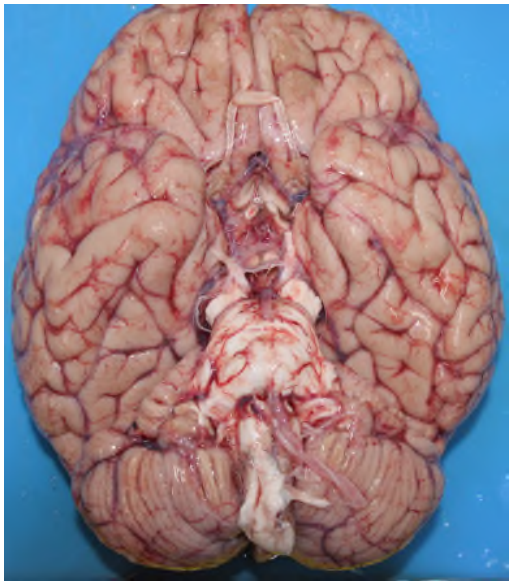


Atherosclerosis: Lesion and region

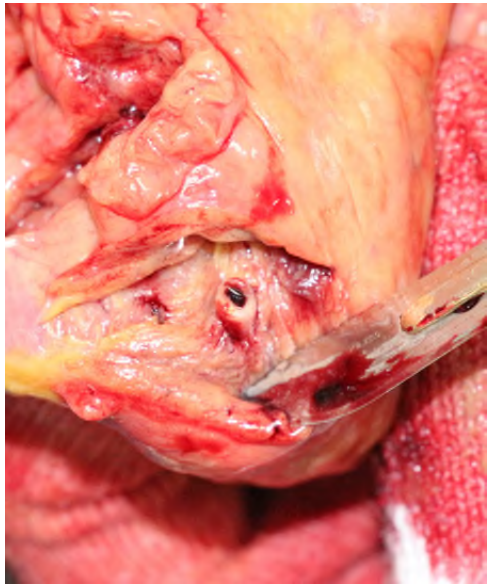
Coronary occlusion



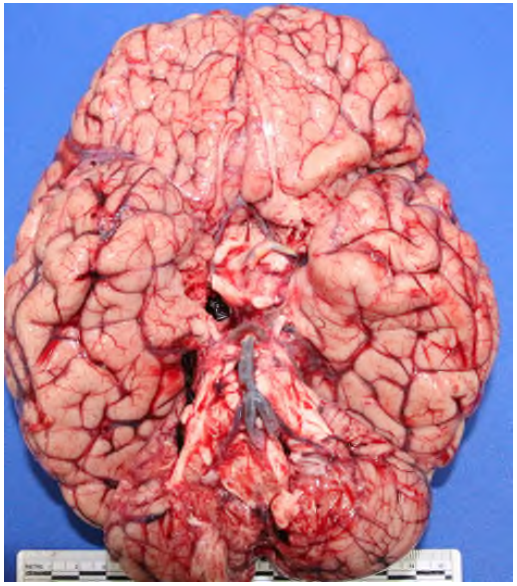
ICA & MCA non-occlusion



Coronary occlusion



ICA & MCA occlusion



Introduction

- 죽상동맥경화증
  - 혈관 연구자의 영원한 연구 주제?
- 동물 모델의 한계점
  - 병변은 심장동맥, 중대뇌동맥이 주류인데….
  - 혈관 병태생리가 다른데….

- Circulatome
  - Although many risk factors such as hyperlipidemia, diabetes, and hypertension are systemic, distinct vascular regions frequently display differential disease susceptibility or resistance…… (from 1964 to 2018..)

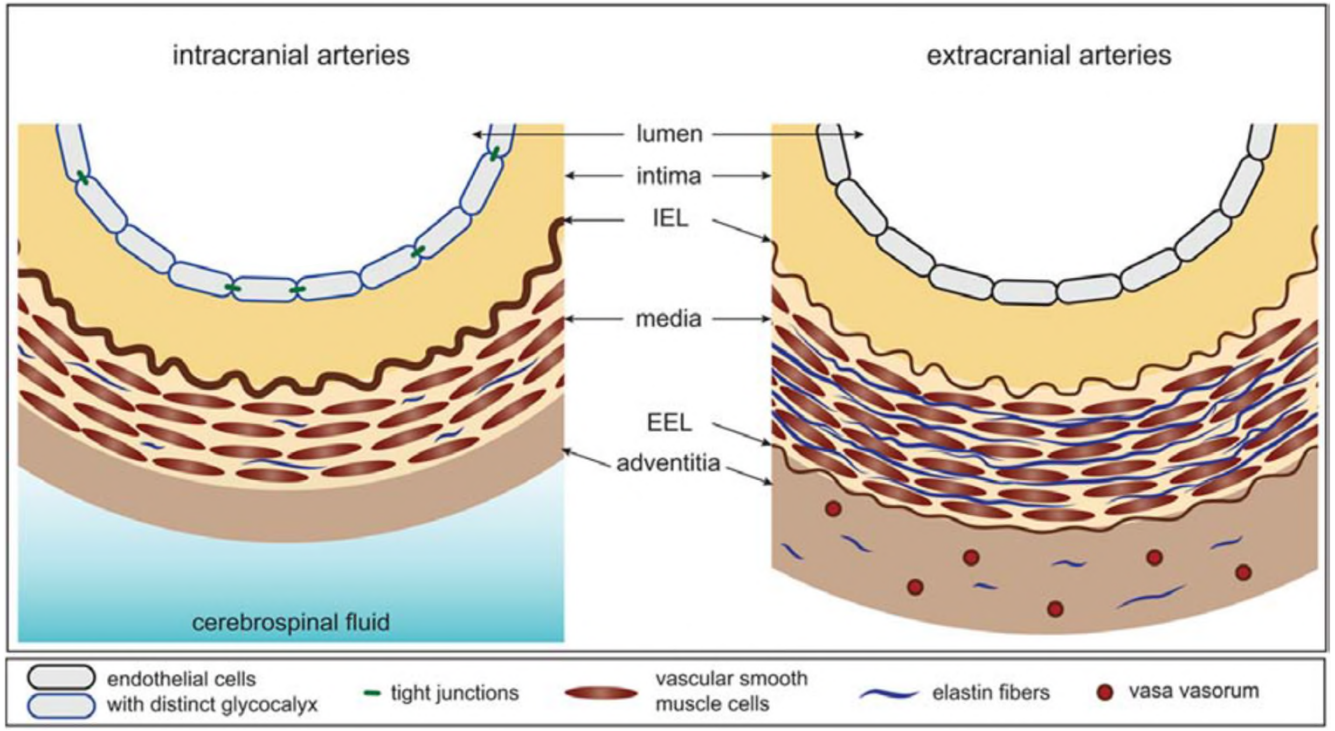
Introduction

- **Histological difference**
  - Intracranial arteries

    : muscular-type

  - Extracranial arteries

    : elastin filament rich



Circulation. 2014;130:1407-1414.

Introduction

- **Physiological difference**
  - ICA: Greater antioxidant enzyme activities than ECA

	Abdominal Aorta	Carotid Artery	Middle Cerebral Artery	Basilar Artery
No. of segments	12	15	15	12
Glutathione peroxidase, mU/mg protein	70.6±11.5	67.5±14.5	84.8±16.5	80.2±11.5
Catalase, IU/mg protein	15.4±8.5	13.6±7.5	19.1±6.5	18.4±5.9
Cu/Zn-SOD, IU/mg protein	6.8±0.9	7.2±1.0	6.5±0.9	6.6±0.9
Mn-SOD, IU/mg protein	2.0±0.4	1.6±0.4	3.2±0.6*	3.1±0.6*

Stroke. 2001;32:2472-2480.

Introduction

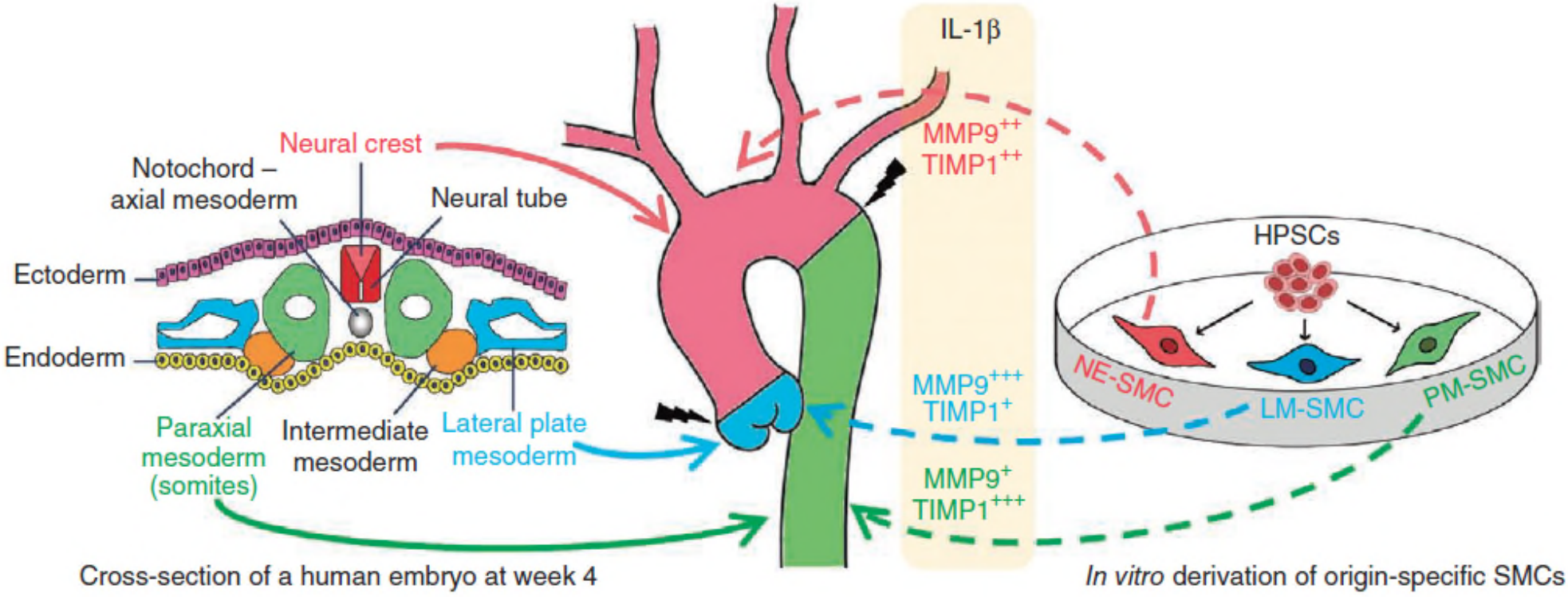
- **Embryonal difference**
  - Lineage tracking studies shows

    vascular SMCs in different vessels have distinct embryological origins

  - The diversity of SMC origins

    contribute to the site-specific localization of vascular diseases

  - Origin of intracranial arteries : **neuroectoderm**



Nat Biotechnol. 2012 January 15; 30: 165–73

Part I.

- **The goal of this study**
  - Compare the gene profile of human vascular smooth muscle cells (Intracranial / extracranial)
  - Identify the differentially expressed genes (DEGs) to understand vascular diseases

Material and Method

- **Human vessel sampling**

  10 autopsy cases, Vascular disease risk factor (-)

  Intracranial artery – Middle cerebral artery

  Extracranial artery – Left descending coronary artery

  Vascular smooth muscle cells were isolated manually from each arteries

- **RNA extraction**

  Using TRIzol® Reagent following the manufacturer's instructions

  Checked for an RIN number to inspect RNA integration

Material and Method

- **Microarray and analysis**
  - Each gene expression profiles were obtained and compared using the Agilent Human Gene Expression 4×44K v2 Microarray kit
  - Fluorescently labelled cDNA was obtained from a single round of labelling using a kit in the presence of fluorescent dNTP
  - Statistical analysis of mRNA microarray data was performed by Genespring GX 9.0 Software

Material and Method

- **Bioinformatic analysis**
  - Gene ontolgy analysis
  - KEGG pathway analysis
  - Gene-associated gene analysis : Database for Annotation, Visualization and Integrated Discovery
- **Reverse transcription polymerase chain reaction**
  - 10 sets of MCA and LAD extracted from autopsy
  - Selected genes : Fivefold upregulated and P-value<0.05

Results

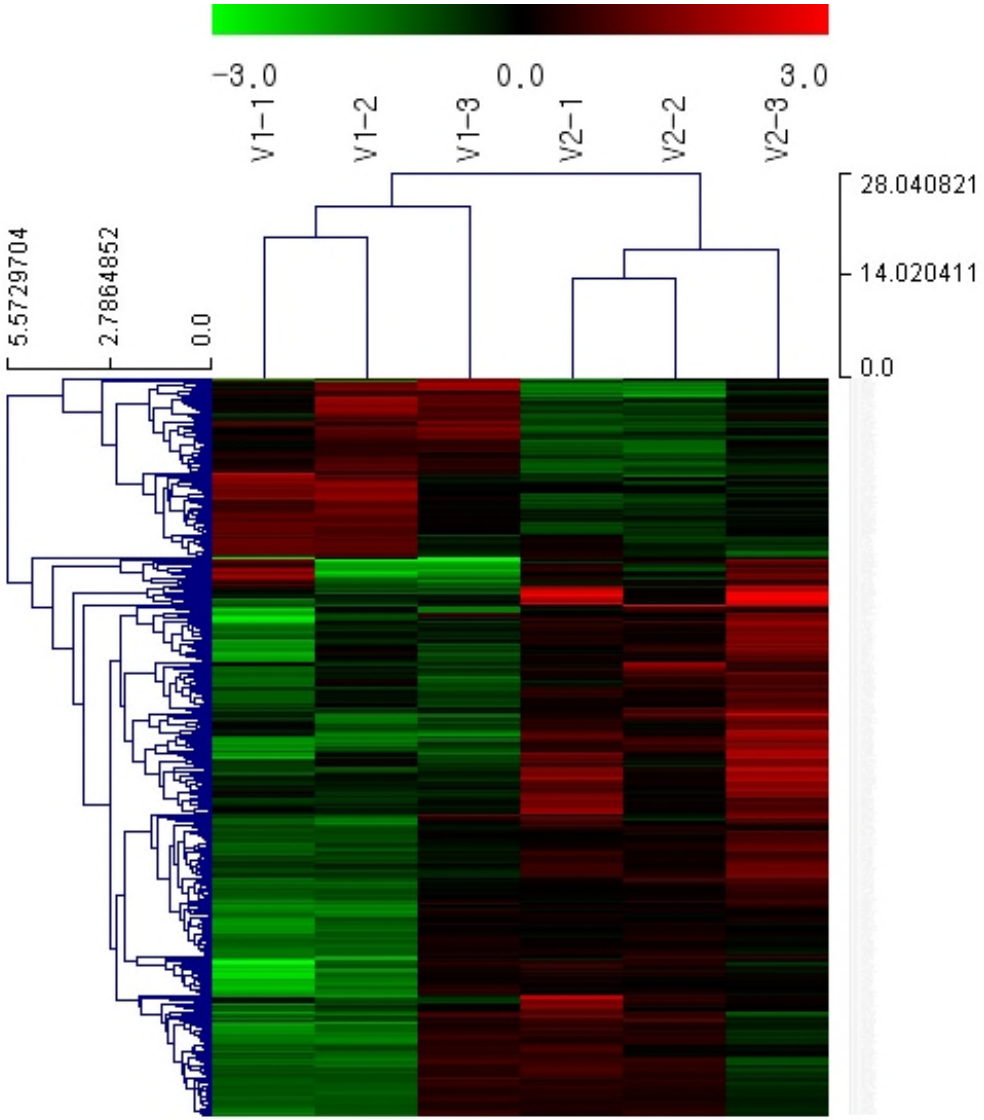
- **Whole-genome mRNA expression profiling**
  - Approximately 34,000 genes identified
  - Differentially-expressed genes were 359

    : Upregulated 272 / Downregulated 87

    (V2/V1, Fold-change > 2 or < 0.5 and p-value < 0.05)

Results

Fig. 1 (A)



Results

- **Gene Ontology (GO) enrichment**

  The percentage of 359 DEGs involved in each GO

  Angiogenesis (4.5%)

  Extracellular matrix (4.3%)

  Cell migration (2.9%), neurogenesis (2.9%)

  Cell proliferation (2.7%)

  Inflammatory response (2.0%)

Results

Fig. 1 (B)

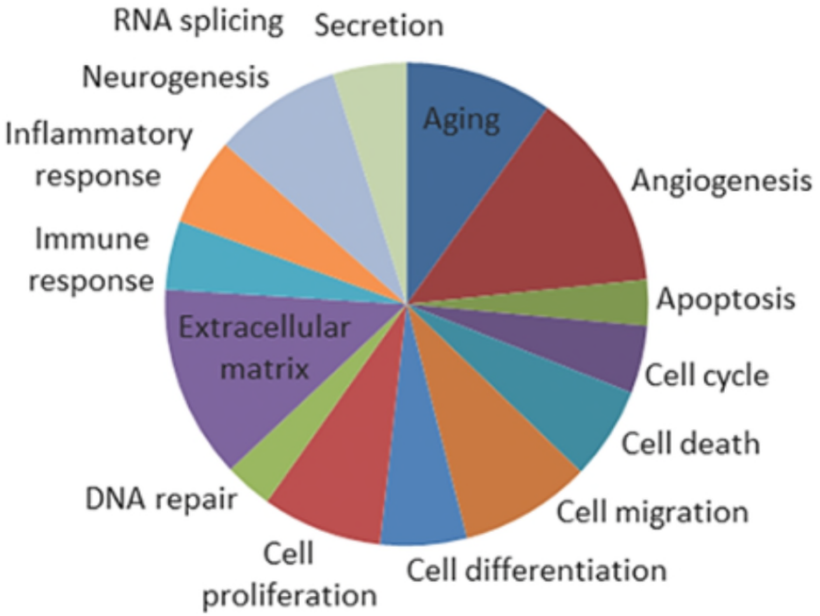
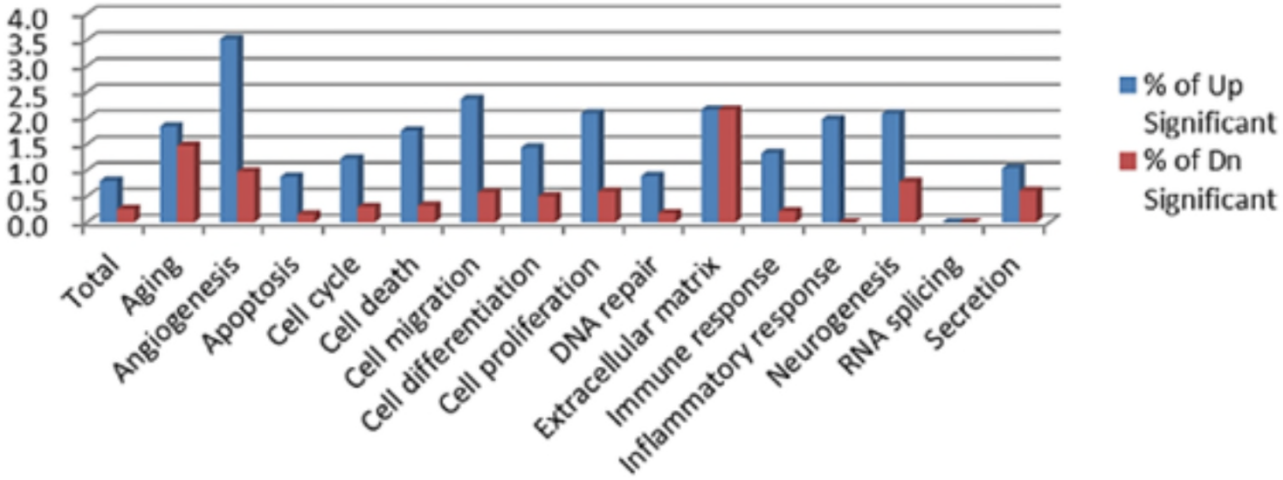


Fig. 1 (C)



Results

Table 1 (A)

GenebankID	Symbol	Fold Change	P-value
Angiogenesis			
NM_001647	APOD	11.494	0.000
NM_001993	F3	6.171	0.005
NM_000584	IL8	5.331	0.014
NM_000104	CYP1B1	4.191	0.005
NM_000358	TGFBI	3.367	0.003
NM_004040	RHOB	3.108	0.000
NM_002970	SAT1	3.082	0.000
NM_017617	NOTCH1	2.855	0.000
NM_001040708	HEY1	2.825	0.002
NM_001025366	VEGFA	2.787	0.000
NM_030817	APOLD1	2.592	0.026
NM_002737	PRKCA	2.520	0.001
NM_002228	JUN	2.337	0.001
NM_002165	ID1	2.307	0.031
NM_033238	PML	2.210	0.004
NM_002135	NR4A1	2.173	0.033
NM_002970	SAT1	2.110	0.000
NM_002210	ITGAV	2.060	0.021

Results

Table 1 (B)

GenebankID	Symbol	Fold Change	P-value
Extracellular matrix			
NM_001993	F3	6.171	0.005
NM_004822	NTN1	5.320	0.000
NM_133507	DCN	4.489	0.002
NM_006486	FBLN1	4.398	0.002
NM_001920	DCN	4.121	0.000
NM_001996	FBLN1	3.876	0.010
NM_182487	OLFML2A	3.846	0.007
NM_000358	TGFBI	3.367	0.003
NM_001025366	VEGFA	2.787	0.000
NM_002345	LUM	2.395	0.035
NM_006988	ADAMTS1	2.286	0.003
NM_030761	WNT4	2.276	0.000

Results

Table 1 (C)

GenebankID	Symbol	Fold Change	P-value
Cell migration			
NM_001647	APOD	11.494	0.000
NM_001993	F3	6.171	0.005
NM_003641	IFITM1	5.956	0.003
NM_004472	FOXD1	5.346	0.000
NM_000584	IL8	5.331	0.014
NM_004822	NTN1	5.320	0.000
NM_014331	SLC7A11	4.319	0.045
NM_004098	EMX2	4.308	0.001
NM_000104	CYP1B1	4.191	0.005
NM_005654	NR2F1	3.919	0.008
NM_006186	NR4A2	3.169	0.000
NM_002613	PDPK1	2.889	0.000
NM_017617	NOTCH1	2.855	0.000
NM_001453	FOXC1	2.820	0.001
NM_001025366	VEGFA	2.787	0.000
AK056079	JAM2	2.605	0.015
NM_001679	ATP1B3	2.544	0.001
NM_002737	PRKCA	2.520	0.001
NM_004972	JAK2	2.514	0.000
NM_002165	ID1	2.307	0.031
NM_002613	PDPK1	2.296	0.001
NM_016038	SBDS	2.211	0.008
NM_002135	NR4A1	2.173	0.033
NM_016951	CKLF	2.139	0.029
NM_178012	TUBB2B	2.134	0.006
NM_002206	ITGA7	2.122	0.001
NM_005704	PTPRU	2.084	0.002
NM_002210	ITGAV	2.060	0.021
NM_003641	IFITM1	2.032	0.001

Results

- **Candidate genes**
  - 14 upregulated genes

    V2/V1, Fold-change > 5, P-value <0.05
  - 1 downregulated gene

    V2/V1, Fold-change < 0.2, P-value <0.05

Table 4

GenebankID	Symbol	Fold Change	P-value
Upregulated			
NM_001647	APOD	11.494	0.000
NM_001927	DES	9.051	0.000
NM_005602	CLDN11	8.659	0.008
NR_026943	LOC642852	6.578	0.003
NM_001993	F3	6.171	0.005
NM_000702	ATP1A2	5.977	0.003
NM_003641	IFITM1	5.956	0.003
NM_030926	ITM2C	5.355	0.014
NM_004472	FOXD1	5.346	0.000
NM_000584	IL8	5.331	0.014
NM_004822	NTN1	5.320	0.000
NM_020311	CXCR7	5.242	0.000
NM_000518	HBB	5.129	0.003
NM_002677	PMP2	5.025	0.002
Downregulated			
NR_002989	SNORA81	0.188	0.007

Results

- **Confirmation of microarray data**
  - 8 genes were selected to verify the analyzed microarray data
  - 10 sets of MCA and LAD extracted from autopsy and analyzed by RT-PCR
  - All of them were highly expressed in MCA

Fig. 3

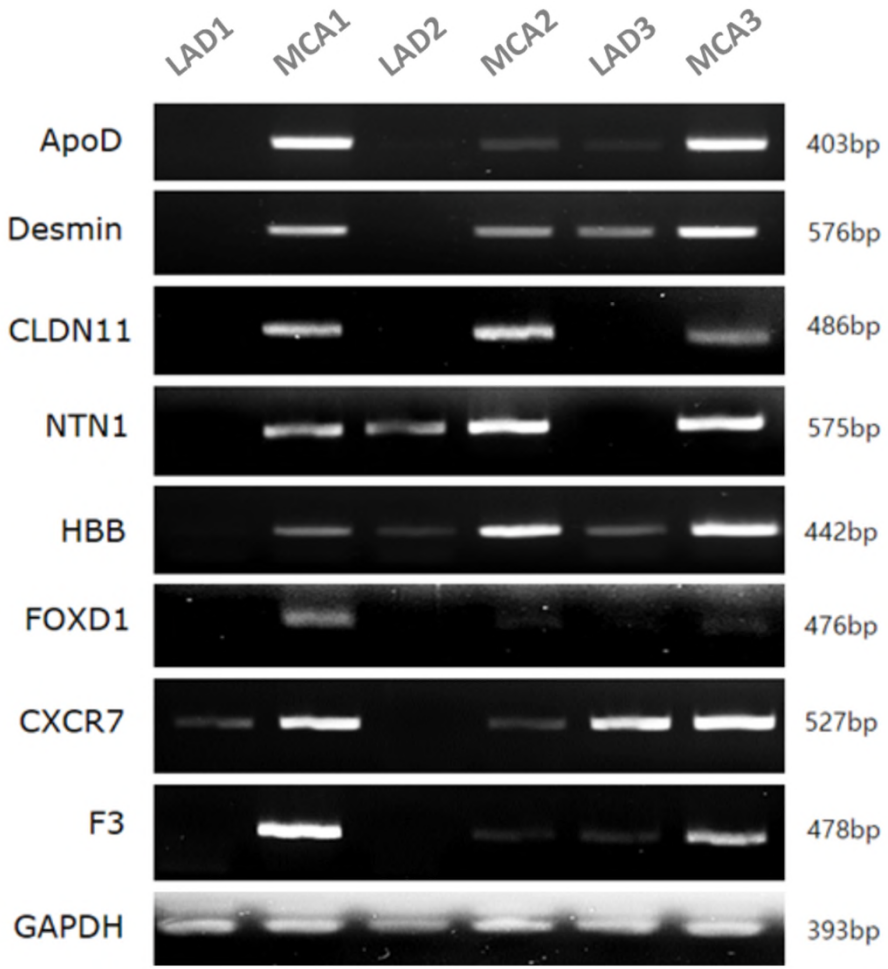


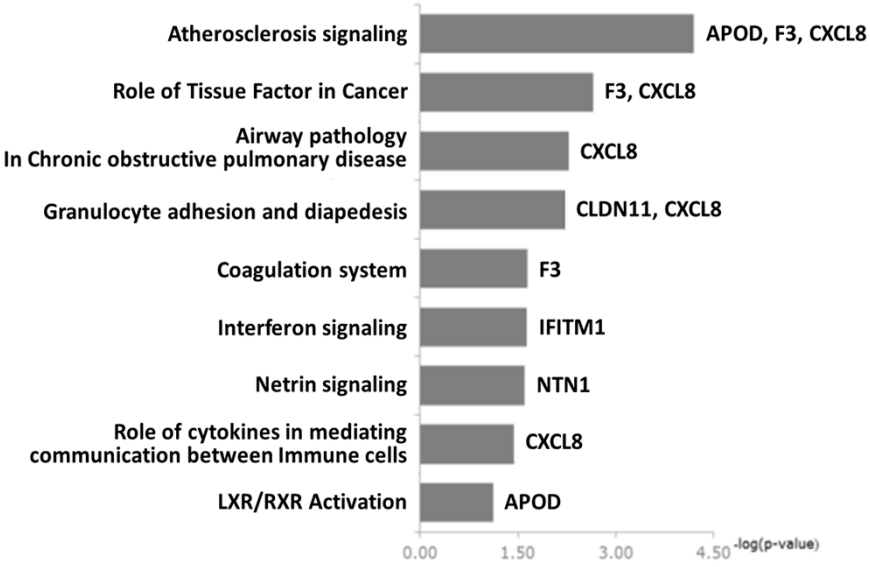
Table 5

Gene	Sequence	Primer size
ApoD	CCTGCCAAGCTGGAAGTTAAGTT AACAGGGTAGGGCATGGTTACAT	403bp
Desmin	ACGCGGTGAACCAGGAGTTTC TAGCCGCGATGGTCTCATACTGA	576bp
CLDN11	CTTCTCCCTTTCGGCTTAGTTTC CCCATGAAGCCAAACTTAACAGT	486bp
NTN1	TGTGAATTCTCAAGCCCGTAGTGT AATAGTGTCACTGCCGTAAACCCA	575bp
HBB	CTGAGGAGAAGTCTGCCGTTACT GCAAGAAAGCGAGCTTAGTGATA	442bp
FOXD1	CTGCCCTGTCCAGTGTCGAGAACT GCTGGCATTCTTCAAGACCTTTAC	476bp
CXCR7	TTCCCTTCTCCATTATCGCTGTC CAAGCATCAAGACCCGAAGCTAC	527bp
F3	GTGTGACCTCACCGACGAGATTG CCCTTTCTCCTGGCCCATACACT	478bp
GAPDH	GGGAAACTGTGGCGTGATG CCTGTTGCTGTAGCCAAATTCGT	393bp

Results

- **Ingenuity pathway analysis (IPA)**
  - To identify potential pathogenic pathways
  - The top canonical pathway : atherosclerosis signaling

    Related genes : APOD, F3, CXCL8



Results

- **Gene-associated disease analysis**
  - Used DAVID to identify DEGs-related disease using 14 upregulated genes
  - Type 2 diabetes and Hypertension were the most relevant

    APOD, F3 and DES are associated with type 2 DM

    ATP1A2 and HBB are associated with both disease

Table 6.

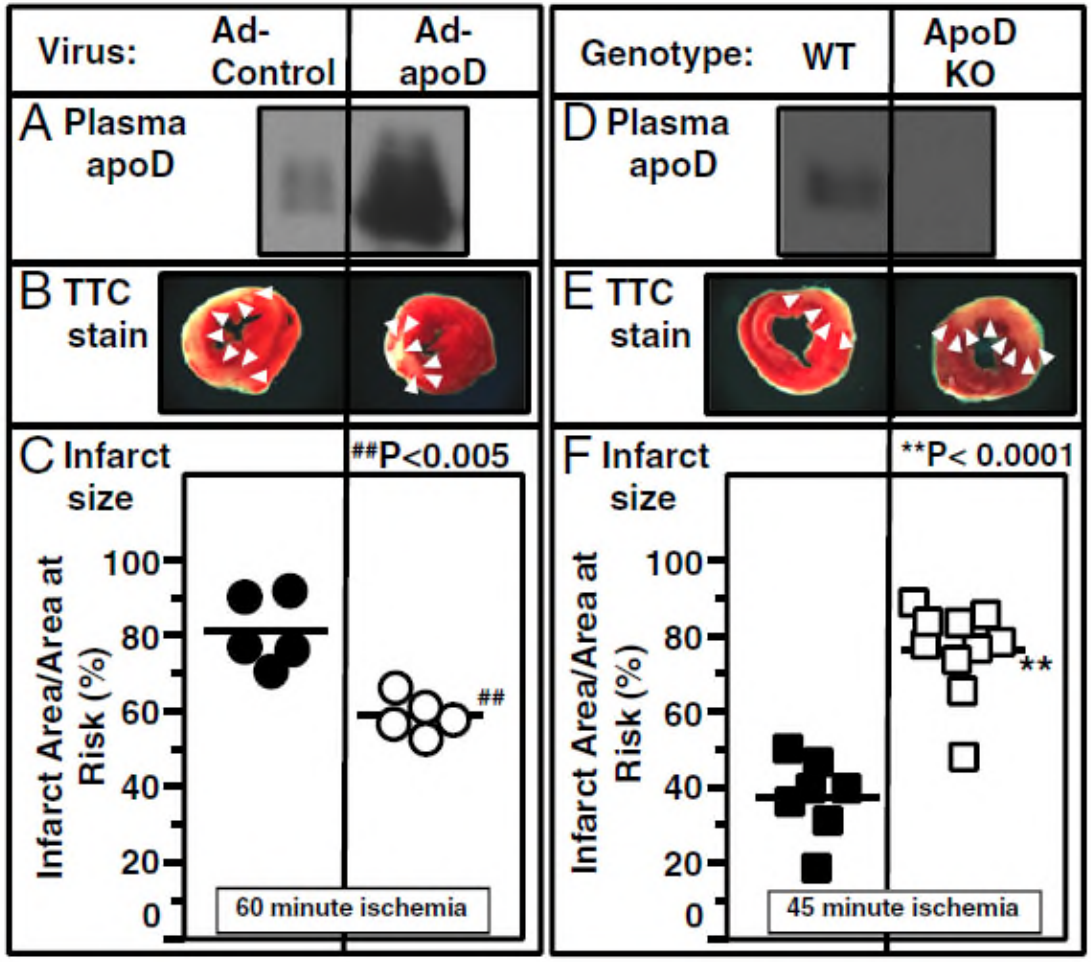
Term	Gene count	P-value	Fold enrichment
Hypertension	3	8.2E-2	5.5
Type 2 Diabetes l edema l rosiglitazone	5	5.1E-2	3.0

OFFICIAL_GENE_SYMBOL	GENE NAME
Type 2 Diabetes related	
ATP1A2	ATPase Na+/K+ transporting subunit alpha 2
APOD	Apolipoprotein D
F3	Coagulation factor III, tissue factor
DES	Desmin
HBB	Hemoglobin subunit beta
Hypetenesion related	
ATP1A2	ATPase Na+/K+ transporting subunit alpha 2
HBB	Hemoglobin subunit beta
ITM2C	Integral membrane protein 2C

Discussion

- **Apolipoprotein D (APOD)**
  - A component of HDL that no marked similarity to other apolipoprotein sequences
  - Intracellular accumulation selectively inhibit PDGF-BB-induced VSMC proliferation
  - Cardioprotective as an antioxidant

Discussion

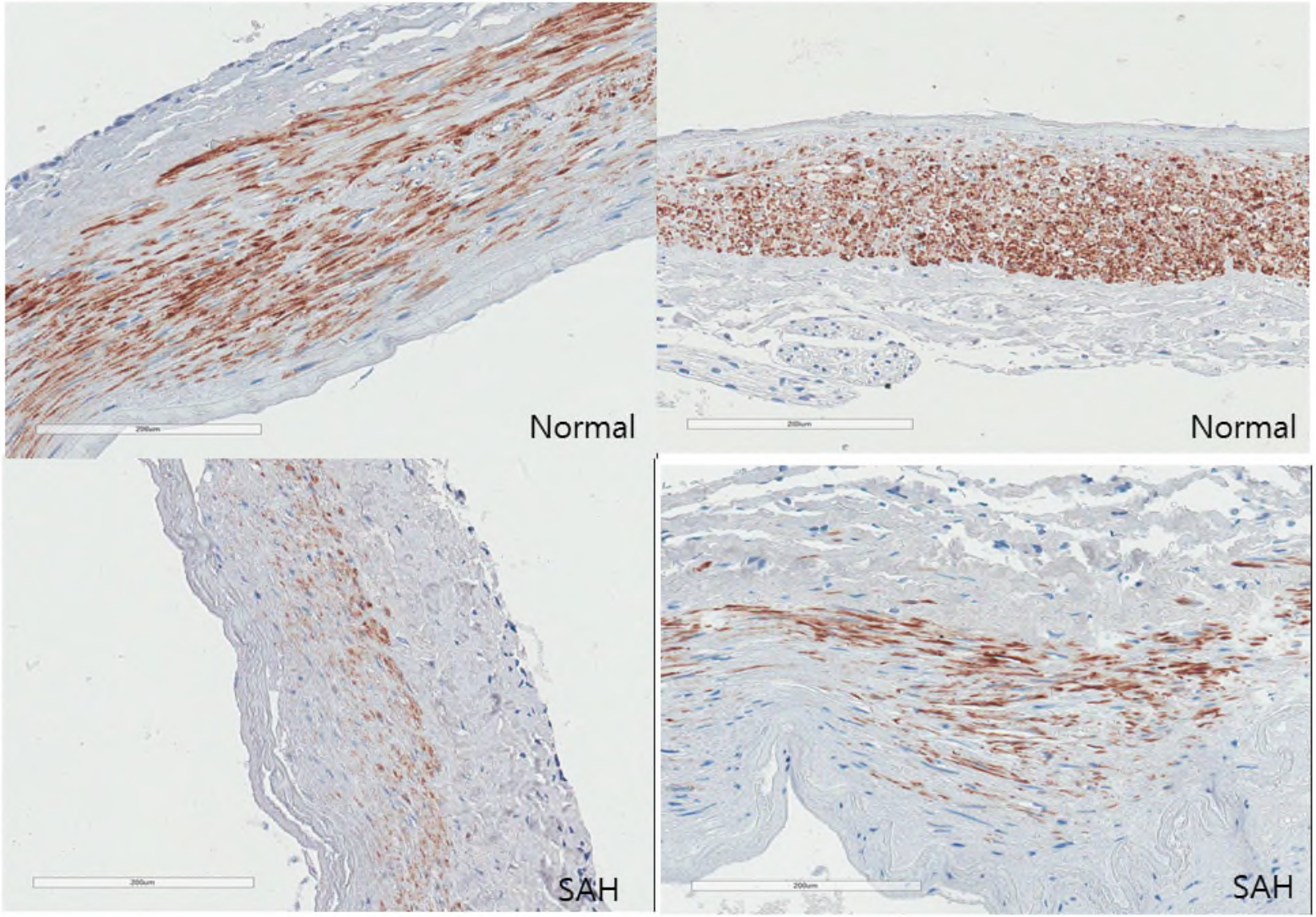


Proc Natl Acad Sci U S A. 2013;110(42):17023-8.

Discussion

- **Desmin (DES)**
  - A key subunit of the intermediate filament in cardiac and skeletal muscles
    - Maintenance of structural and mechanical integrity of the contractile apparatus in muscle tissues
  - In vSMC, especially intracranial
    - Control cerebral arteries: strongly immunostained
    - vSMCs in both non-ruptured and ruptured aneurysmal walls: no staining for desmin

Desmin expression in middle cerebral artery (CNU Cases)



Conclusion

This dataset provides a resource for understanding the different arterial regulation and disease susceptibility in IA and EA, especially atherosclerosis and diabetes, and may also aid in the development of diagnostic and therapeutic markers

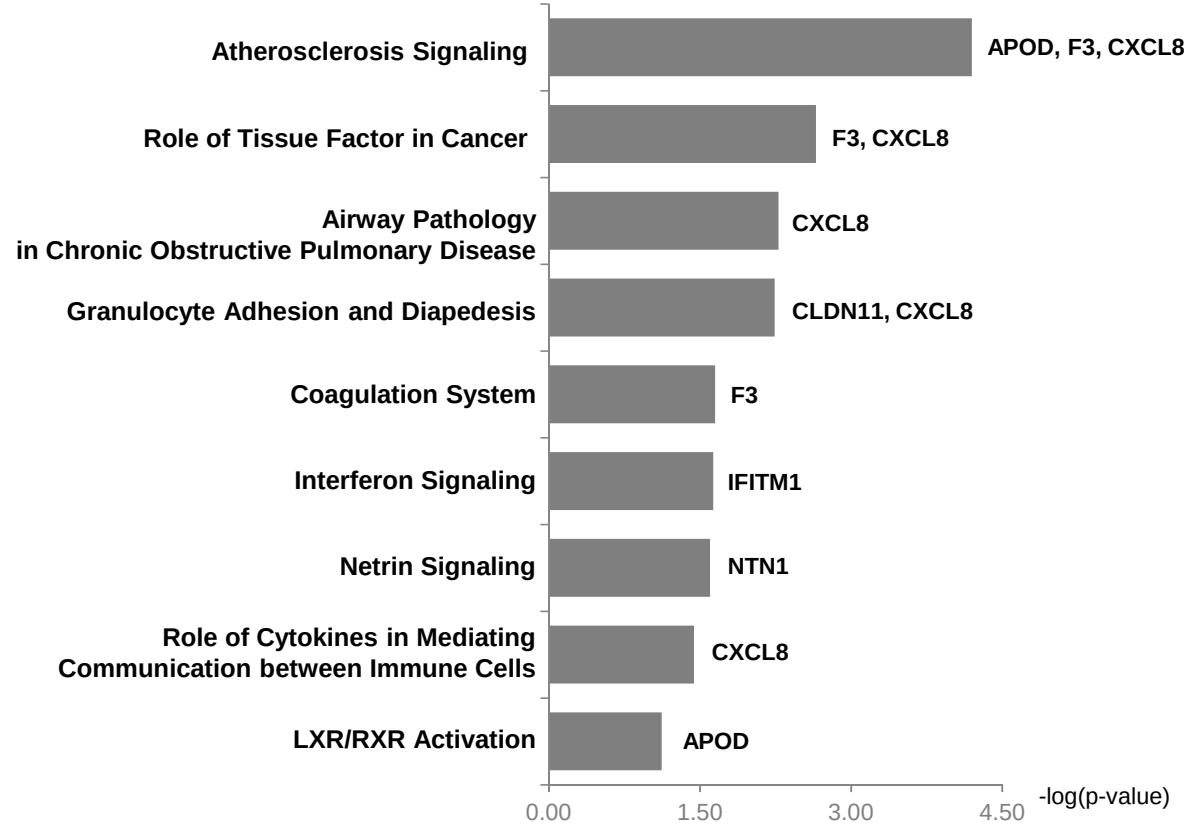
Part II.

CLDN11 Expression in Vascular Smooth Muscle Cell and role for Cardiovascular Disease

5 Fold_increased in ICA

Gene	Fold
APOD	11.494
DES	9.051
CLDN11	8.659
LOC642852	6.578
F3	6.171
ATP1A2	5.977
IFITM1	5.956
ITM2C	5.355
FOXD1	5.346
IL8	5.331
NTN1	5.320
CXCR7	5.242
HBB	5.129
PMP2	5.025

[Canonical pathway]



[Networks]

Molecules in Network	Focus molecules	Top Diseases and Functions
ACKR3, APOD, ATP1A2, CXCL8, DES, F3, FOXD1, HBB, IFITM1, NTN1, PMP2	11	Cancer, Organismal Injury and Abnormalities, Reproductive System Disease
CLDN11, ITM2C	2	Cell-To-Cell Signaling and Interaction, Cellular Assembly and Organization, Cellular Function and Maintenance

CLDN11 Gene (Protein Coding) ★

Claudin 11

GCID: GC03P170418 ?
GIFtS: 57 ?

Genes
Participants

Undiagnosed Diseases Network

Jump to section

Aliases Disorders Domains Drugs Expression Function Genomics Localization Orthologs
Paralogs Pathways Products Proteins Publications Sources Summaries Transcripts Variants

Aliases for CLDN11 Gene

Aliases for CLDN11 Gene

Claudin 11 [2 3 5]

Oligodendrocyte Transmembrane Protein [2 3]

Oligodendrocyte-Specific Protein [3 4]

OTM [3 4]

OSP [3 4]

Claudin-11 [3]

External Ids for CLDN11 Gene

HGNC: 8514 Entrez Gene: 5010 Ensembl: ENSG00000013297 OMIM: 601326 UniProtKB: O75508

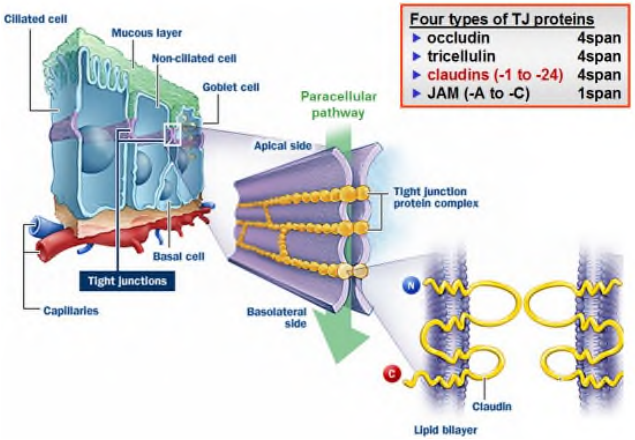
Previous HGNC Symbols for CLDN11 Gene

OTM

Previous GeneCards Identifiers for CLDN11 Gene

GC03P167279, GC03P171185, GC03P171538, GC03P171457, GC03P171619, GC03P170136, GC03P167506

Export aliases for CLDN11 gene to outside databases



Summaries for CLDN11 Gene

Entrez Gene Summary for CLDN11 Gene

This gene encodes a member of the claudin family. Claudins are integral membrane proteins and components of tight junction strands. Tight junction strands serve as a physical barrier to prevent solutes and water from passing freely through the paracellular space between epithelial or endothelial cell sheets, and also play critical roles in maintaining cell polarity and signal transductions. The protein encoded by this gene is a major component of central nervous system (CNS) myelin and plays an important role in regulating proliferation and migration of oligodendrocytes. Mouse studies showed that the gene deficiency results in deafness and loss of the Sertoli cell epithelial phenotype in the testis. This protein is a tight junction protein at the human blood-testis barrier (BTB), and the BTB disruption is related to a dysfunction of this gene. Alternatively spliced transcript variants encoding different isoforms have been identified.[provided by RefSeq, Aug 2010]

GeneCards Summary for CLDN11 Gene

CLDN11 (Claudin 11) is a Protein Coding gene. Diseases associated with CLDN11 include Appendiceal Neoplasm and Multiple Sclerosis, Disease Progression, Modifier Of. Among its related pathways are Blood-Brain Barrier and Immune Cell Transmigration: VCAM-1/CD106 Signaling Pathways and Blood-Brain Barrier Pathway: Anatomy. GO annotations related to this gene include *identical protein binding* and *structural molecule activity*.

UniProtKB/Swiss-Prot for CLDN11 Gene CLD11_HUMAN,O75508

Plays a major role in tight junction-specific obliteration of the intercellular space, through calcium-independent cell-adhesion activity.

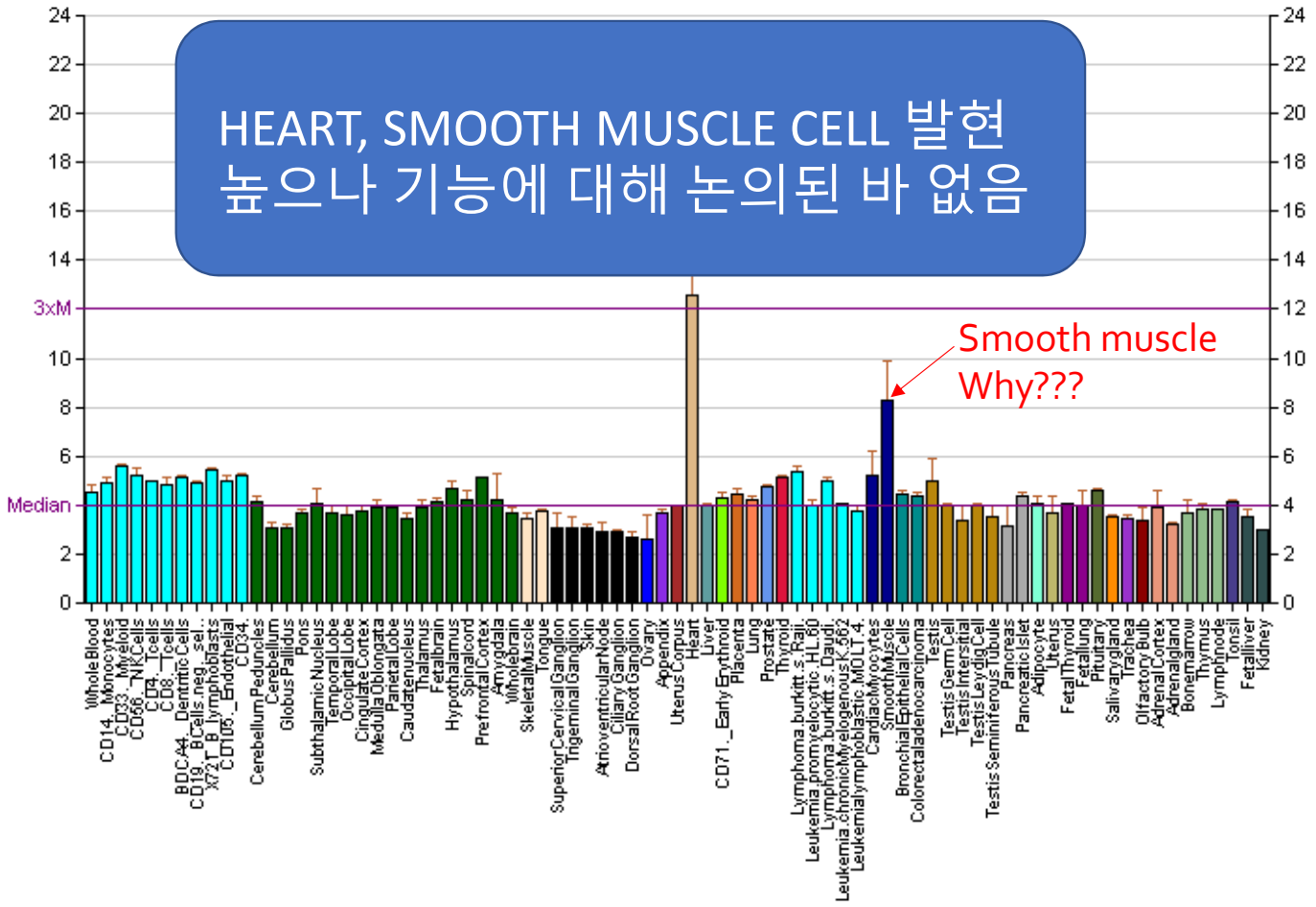
Gene Wiki entry for CLDN11 Gene

Biological Roles of CLDN11 in cancer

- Potential tumor suppressor gene located at chromosome 3 (3q26.2)
- Silencing of *CLDN11* expression
  - Associated with increased invasiveness in various cancers
  - Poor outcome of patients with meningiomas was associated with reduced *CLDN11* expression
  - Promoter hypermethylation in gastric cancer and malignant melanoma

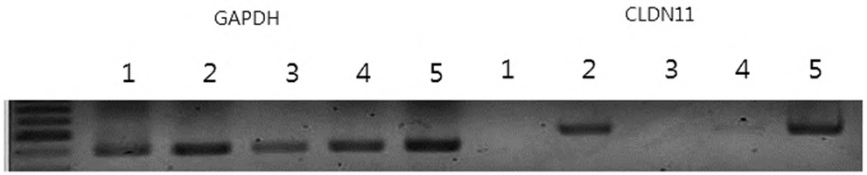
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5541974/

CLDN11 RNA Expression Profile in Human tissues

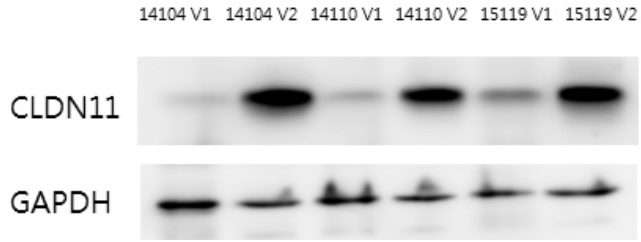


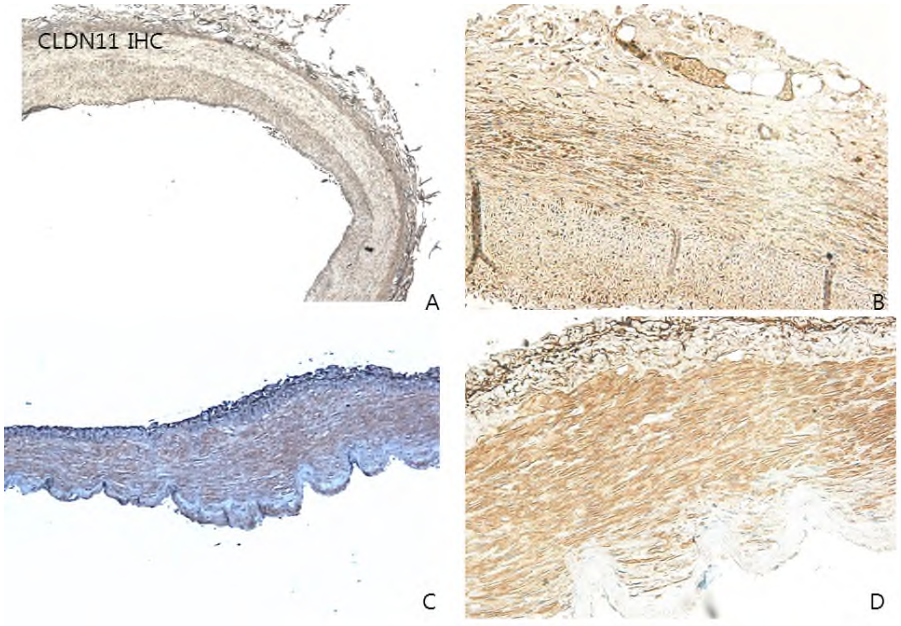
Ref: http://biogps.org/#goto=genereport&id=5010

CLDN11 Expression in Human Vasculature



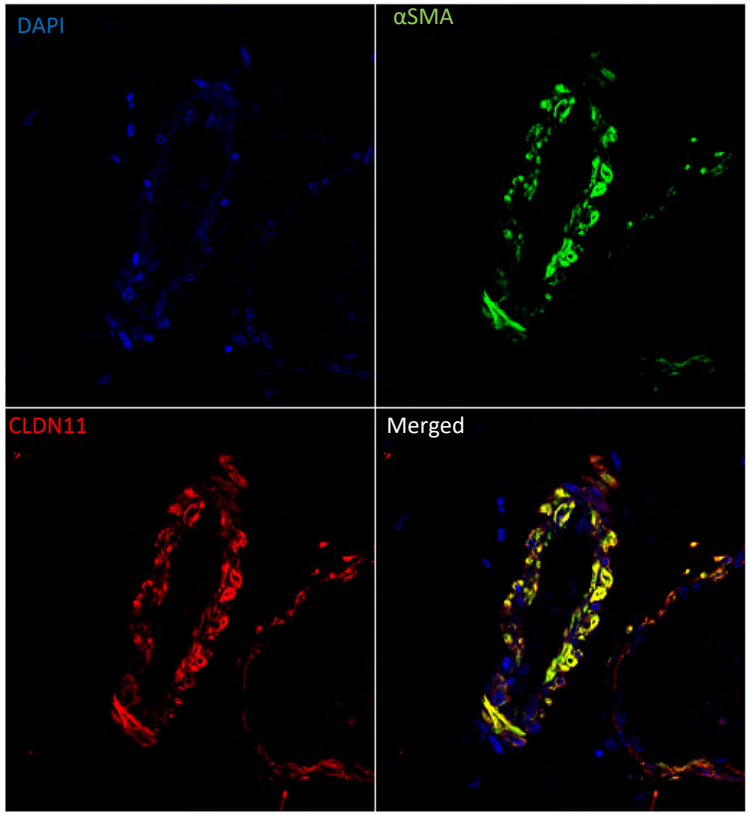
1 : 16101-V1 (LAD)/2 : 16101-V2 (MCA)
3 : 16180-V1 (LAD)/4 : 16180-V2 (MCA)
5 : 16185(Human brain, Cldn11 Control)



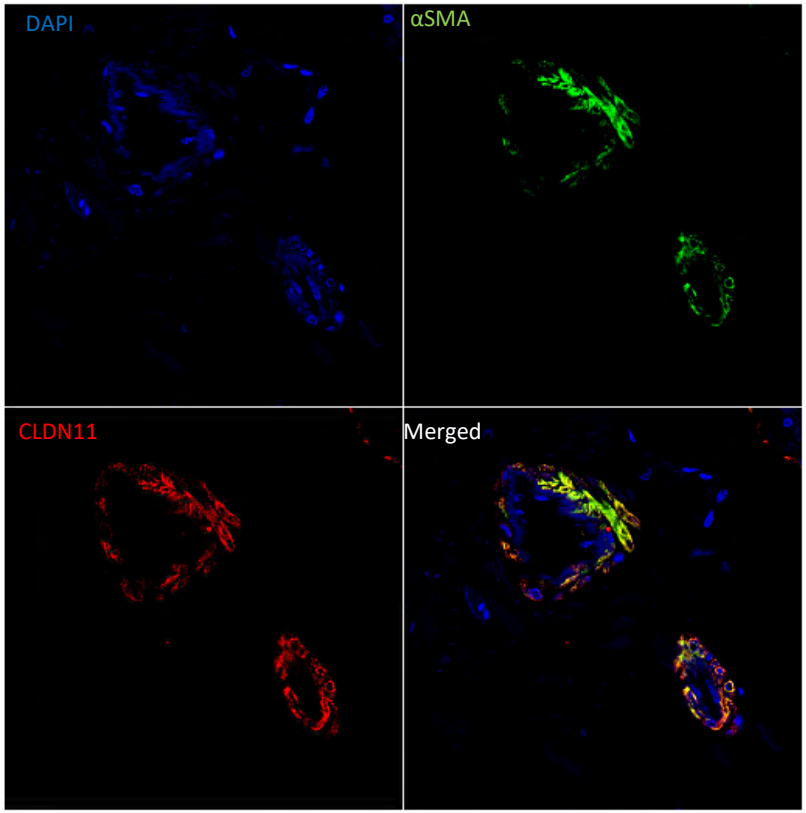


A, B: Coronary artery (Left Ant. Descending, LAD)
C, D: Middle cerebral artery (MCA)

CLDN11 Expression in Human Coronary artery

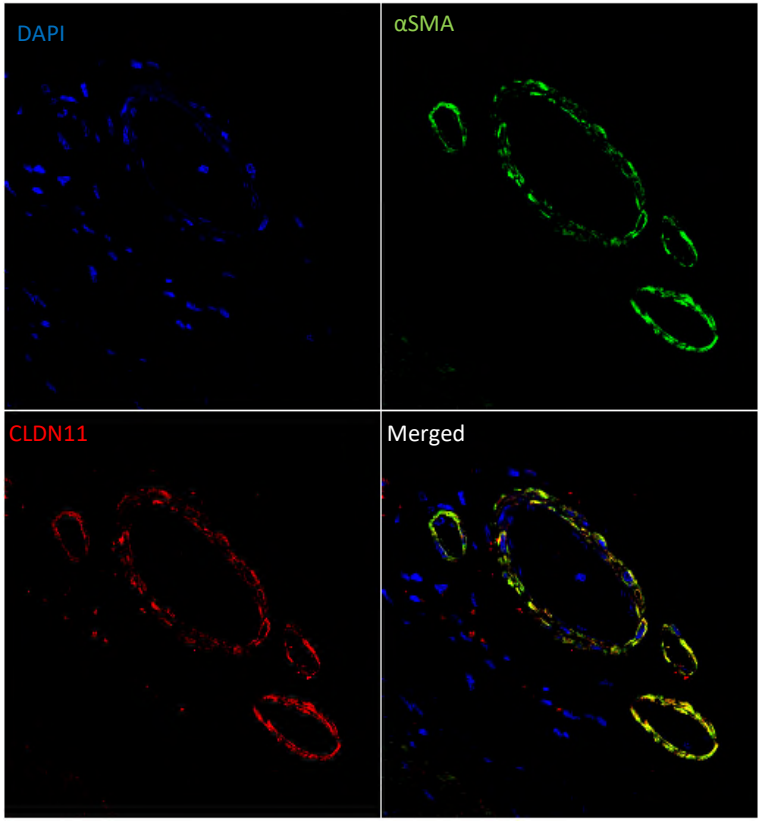


400X



400X

CLDN11 Expression in Human Middle Cerebral Artery



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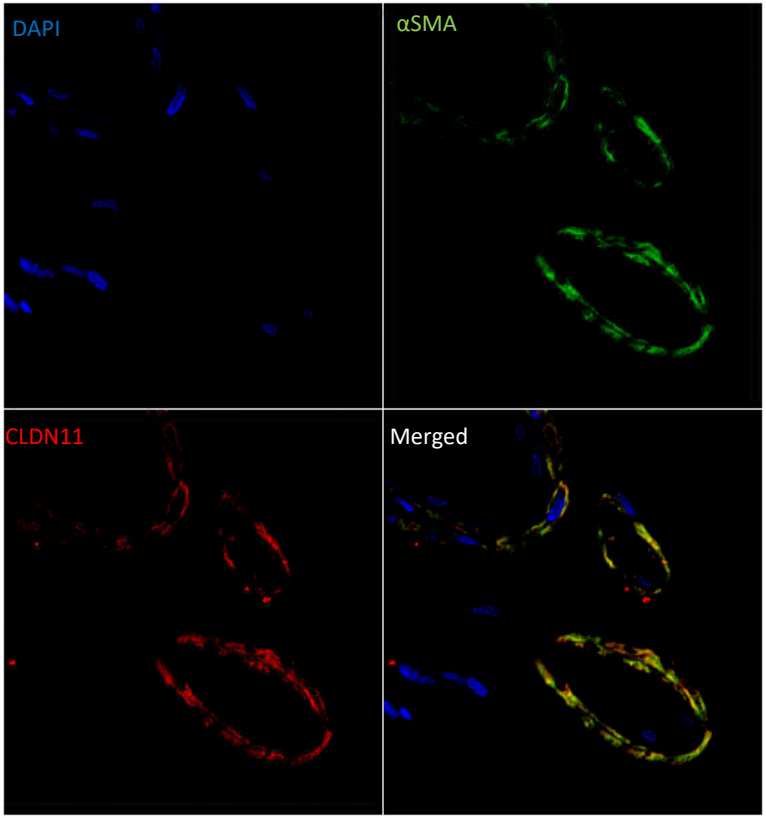

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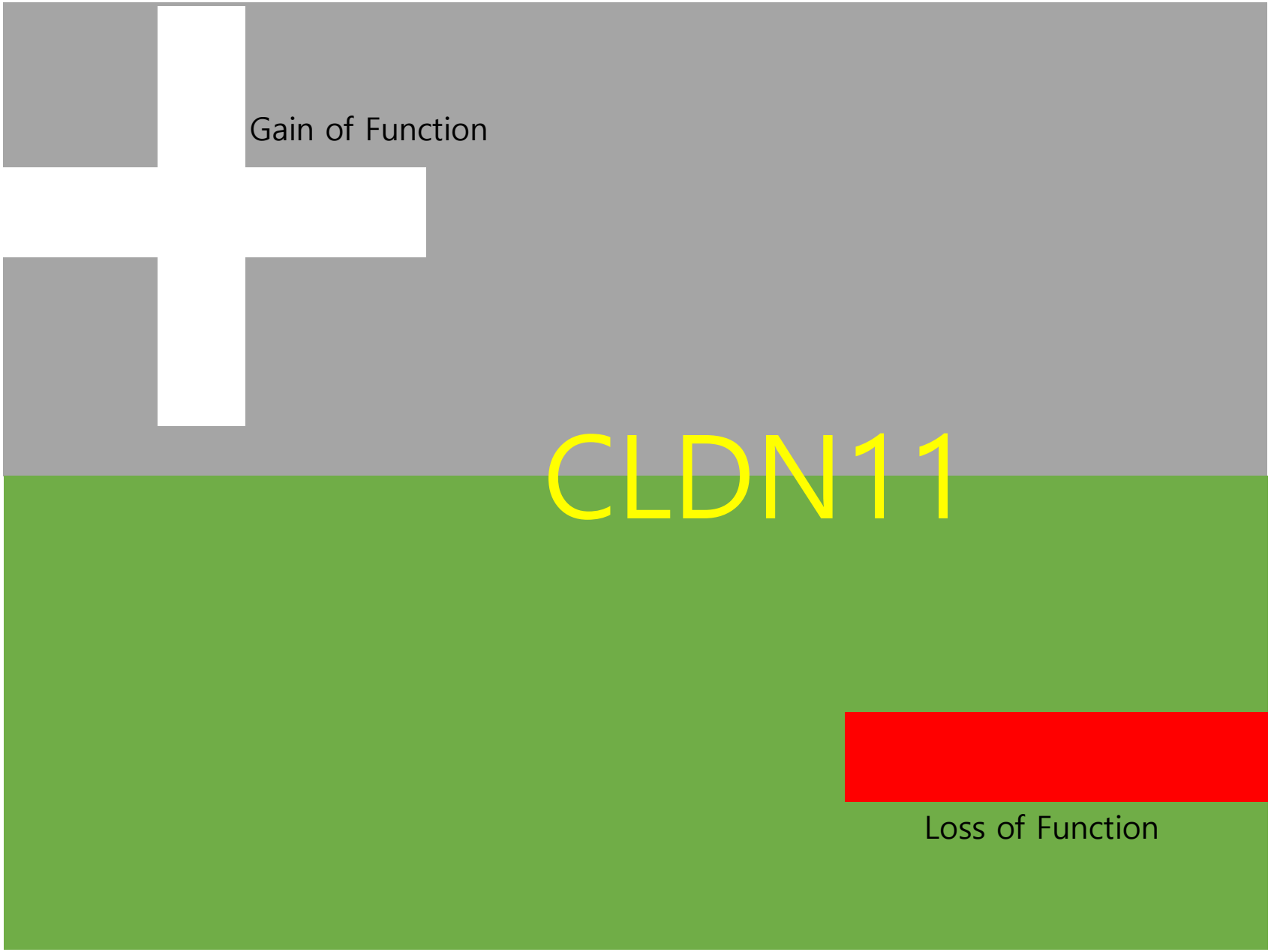
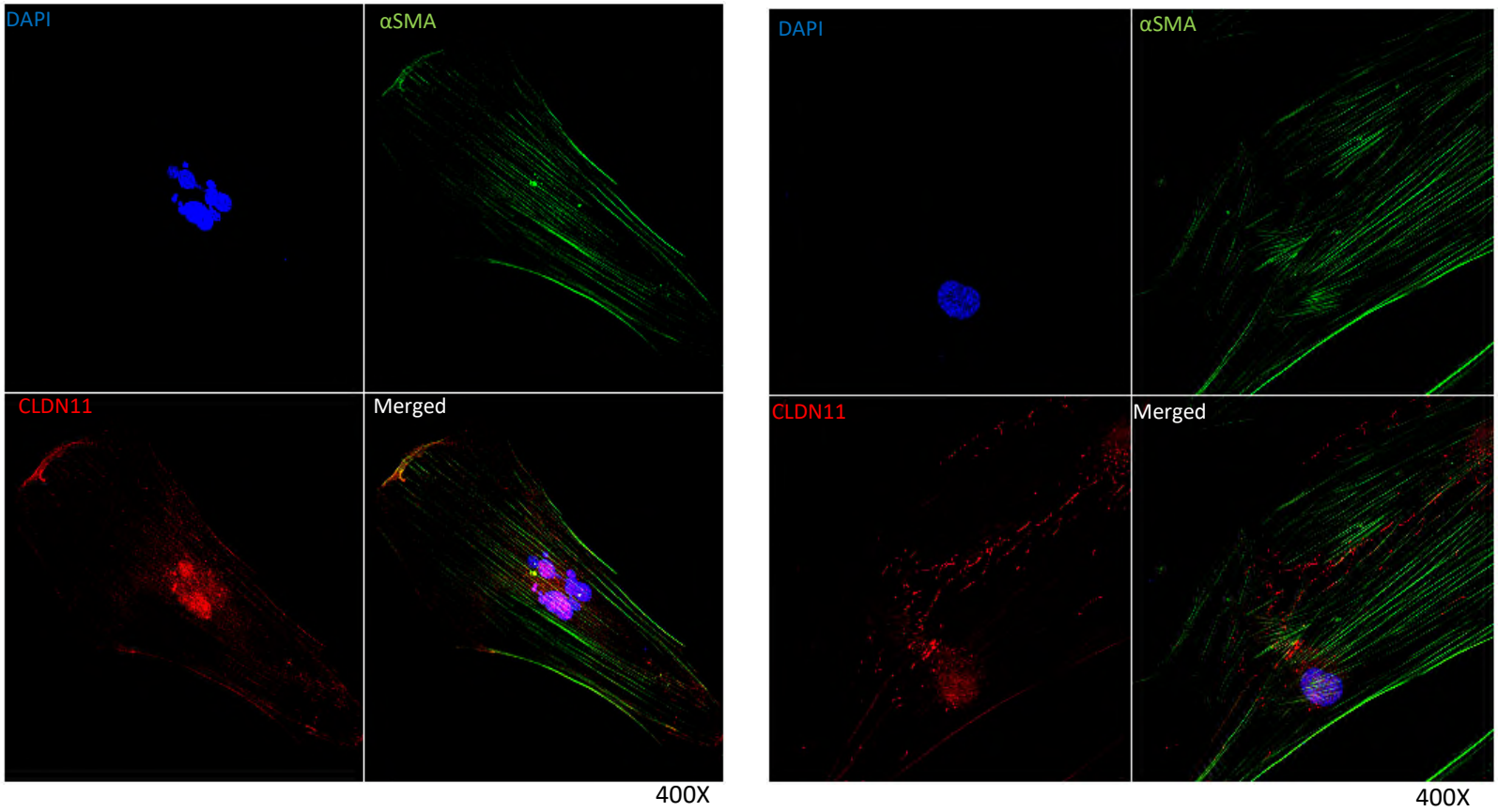
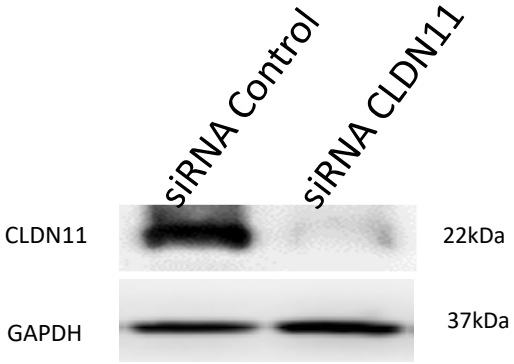
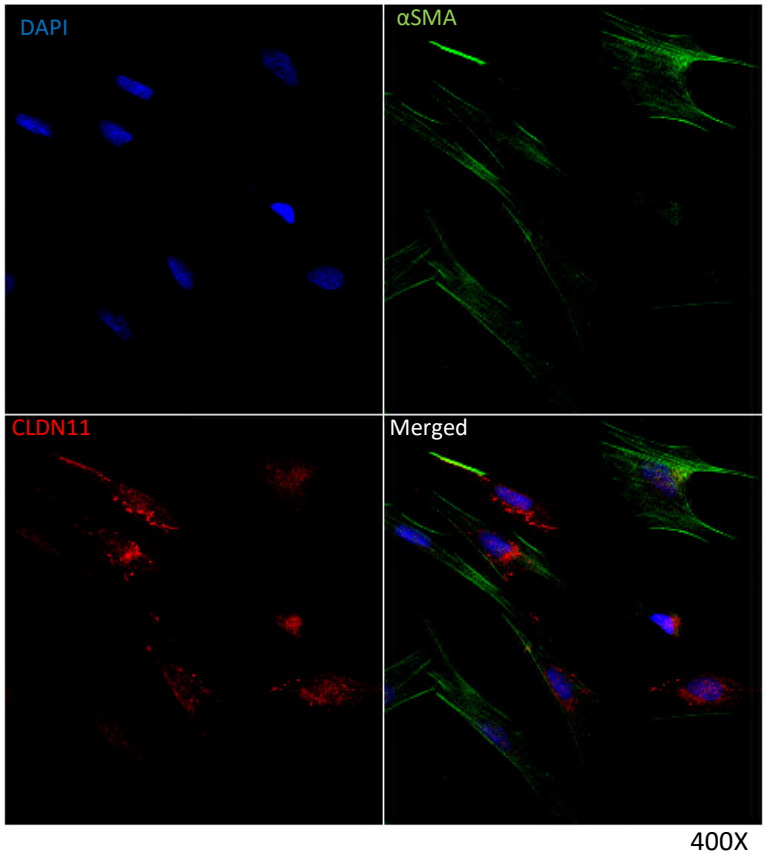

Gain of Function
CLDN11
Loss of Function

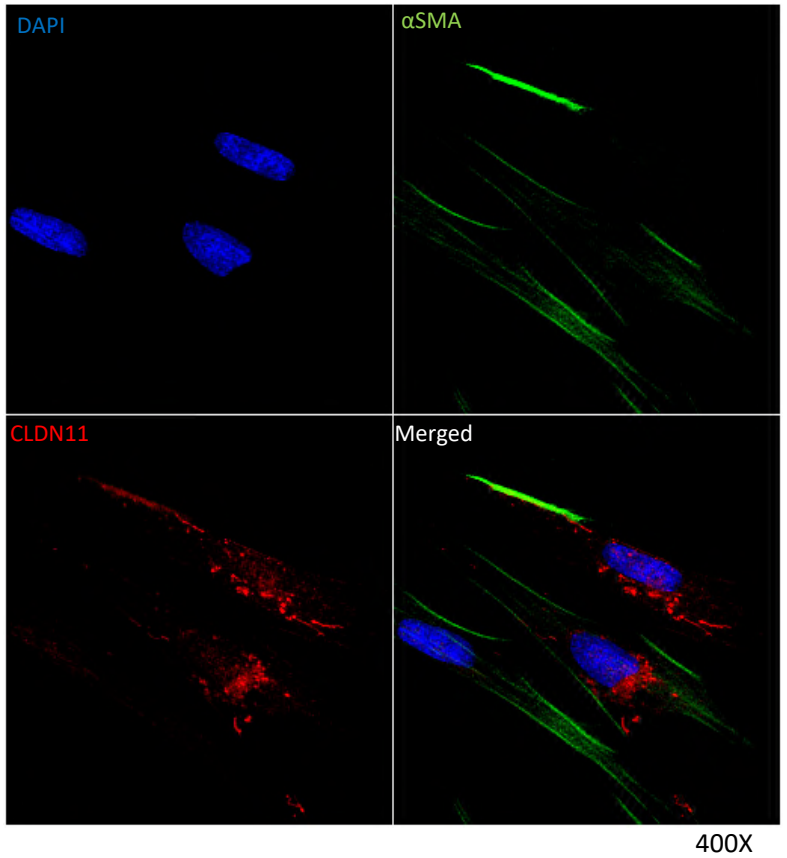
CLDN11 expression in human vascular smooth muscle cell line



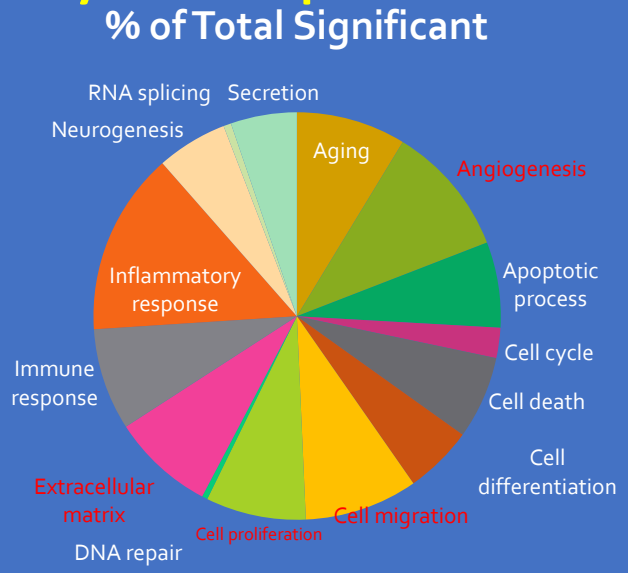
CLDN11 re-distribution in vSMC following siRNA CLDN11 treatment

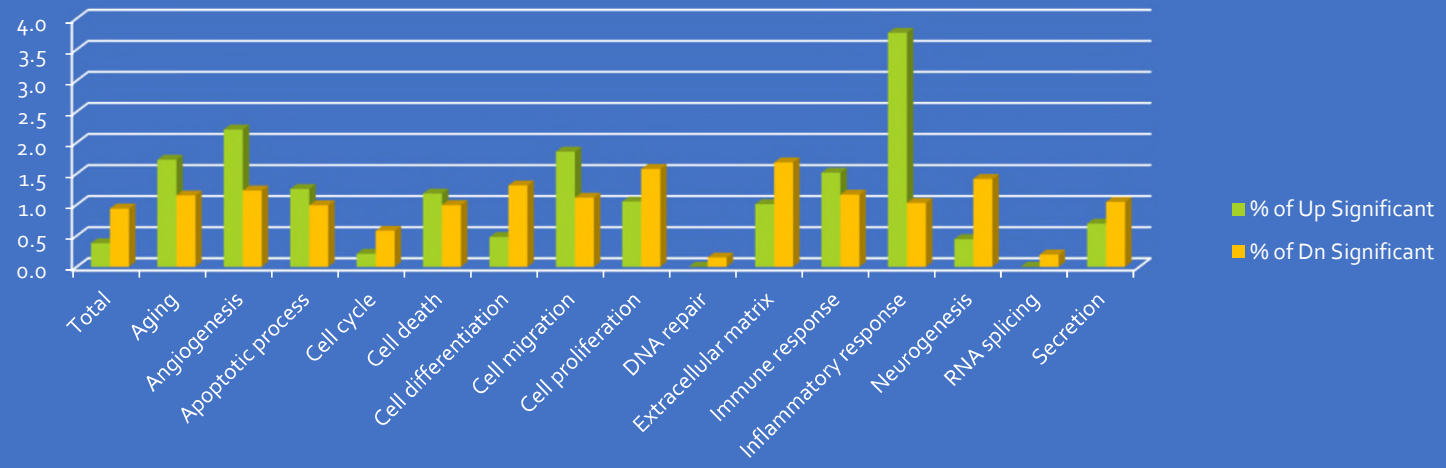


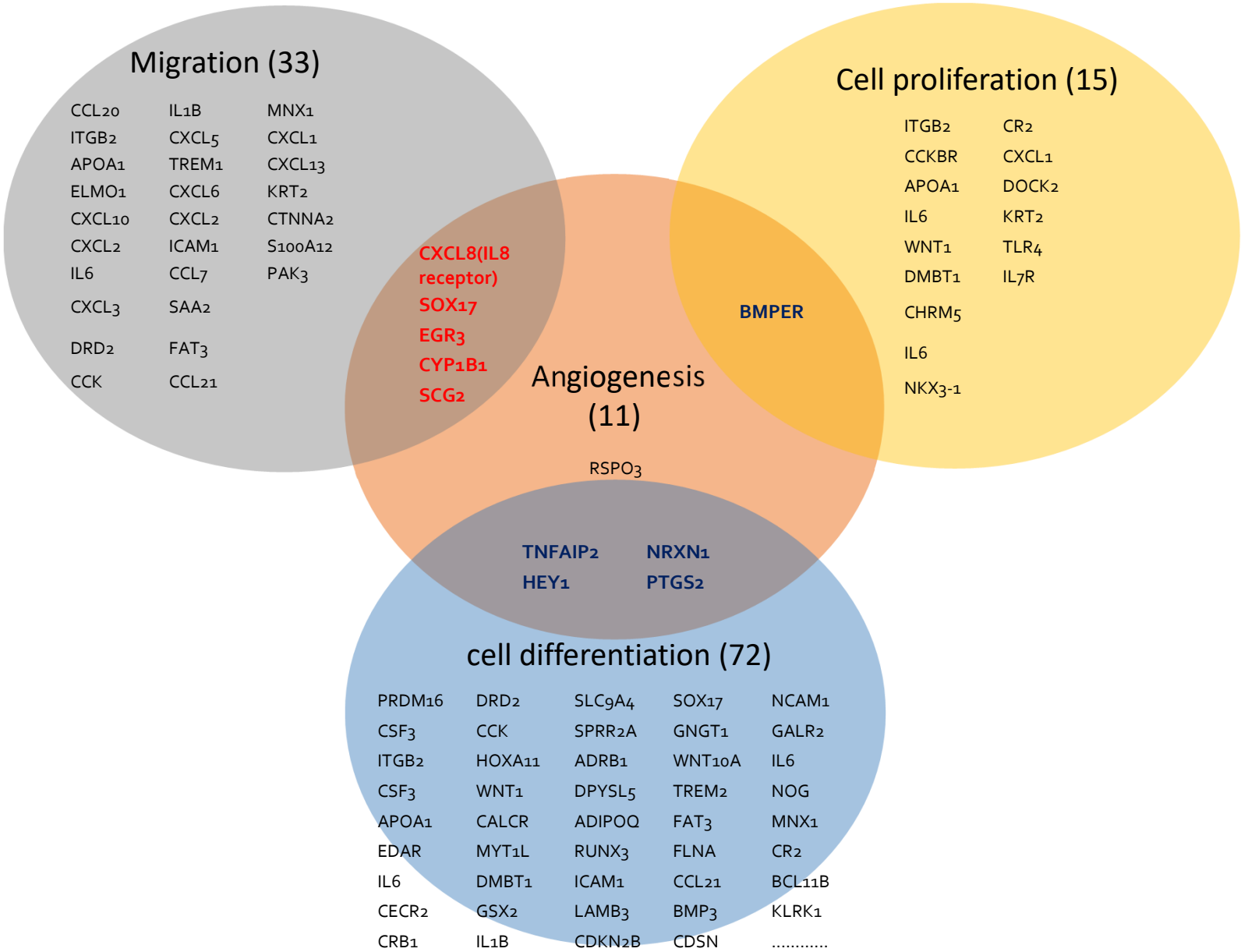




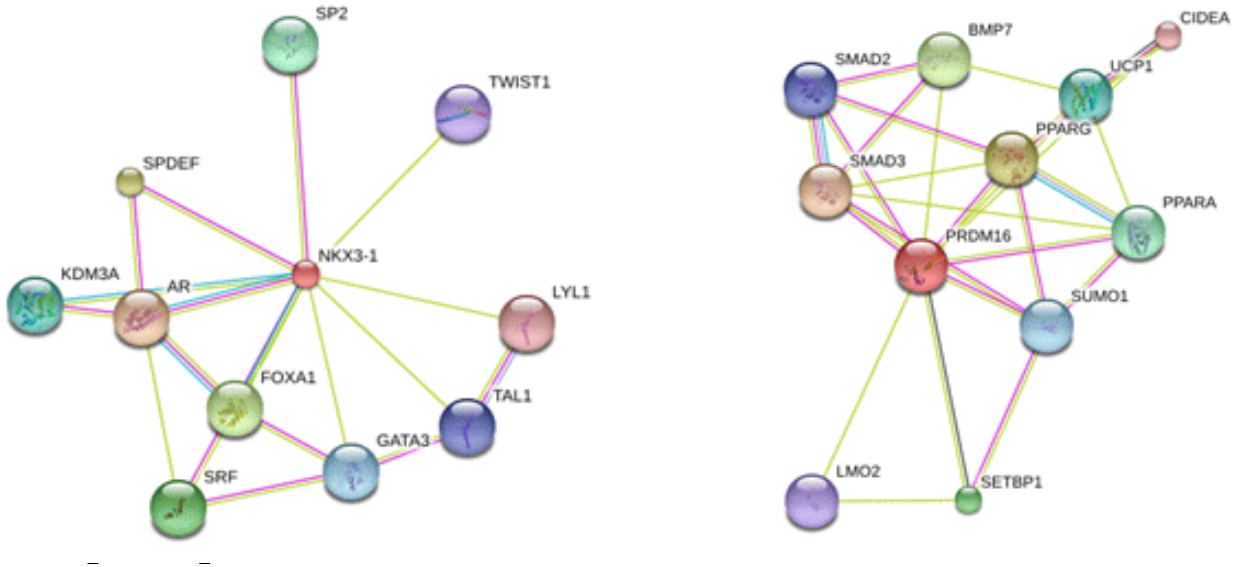
Gene Ontology Analysis Report






Migration (33)
CCL20 IL1B MNX1
ITGB2 CXCL5 CXCL1
APOA1 TREM1 CXCL13
ELMO1 CXCL6 KRT2
CXCL10 CXCL2 CTNNA2
CXCL2 ICAM1 S100A12
IL6 CCL7 PAK3
CXCL3 SAA2
DRD2 FAT3
CCK CCL21
Cell proliferation (15)
ITGB2 CR2
CCKBR CXCL1
APOA1 DOCK2
IL6 KRT2
WNT1 TLR4
DMBT1 IL7R
CHRM5
IL6
NKX3-1
CXCL8(IL8 receptor)
SOX17
EGR3
CYP1B1
SCG2
BMPER
Angiogenesis (11)
RSPO3
TNFAIP2 NRXN1
HEY1 PTGS2
cell differentiation (72)
PRDM16 DRD2 SLC9A4 SOX17 NCAM1
CSF3 CCK SPRR2A GNGT1 GALR2
ITGB2 HOXA11 ADRB1 WNT10A IL6
CSF3 WNT1 DPYSL5 TREM2 NOG
APOA1 CALCR ADIPOQ FAT3 MNX1
EDAR MYT1L RUNX3 FLNA CR2
IL6 DMBT1 ICAM1 CCL21 BCL11B
CECR2 GSX2 LAMB3 BMP3 KLRK1
CRB1 IL1B CDKN2B CDSN .....

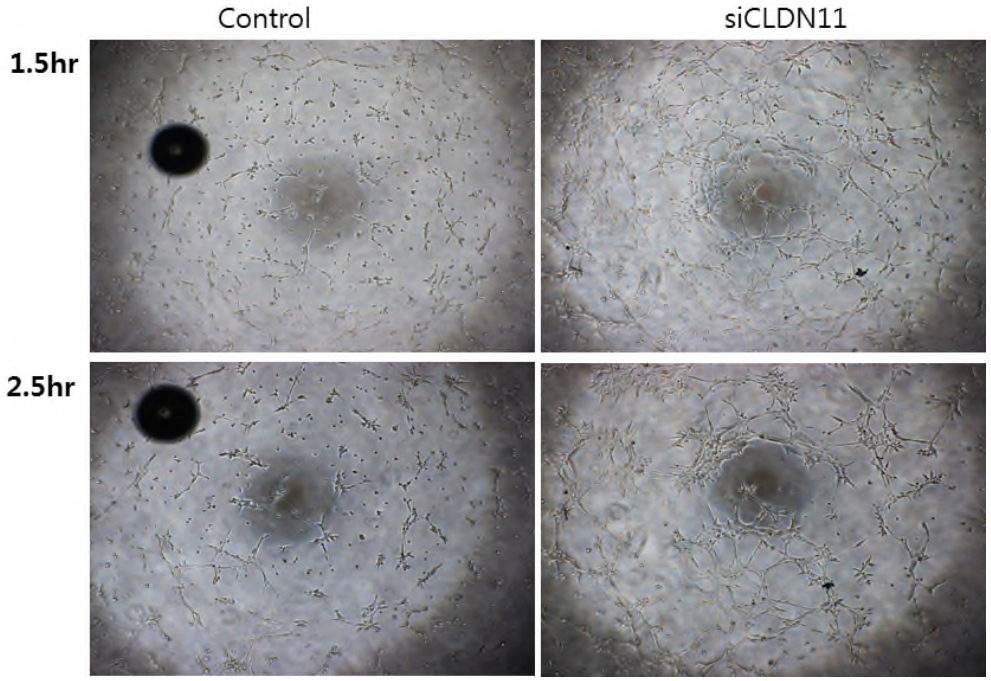
PPI (Protein-protein interaction) analysis for up-regulated gene cluster following siRNA-CLDN11 treatment

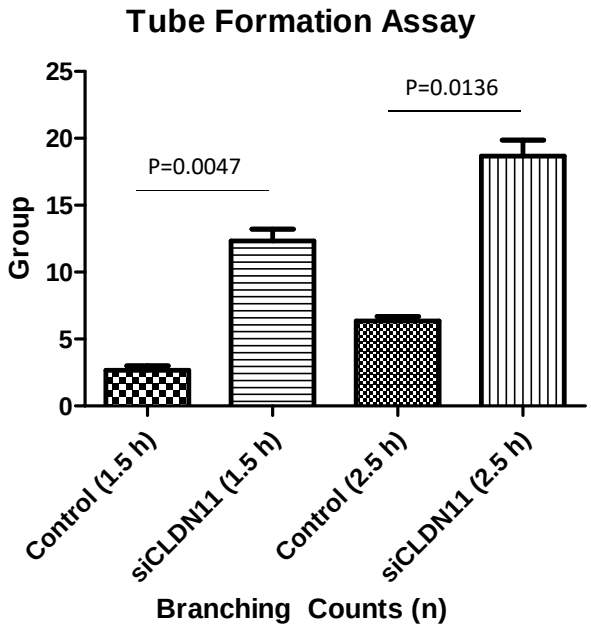


C=5; O=2; E=0.02; R=130.78;
PValue=9.07e-05; FDR=7.11e-02

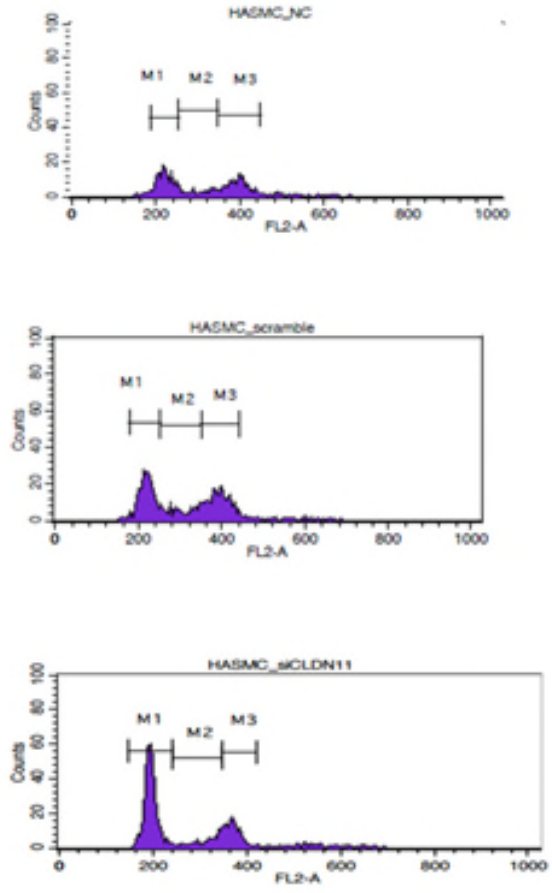
userid	Gene Symbol	Gene Name	Entrez Gene
A_33_P3239347	NKX3-1	NK3 homeobox 1	4824
A_33_P3348872	PRDM16	PR/SET domain 16	63976

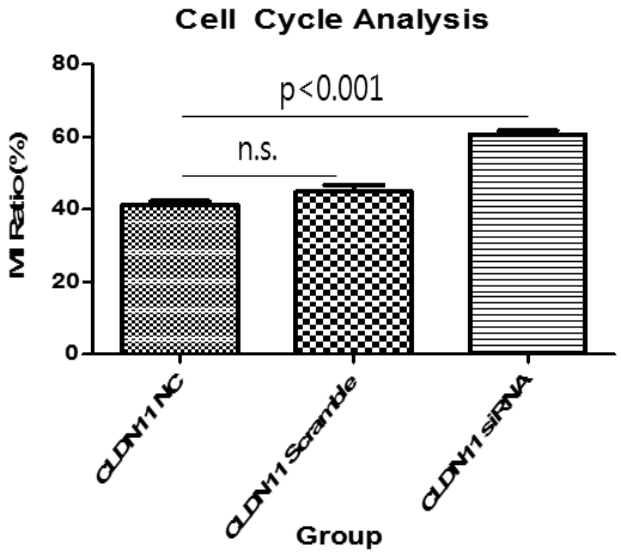
Functional Evaluation: Tube Formation





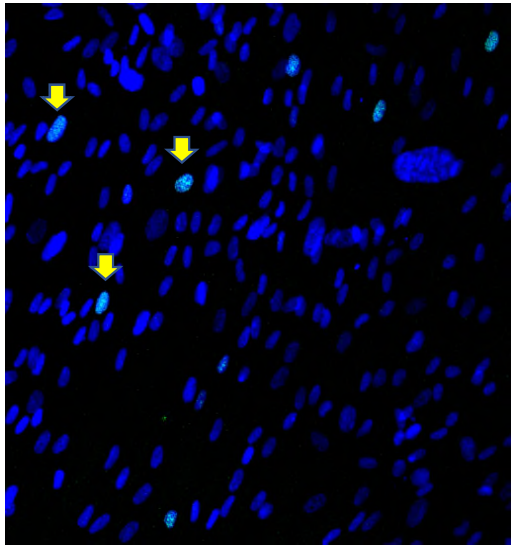
Functional Evaluation: Cell cycle analysis



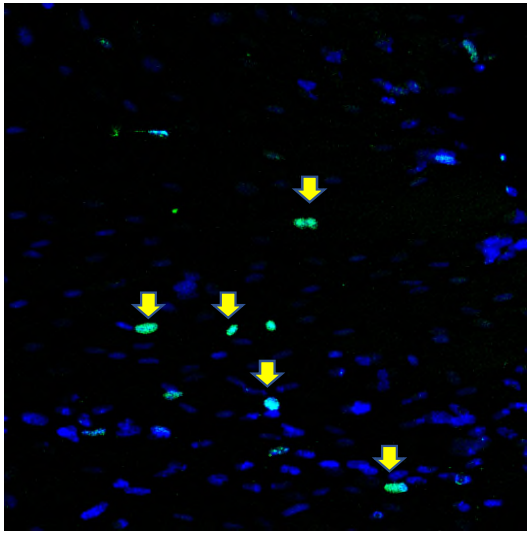


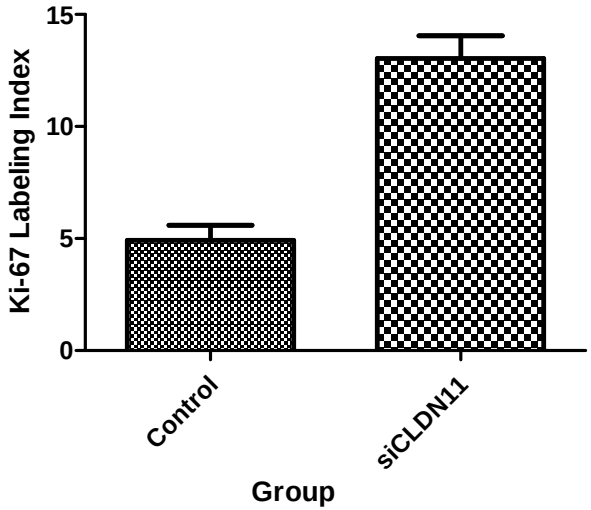
Ki-67 Labeling Index following siCLDN11 treatment

Control

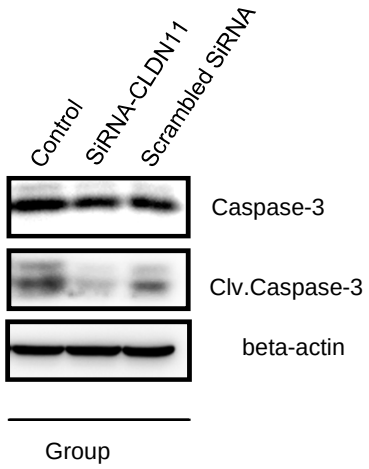


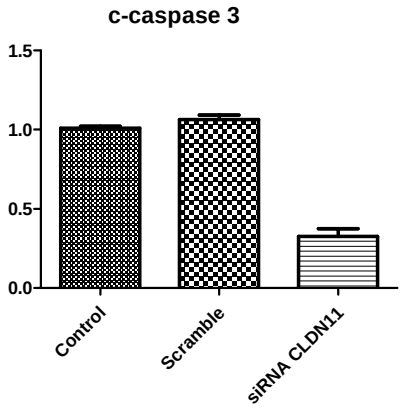
siCLDN11





Caspase-3 expression following siRNA-CLDN11 in vSMC





The Role of CLDN11 in Atherosclerosis

- Modified American Heart Association (AHA) classification of atherosclerosis based on morphological description

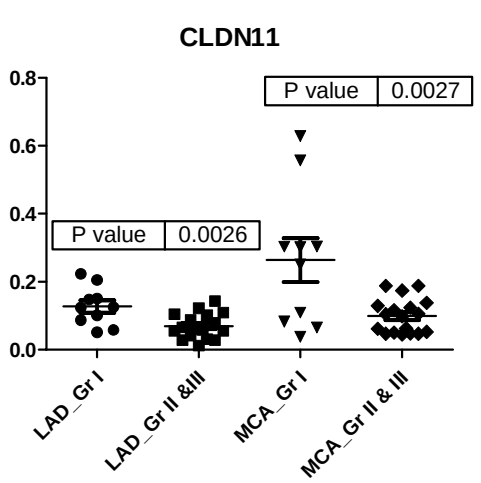
	Description	Thrombosis
Non–atherosclerotic lesions		
Intimal thickening	The normal accumulation of Smooth Muscle Cells (SMCs) in the intima in the absence of lipid or macrophage foam cells	Absent
Intimal xanthoma, or "fatty streak"	Luminal accumulation of foam cells without a necrotic core or fibrous cap. Based on animal and human data, such lesions usually regress.	Absent
Progressive atherosclerotic lesions		
Pathological intimal thickening	SMCs in a proteoglycan-rich matrix with areas of extracellular lipid accumulation without necrosis	Absent
Erosion	Luminal thrombosis; plaque same as above	Thrombus mostly mural and infrequently occlusive
Fibrous cap atheroma	Well-formed necrotic core with an overlying fibrous cap	Absent
Erosion	Luminal thrombosis; plaque same as above; no communication of thrombus with necrotic core	Thrombus mostly mural and infrequently occlusive
Thin fibrous cap atheroma	A thin fibrous cap infiltrated by macrophages and lymphocytes with rare SMCs and an underlying necrotic core	Absent; may contain intraplaque hemorrhage/fibrin
Plaque rupture	Fibroatheroma with cap disruption; luminal thrombus communicates with the underlying necrotic core	Thrombus usually occlusive
Calcified nodule	Eruptive nodular calcification with underlying fibrocalcific plaque	Thrombus usually nonocclusive
Fibrocalcific plaque	Collagen-rich plaque with significant stenosis usually contains large areas of calcification with few inflammatory cells; a necrotic core may be present.	Absent

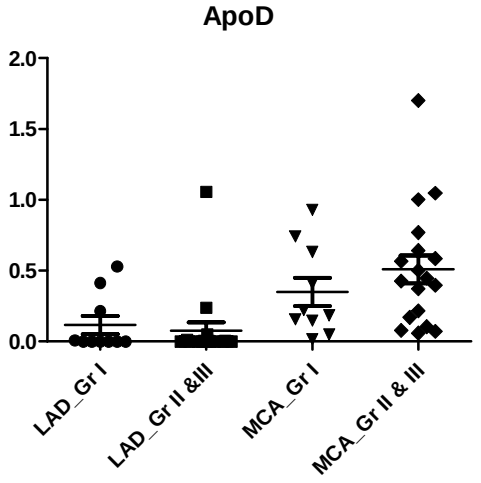
Group I

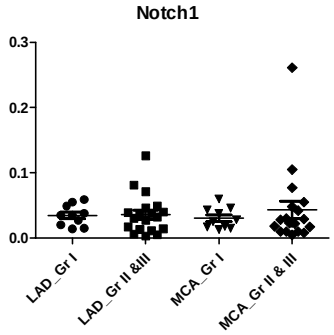
Group II

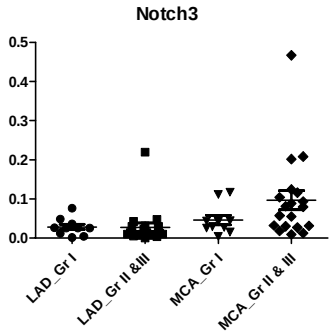
Group III

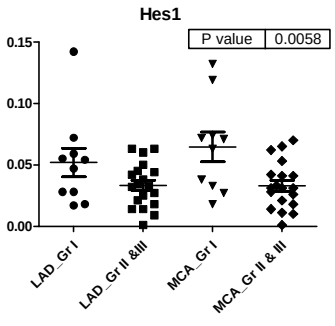
Target gene analysis according to atherosclerosis grade : Non-Atherosclerotic lesion vs. Progressive Atherosclerotic lesion

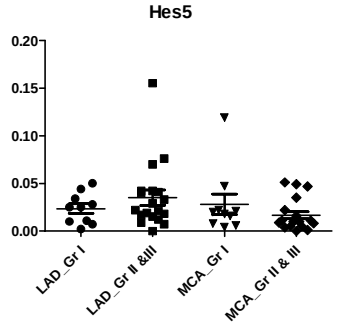




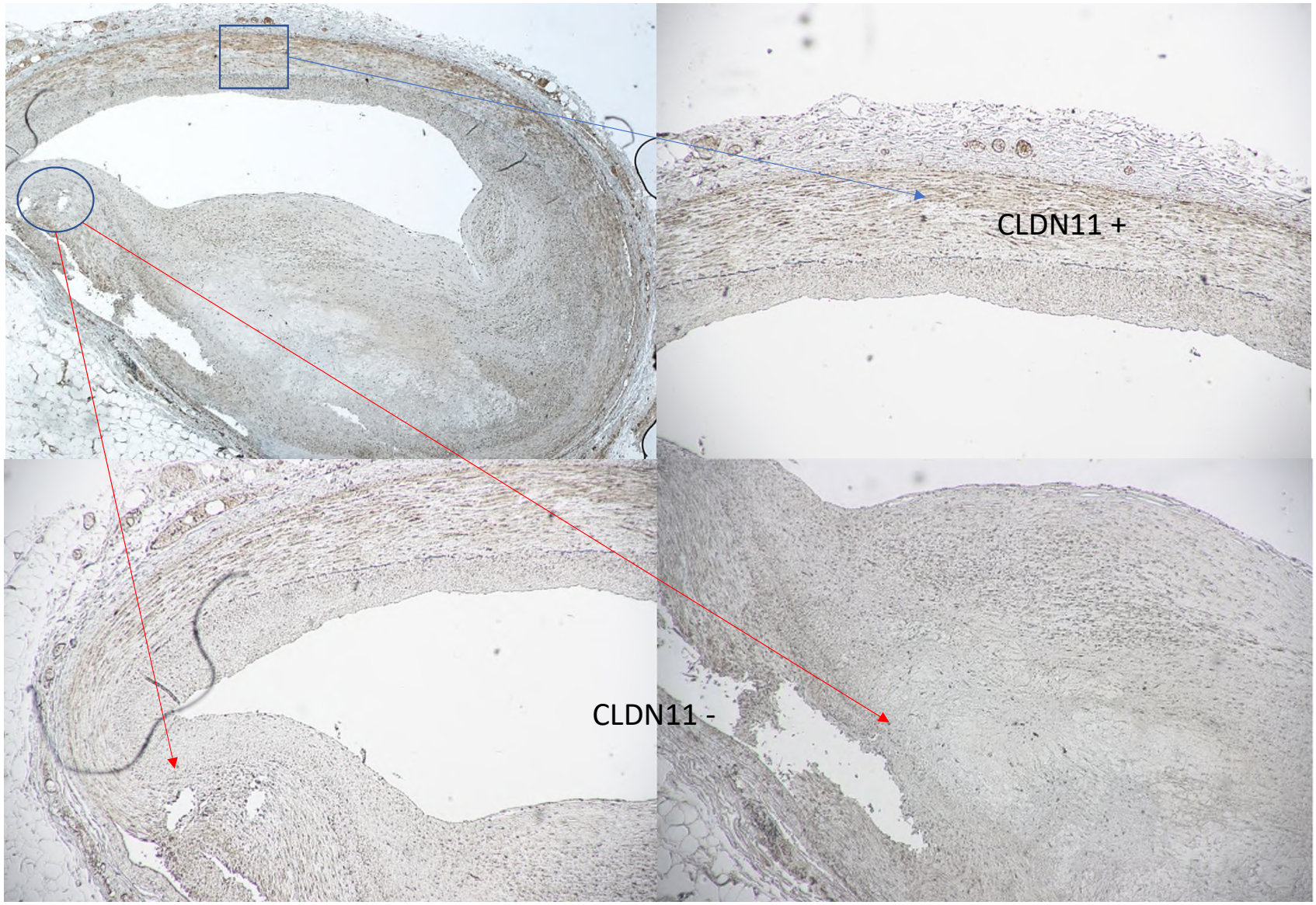








CLDN11 IHC in LAD with CAS



CLDN11 mRNA expression

Between Non-complicated (Gr II) and complicated (Gr III) atherosclerotic lesions

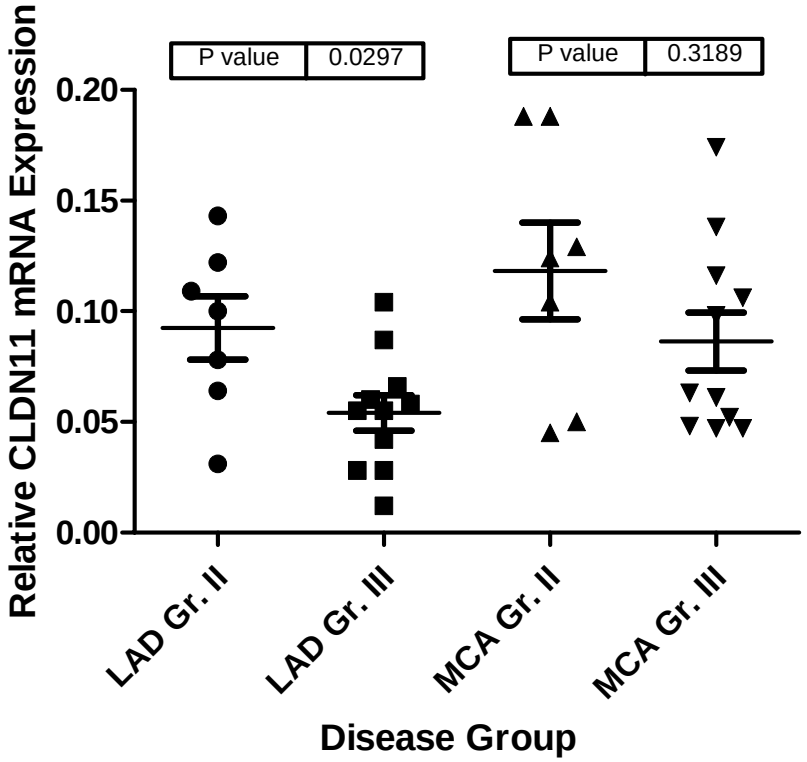
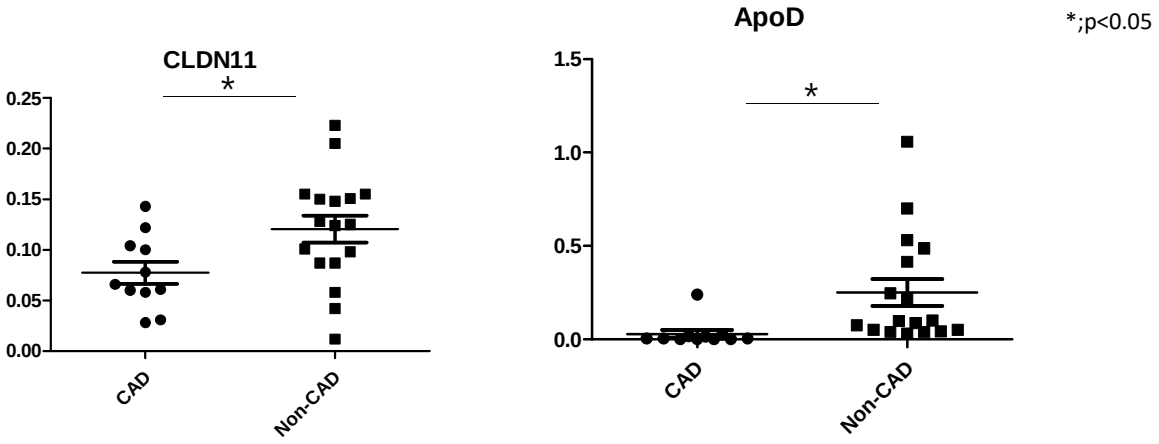


Table 1. Patients List according to cause of death

Index	Age	Sex	Group	Dx
13125	62	M	Ⅱ	관상동맥경화에 의한 허혈성 심장질환
13134	56	M	Ⅰ	고도의 두부손상
13135	60	M	Ⅲ	고도의 관상동맥경화에 의한 허혈성 심장질환
13140	66	F	Ⅱ	엔도설판 중독
13141	54	M	Ⅱ	관상동맥경화에 의한 허혈성 심장질환
13142	32	M	Ⅱ	간질발작에 의한 사망을 먼저 고려
13143	84	F	Ⅰ	폐렴
13144	51	F	Ⅲ	고도의 관상동맥경화에 의한 허혈성 심장질환
13146	29	M	Ⅱ	중상동맥 경화증에 의한 허혈성 심장질환
13147	39	M	Ⅱ	뇌간부 손상
141	38	M	Ⅰ	급성췌장염
142	55	M	Ⅲ	뇌간압박
143	49	M	Ⅱ	약물중독
146	50	M	Ⅰ	식도정맥류 파열
149	63	M	Ⅲ	관상동맥경화에 의한 허혈성 심장질환
1410	48	F	Ⅱ	좌측경부 자절창에 의한 허혈성 심장질환
1414	30	M	Ⅱ	비외상성지주막하출혈
1422	48	F	Ⅰ	고도의 흉부손상
1423	28	M	Ⅰ	고도의 두부손상
1430	42	M	Ⅰ	경부압박질식사 (액사)
1433	50	M	Ⅰ	일산화탄소 중독
1436	57	M	Ⅰ	경부압박질식사
1451	16	F	Ⅰ	엔도설판 중독
1465	72	M	Ⅱ-Ⅲ	고도의 관상동맥경화에 의한 허혈성 심장질환
1467	59	M	Ⅱ	관상동맥경화에 의한 허혈성 심장질환
1477	57	M	Ⅱ-Ⅲ	고도의 관상동맥경화에 의한 허혈성 심장질환
14104	54	M	Ⅱ	죽상관상동맥경화에 의한 허혈성 심장질환
15119	35	M	Ⅱ-Ⅲ	관상동맥경화에 의한 허혈성 심장질환(심근경색)
15165	53	M	Ⅱ-Ⅲ	죽상관상동맥경화에 의한 허혈성 심장질환

Target gene analysis
According to cause of death
: Coronary a. disease (CAD) vs. Non-CAD



CLDN11 expression in human vascular smooth muscle

- Tightly regulate the vascular smooth muscle physiology
- CLDN11 might play a certain role for atherosclerosis initiation and propagation to regulate the vSMCs plasticity
- Possible for new biological marker for cardiovascular events in clinical and forensic diagnosis

감사합니다.

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  - Prof. 김인준
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경청해 주셔서 감사합니다.