Claudin-low breast cancers: clinical, pathological, molecular and prognostic characterization

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Sweave report

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1 Preparation of public data

1.1 Loading description file sets with their location:

```
> library(xtable)
> library(affy)
> library(e1071)
> Path <- "G:/D_Old/DATA/CLDN/20140404_Papier_RS/20140807_retourRev/docs_Prep_SweaveR/Prep_Obj_Sweav
> Set <- read.delim(paste(Path, "Description_32sets.txt", sep="/"))
> print(xtable(Set[,c(3,5,7)]), size="footnotesize",include.rownames = FALSE)
```

File_Name	DataSet_ID	Platform
2006.Ivshina06.Upp.Sing.Stock.448BC.GSE4922_1456.RMA.RData	GSE4922_1456	hgu133ab
2006.Sotiriou.189BC.GSE2990.RMA.RData	GSE2990	hgu133a
2008.Schmidt.200BC.GSE11121.RMA.RData	GSE11121	hgu133a
2007.Desmedt.198BC.GSE7390.RMA.RData	GSE7390	hgu133a
2002.van.t.Veer.117BC.Proc.RData	vVeer	vVeerchip
2002.van.de.Vijver.295BC.Proc.RData	vVijver	vVijverchip
2005.Wang.286BC.GSE2034.RMA.RData	GSE2034	hgu133a
2006.Hess.133BC.MDA133.RMA.RData	MDA133	hgu133a
IPC372_RMA_S4.RData	IPC_BCSet	hgu133plus2
2007.Bonnefoi.161BC.GSE6861.RMA.RData	GSE6861	hgu133x3p
2011.Hatzis.GSE25066.508BC.RMA.RData	GSE25066	hgu133a
2011.Guedj.EMTAB365.537BC.RMA.RData	ETABM365	hgu133plus2
2011.Desmedt.GSE16446.120BC.RMA.RData	GSE16446	hgu133plus2
2005.ExpO.GSE2109.348BC.RMA.RData	GSE2109	hgu133plus2
2005.Farmer.GSE1561.49BC.RMA.RData	GSE1561	hgu133a
2005.Minn.GSE2603.99BC.RMA.RData	GSE2603	hgu133a
2007.Miller.GSE5462.58x2BC.RMA.RData	GSE5462	hgu133a
2007.Seitz.GSE6596.24BCs2NL.RMA.RData	GSE6596	hgu133a
2008.Hoeflich.GSE12763.30BC.RMA.RData	GSE12763	hgu133plus2
2008.Marty.GSE13787.23BC.RMA.RData	GSE13787	hgu133plus2
2008.Merritt.ETABM158.130BC.RMA.RData	ETABM158	u133aaofav2
2008.Yu.GSE5364.183BC13NL_MAS5.RData	GSE5364	hgu133a
2009.Bos.GSE12276.204BC.RMA.RData	GSE12276	hgu133plus2
2009.Zhang.GSE12093.136BC.RMA.RData	GSE12093	hgu133a
2010.Barry.GSE23593.50BC.18x2ou3.RMA.RData	GSE23593	hgu133plus2
2010.Korde.GSE18728.30BC.61echts.RMA.RData	GSE18728	hgu133plus2
2010.Prat.GSE18229.eSet.337BC.RMA.RData	GSE18229	GPLPrat
2010.Silver.GSE18864.84BC9repl.RMA.RData	GSE18864	hgu133plus2
2011.Chen.GSE10780.42BC143pNl.RMA.RData	GSE10780	hgu133plus2
2012.Popovoci.GSE20194.278BC.RMA.RData	GSE20194	hgu133a
2010.Iwamoto.PoolGSE22093_23988.RMA.RData	GSE22093_GSE23988	hgu133a
2010.Tabchy.GSE20271.RMA.RData	GSE20271	hgu133a

Public sets[1]

[1]Each of .RData objects listed were previously constructed from expression data and phenodata available. Phenodata were cleaned and homogenized across data sets. For Agilent-based data sets, we applied quantile normalization (*limma* package) to processed data. For Affymetrix-based data sets, we used Robust Multichip Average (RMA, *affy* package) on the raw .CEL files. Updated genechips annotation were integrated in their respective .RData object.

1.2 Merging phenodata from .RData objects

```
> PublicSet <- list(HC=c()) ; require(affy)
> for (i in seq_along(Set$Nom_ObjHC)){
+   load(paste(Path, "RData_ObjSets", Set$File_Name[i], sep="/"))
+   PublicSet$HC <- rbind(PublicSet$HC, pData(Eset_Obj)) ; rm(Eset_Obj)
+ }
> print(xtable(data.frame(table(PublicSet$HC$SetName)),
+              caption="Merged phenodata effectif"),
+       size="footnotesize",
+       include.rownames = FALSE)
```

Var1	Freq
2006.Ivshina.448BC.GSE4922.1456	448
2006.Sotiriou.189BC.GSE2990	189
2008.Schmidt.200BC.GSE11121	200
2007.Desmedt.198BC.GSE7390	198
2002.van.t.Veer.117BC	117
2002.van.de.Vijver.295BC	295
2005.Wang.286BC.GSE2034	286
2006.Hess.133BC.MDA133	133
IPC372_RMA_S4.RData	372
2007.Bonnefoi.161BC.GSE6861	161
2011.Hatzis.GSE25066.508BC	508
2011.Guedj.EMTAB365.537BC	537
2011.Desmedt.GSE16446.120BC	120
2005.ExpO.GSE2109.348BC	348
2005.Farmer.GSE1561.49BC	49
2005.Minn.GSE2603.99BC	99
2007.Miller.GSE5462.58x2BC	116
2007.Seitz.GSE6596.24BCs2NL	26
2008.Hoeflich.GSE12763.30BC	30
2008.Marty.GSE13787.23BC	23
2008.Merritt.ETABM158.130BC	130
2008.Yu.GSE5364.183BC13NL	196
2009.Bos.GSE12276.204BC	204
2009.Zhang.GSE12093.136BC	136
2010.Barry.GSE23593.50BC.18x23	50
2010.Korde.GSE18728.30BC.61e	61
2010.Prat.GSE18229.337BC	337
2010.Silver.GSE18864.84BC9repl	84
2011.Chen.GSE10780.42BC143pNl	185
2012.Popovoci.GSE20194.278BC	278
2010.Iwamoto.GSE22093.23988.164	164
2010.Tabchy.GSE20271.178BC	178

Merged phenodata effectif

```
> nrow(PublicSet$HC)
```

[1] 6258

1.3 Selection of primary breast cancer samples without duplicate mesurement

```
> sel_Primaire <- which(PublicSet$HC$Type %in% "PrimaryBC"
+                       & PublicSet$HC$Duplicate %in% "unique")
> length(sel_Primaire)
```

```
[1] 5447
```

2 Export markers & classification

2.1 Export markers (ESR1, PGR, ERBB2) & GMM groups:

Define genes by their Entrez Gene ID for matching

```
> ref_EntrezGeneID <- list(ESR1="2099", PGR="5241", ERBB2="2064")
```

Probes selection based on signal levels and variance

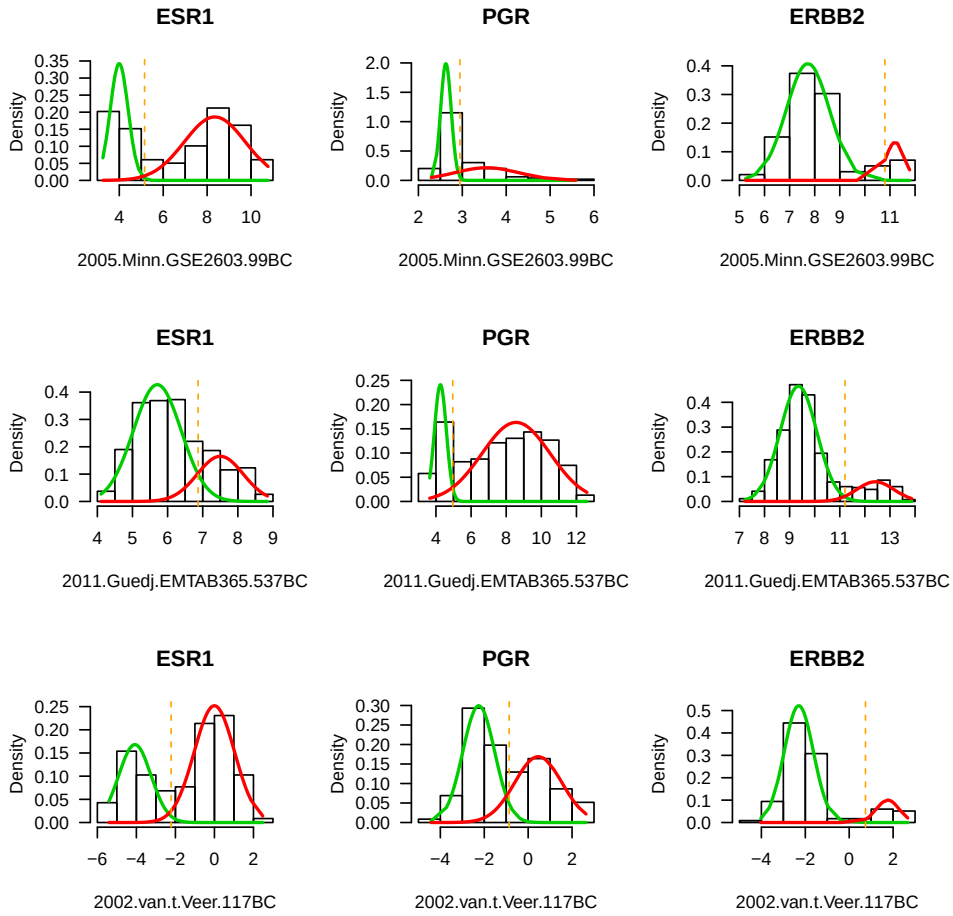
```
> source("G:\\Ori Tools\\Prog\\Rwork\\Script\\20120828_ExportGene_S4Obj.r")
>   # batch function
> VAR_GeneCtrl <- Batch_ExportGene_PF(ref_EntrezGeneID, SET=Set)
```

Gaussian Mixture Models (GMM) segmentation function based on the mixtools R package

```
> source("G:/Ori Tools/Prog/Rwork/Script/20130118_GMMnK_EMsegmentation.r")
> GMM_Sets <- list()
> require(limma)
> for (i in seq_along(VAR_GeneCtrl)){
+   cat(paste(names(VAR_GeneCtrl)[i], ":"))
+   GMM_Sets[[i]] <- Seg_EM_PF(VAR_GeneCtrl[[i]]$Expres, Nom=names(VAR_GeneCtrl)[i])
+   cat("done.\n\n")
+ }
```

Plot GMM from 3 random sets:

```
> require(mixtools)
> par(mfrow=c(3,3))
>  for (i in sample(seq(32),3)){
+   for(j in seq(3)){
+     plot(GMM_Sets[[i]][[j]]$mixmdl, which=2, las=1,
+          main2=names(GMM_Sets[[i]])[j],
+          col2=c(3,2), xlab2=names(GMM_Sets)[i])
+     abline(v=GMM_Sets[[i]][[j]]$Cut_off, col="orange", lty=2)
+   }
+ }
```



GMM segmentation & merge *ESR1*, *PGR* & *ERBB2* genes

```
> VAR_Gene <- c()
> for (i in seq_along(GMM_Sets)){
+      VAR_Gene <- rbind(VAR_Gene, cbind(
+          ESR1=ifelse(VAR_GeneCtrl[[i]]$Expres$ESR1 >
+                        GMM_Sets[[i]]$ESR1$Cut_off, 1,
+                      ifelse(VAR_GeneCtrl[[i]]$Expres$ESR1 <=
+                               GMM_Sets[[i]]$ESR1$Cut_off, 0, NA )),
+          PGR=ifelse(VAR_GeneCtrl[[i]]$Expres$PGR >
+                       GMM_Sets[[i]]$PGR$Cut_off, 1,
+                     ifelse(VAR_GeneCtrl[[i]]$Expres$PGR <=
+                               GMM_Sets[[i]]$PGR$Cut_off, 0, NA )),
+          ERBB2=ifelse(VAR_GeneCtrl[[i]]$Expres$ERBB2 >
+                         GMM_Sets[[i]]$ERBB2$Cut_off, 1,
+                       ifelse(VAR_GeneCtrl[[i]]$Expres$ERBB2 <=
+                                GMM_Sets[[i]]$ERBB2$Cut_off, 0, NA )) ))
+ }
> VAR_Gene <- data.frame(VAR_Gene)
```

2.2 GES Classifications & metagenes, 32 data sets

```
> RES_List <- list()
> for ( i in 1:nrow(Set)){
+   load(paste(Path, "RData_ObjSets", Set$File_Name[i], sep="/"))
+   #### import chip
+   load(paste(Path, "/RData_ObjSets/chip/", annotation(Eset_Obj), ".RData", sep=""))
+   CHIP <- CHIP[match(featureNames(Eset_Obj), CHIP$PID),]  # ctrl
+   #### data matrix
+   DATA <- exprs(Eset_Obj)
+   #### select samples set
+   sel_sampleloop <- which(PublicSet$HC$SetName %in% Set$Nom_ObjHC[i])
+   ################################
+   ##### Classification
+   ##### PAM50 & ROR_P :
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20100929_Classif.SSP_PAM50.r")
+   PAM50_Tmp <- PAM50.PF(DATA, CHIP$GeneID, Set$Nom_ObjHC[i])
+   RES_PAM50_Tmp <- cbind(PAM50_Tmp[,6:12])
+   ##### CLDN-low (Prat et al.) :
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20101123_Classif.Claudin_Low_PratBCL.r")
+   CLDN_Tmp <- Claudin_Low.Classifier(DATA, CHIP$GeneID, Set$Nom_ObjHC[i])
+   RES_CLDN_Tmp <- CLDN_Tmp$Grp
+   ##### Differentiation Score (Prat et al. /w Lum Prog., MaSC & Mat. Lum Lim et al.) :
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20101203_Classif.Diff_Prat.r")
+   DiffPrat_Tmp <- Diff_Prat_Classifier(DATA, CHIP, Set$Nom_ObjHC[i])
+   RES_DiffPrat_Tmp <- DiffPrat_Tmp
+   ##### Amsterdam 70g (vant Veer et al.)
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20100922_Classif.70g_vVeer.r")
+   vV70g_Tmp <- vV70g.Classifier(DATA, CHIP$GeneID, Set$Nom_ObjHC[i])
+   RES_vV70g_Tmp <- vV70g_Tmp$Classif
+   ##### GGI (Loi et al.)
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20100720_GGI.r")
+   GGI_Tmp <- GGI.Classifier(DATA, CHIP$GeneID,
+                             Grd=PublicSet$HC$Grade[sel_sampleloop],
+                             Set$Nom_ObjHC[i])
+   RES_GGI_Tmp <- GGI_Tmp$Classif[,1:2]
+   ##### Recurent Score (Paik et al.)
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20100922_Classif.RS.Paik.R")
+   RSPaik_Tmp <- RS.Paik.Classifier(DATA, CHIP$GeneID, Set$Nom_ObjHC[i])
+   RES_RSPaik_Tmp <- RSPaik_Tmp$Classif
+   ##### Immune Response (Caldas et al.)
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20121128_Classif.IR.Caldas.r")
+   IR_Tmp <- IR.Caldas_PF(DATA, CHIP, ER=VAR_Gene$ESR1[sel_sampleloop],
+                          Set$Nom_ObjHC[i])
+   RES_IR_Tmp <- data.frame(IR_Tmp)
+   ##### LCK (Rody et al.)
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20121129_Classif.LCK.Rody.r")
+   LCK_Tmp <- LCK.Rody_PF(DATA, CHIP, Set$Nom_ObjHC[i])
+   RES_LCK_Tmp <- data.frame(LCK_Tmp)
+   ##### Stroma (Bianchini et al.)
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20101007_Classif.Stromal_Bianchini.r")
+   StromaBianchini_Tmp <- Bianchini_Stroma.Classifier(DATA,
+                                    SSP = PAM50_Tmp$PAM50 , CHIP$GeneID, Set$Nom_ObjHC[i])
+   RES_StromaBianchini_Tmp <- StromaBianchini_Tmp$Classif
+   ##### Immune28g (Sabatier et al.)
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20111214_Classif.K.Imm_28g_RS.r")
+   Kimm28g_Tmp <- K.Imm_28g.Classifier(DATA, CHIP$GeneID,
+                                       SSP = PAM50_Tmp$PAM50, Set$Nom_ObjHC[i])
+   RES_Kimm28g_Tmp <- Kimm28g_Tmp$Classif[,1:2]
```

```
+   ##### Lympho metagenes (Palmer et al.)
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20130312_Palmer_MetaG_Lympho.r")
+   Palmer_Tmp <- Palmer_Lympho.PF(DATA, CHIP$GeneID, Set$Nom_ObjHC[i])
+   colnames(Palmer_Tmp) <- paste("Palmer", colnames(Palmer_Tmp), "Module", sep="_")
+   ##### DLDA30 (Hess et al.)
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20120905_Classif.DLDA_30_Hess.r")
+   DLDA30_Tmp <- DLDA30.Classifier_PF(DATA, CHIP$GeneID, Set$Nom_ObjHC[i])
+   RES_DLDA30_Tmp <- data.frame(DLDA30_Tmp$Classif)
+   ##### DCN (Farmer et al.)
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20120906_Classif.DCN.Farmer.r")
+   DCN_Tmp <- DCN.Classifier_PF(DATA, CHIP, Set$Nom_ObjHC[i], ER=VAR_Gene$ESR1[sel_sampleloop])
+   RES_DCN_Tmp <- data.frame(DCN_Tmp$Classif)
+   #### A_Score (Desmedt et al.)
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20120907_Classif.A_Score.Desmedt2k11.r")
+   A_Score_Tmp <- A_Score.Classifier_PF(DATA, CHIP, Set$Nom_ObjHC[i],
+                                        ER=VAR_Gene$ESR1[sel_sampleloop], ESR1_UNC=TRUE)
+   RES_A_Score_Tmp <- data.frame(A_Score_Tmp$Classif)
+   ##### RBloss Ertel
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20121129_Classif.RB_Ertel.r")
+   RBloss_Tmp <- RBloss.Ertel_PF(DATA, CHIP, ER=VAR_Gene$ESR1[sel_sampleloop],
+                                 SSP=PAM50_Tmp$PAM50 , Set$Nom_ObjHC[i])
+   RES_RBloss_Tmp <- data.frame(RBloss_Tmp[1:3])
+   ##### Taube EMT core
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20140606_Taube_EMT_MetaG.r")
+   RES_Taube_Tmp <- Taube_EM.PF(DATA, CHIP$GeneID, Set$Nom_ObjHC[i])
+   ##### Lum & Prolif cluster metagene, CH IPC BC
+   source("g:/Ori Tools/Prog/Rwork/Script/Classifier/20140106_MetaG_Lum_Prolif_CH353IPC.r")
+   MetaG_CH_IPC_Tmp <- MetaG_LumProlif.PF(DATA, CHIP$GeneID, Set$Nom_ObjHC[i])
+   ############################
+   ##### Pool GESs
+   RES_Glob_Tmp <- cbind( RES_PAM50_Tmp, RES_CLDN_Tmp, RES_DiffPrat_Tmp,
+                          RES_vV70g_Tmp, RES_GGI_Tmp, RES_RSPaik_Tmp,
+                          RES_IR_Tmp, RES_LCK_Tmp, RES_StromaBianchini_Tmp,
+                          RES_Kimm28g_Tmp, RES_DLDA30_Tmp, RES_DCN_Tmp,
+                          RES_A_Score_Tmp, RES_RBloss_Tmp, RES_Taube_Tmp,
+                          MetaG_CH_IPC_Tmp )
+   RES_List[[i]] <- RES_Glob_Tmp
+   rm(CHIP, DATA, Eset_Obj)
+ }
> ##### Merge Classification
> RES_Pool <- c()
> for (i in 1:length(RES_List)){
+     RES_Pool <- rbind(RES_Pool, cbind(RES_List[[i]],
+                                       Set=rep(Set$Nom_ObjHC[i], nrow(RES_List[[i]]))))
+ }
> colnames(RES_Pool) <-paste("GES", colnames(RES_Pool), sep="_")
```

Variables preparation before statistics:

```
> ###### standardization Gene Ctrl / PAM50
> VAR_GeneSTDz <- c()
> for (i in seq_along(VAR_GeneCtrl)){
+   VAR_GeneSTDz <- rbind(data.frame(
+     SSPNorm_IPC_PF(VAR_GeneCtrl[[i]], SSP=RES_List[[i]]$PAM50)$EXPRS$NORM))
+ }
> VAR_GeneSTDz <- data.frame(VAR_GeneSTDz)
> colnames(VAR_GeneSTDz) <- paste("mRNA", colnames(VAR_GeneSTDz), "RAW", sep="_")
> colnames(VAR_Gene) <- paste("mRNA", colnames(VAR_Gene), sep="_")
> ###### pool all variables
```

```
> VAR_List <- c(as.list(PublicSet$HC),
+               as.list(VAR_GeneSTDz),
+               as.list(VAR_Gene),
+               as.list(RES_Pool))
> VAR_ListSurv <- list(DFS =
+                        list(Evt=PublicSet$HC$DFS, Del=PublicSet$HC$DFSDel))
```

3 Statistics

3.1 Description PAM50/CLDN-low BC samples

```
> #### PAM50 /w CLDN-low
> VAR_List$PAM50_CL <- ifelse(VAR_List$GES_CLDNLow_Grpe == "Claudin_Low", "CLDNlow",
+                             as.character(VAR_List$GES_PAM50))
> #### TN expression
> VAR_List$TN <- rep(NA, length(VAR_List[[1]]))
> VAR_List$TN[which(VAR_List$mRNA_ESR1==0 &
+                     VAR_List$mRNA_PGR==0 &
+                     VAR_List$mRNA_ERBB2==0)] <- "yes"
> VAR_List$TN[which(VAR_List$mRNA_ESR1==1 |
+                     VAR_List$mRNA_PGR==1 |
+                     VAR_List$mRNA_ERBB2==1)] <- "no"
```

3.1.1 PAM50/CLDNlow, clinicopathological features

```
> source("g:/Ori Tools/Prog/Rwork/Script/Table.PF/Table.PF.r")
> print(xtable(
+   Table_PF(VAR_List$PAM50_CL,
+                list(Age=VAR_List$age.g,
+                Histo_type=VAR_List$Histo_OK,
+                Histo_grade=VAR_List$Grade,
+                pT=VAR_List$pT2K,
+                pN=VAR_List$pN,
+                ESR1_groups=VAR_List$mRNA_ESR1,
+                ESR1_cont = VAR_List$mRNA_ESR1_RAW,
+                PGR_groups=VAR_List$mRNA_PGR,
+                PGR_cont = VAR_List$mRNA_PGR_RAW,
+                ERBB2_groups=VAR_List$mRNA_ERBB2,
+                ERBB2_cont = VAR_List$mRNA_ERBB2_RAW,
+                TN_exp=VAR_List$TN,
+                pCR=VAR_List$response.CT.pCR.no.invasive.cancer.,
+                DFS=VAR_ListSurv$DFS$Evt),
+          Var_Cont=c(7,9,11), Subset=sel_Primaire)[,c(1:3,5,7,4,6,8,9)]
+     , caption="Description PAM50/CLDNlow BCs", table.placement="top"), size="tiny")
```

	Var	Mod	X3	CLDNlow	LumA	Basal	ERBB2	LumB	Normal
1	Age								
2		<=50	1834	238(49%)	470(43%)	423(56%)	224(43%)	328(46%)	151(53%)
3		>50	2005	247(51%)	622(57%)	331(44%)	291(57%)	380(54%)	134(47%)
4	Histo_type								
5		IDC	1181	140(78%)	263(76%)	224(88%)	201(89%)	255(89%)	98(84%)
6		ILC	72	8(4%)	34(10%)	4(2%)	4(2%)	12(4%)	10(9%)
7		MED	24	5(3%)	1(0%)	18(7%)	0(0%)	0(0%)	0(0%)
8		MIX	59	7(4%)	23(7%)	4(2%)	10(4%)	12(4%)	3(3%)
9		other	77	20(11%)	26(7%)	6(2%)	11(5%)	8(3%)	6(5%)
10	Histo_grade								
11		1	489	49(9%)	293(26%)	12(2%)	15(3%)	53(7%)	67(21%)
12		2	1579	180(35%)	605(54%)	104(14%)	170(32%)	367(47%)	153(48%)
13		3	1957	290(56%)	222(20%)	640(85%)	350(65%)	358(46%)	97(31%)
14	pT								
15		pT1	928	106(38%)	343(46%)	130(29%)	89(27%)	163(34%)	97(50%)
16		pT2-3	1542	172(62%)	399(54%)	323(71%)	239(73%)	311(66%)	98(50%)
17	pN								
18		0	1941	182(55%)	561(62%)	386(67%)	236(52%)	395(61%)	181(60%)
19		1	1279	151(45%)	344(38%)	193(33%)	220(48%)	250(39%)	121(40%)
20	ESR1_groups								
21		0	1929	433(64%)	80(5%)	859(86%)	437(58%)	24(2%)	96(21%)
22		1	3518	240(36%)	1414(95%)	144(14%)	312(42%)	1053(98%)	355(79%)
23	ESR1_cont		5447	6.46(-4.93-12.71)	10.55(-2.06-14.78)	5.46(-5.41-13.44)	7.18(-4.98-14.42)	10.76(-1.92-14.85)	9.77(-2.75-14.43)
24	PGR_groups								
25		0	2851	445(66%)	386(26%)	864(86%)	567(76%)	443(41%)	146(32%)
26		1	2594	228(34%)	1108(74%)	139(14%)	181(24%)	634(59%)	304(68%)
27	PGR_cont		5445	4.21(-2.86-11.59)	5.24(-3.45-12.96)	3.54(-6.69-11.13)	4.07(-4.89-12.18)	4.52(-3.06-13.09)	5.07(-3.22-12.38)
28	ERBB2_groups								
29		0	4738	646(96%)	1407(94%)	958(96%)	320(43%)	1011(94%)	396(88%)
30		1	709	27(4%)	87(6%)	45(4%)	429(57%)	66(6%)	55(12%)
31	ERBB2_cont		5447	6.45(-3.95-12.58)	7.5(-2.84-14.27)	6.52(-4.03-13.37)	8.84(-2.41-15.61)	7.59(-3.67-14.19)	7.83(-2.97-15.53)
32	TN_exp								
33		no	4110	321(48%)	1472(99%)	241(24%)	610(82%)	1064(99%)	402(89%)
34		yes	1336	352(52%)	22(1%)	762(76%)	138(18%)	13(1%)	49(11%)
35	pCR								
36		nPCR	992	155(68%)	302(93%)	210(67%)	97(63%)	178(82%)	50(86%)
37		pCR	302	73(32%)	21(7%)	104(33%)	56(37%)	40(18%)	8(14%)
38	DFS								
39		0	2190	223(65%)	736(75%)	396(62%)	222(52%)	395(60%)	218(73%)
40		1	1165	120(35%)	246(25%)	245(38%)	205(48%)	268(40%)	81(27%)

Description PAM50/CLDNlow BCs

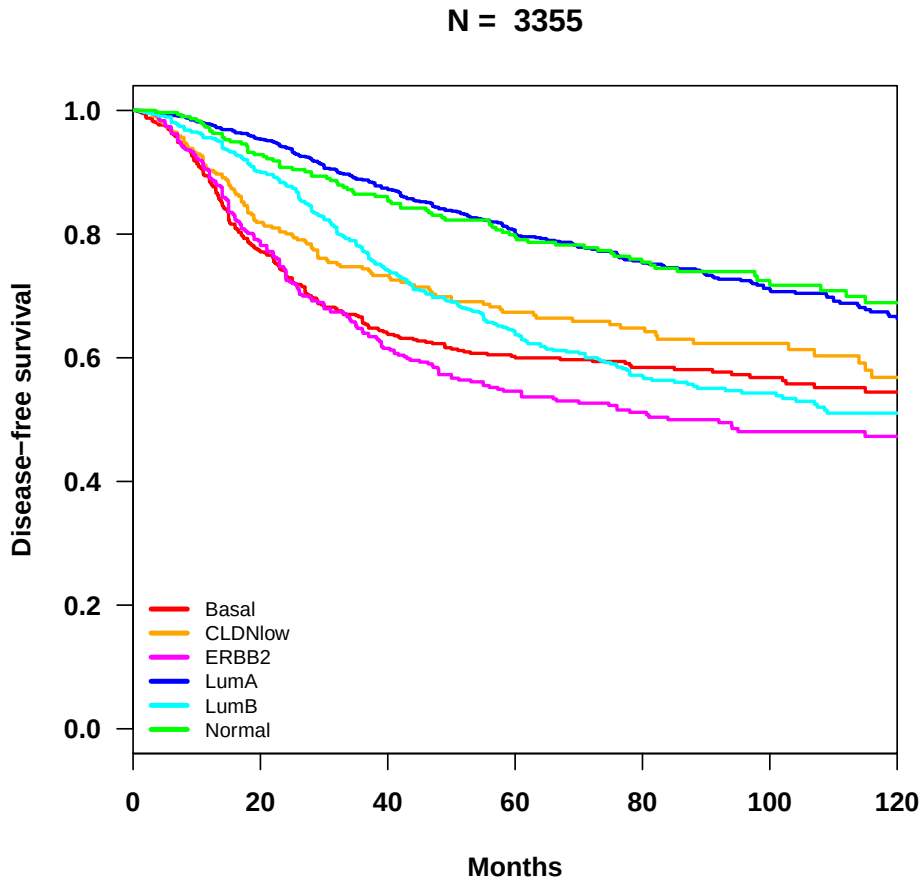
3.1.2 PAM50/CLDNlow, survival description (DFS)

```
> source("g:/Ori Tools/Prog/Rwork/Script/survie.PF/Survival.PF/R/Surv.PF-28072014.r")
> source("g:/Ori Tools/Prog/Rwork/Script/survie.PF/Survival.PF/R/PlotSurv.PF.R")
> #### DFS all
> KM_DFS <- Surv.PF(NULL, VAR_ListSurv$DFS$Evt, VAR_ListSurv$DFS$Del, "Disease-free",
+                       Subset=sel_Primaire)

 Disease-free survival

Call: survfit(formula = Surv(EvtDel, Evt) ~ rep(1, length(Evt)), subset = Subset)

   2092 observations deleted due to missingness
records   n.max n.start  events  median 0.95LCL 0.95UCL
   3355    3355    3355    1165     171     152      NA

N=3355,
5-Year  survival = 68%  (95CI = [0.67-0.7])
50% survival time (month) : 171.4
Follow-up median (months) : 79

> #### DFS CLDNlow
> KM_DFS_CL <- Surv.PF(NULL, VAR_ListSurv$DFS$Evt, VAR_ListSurv$DFS$Del, "Disease-free",
+                       Subset=intersect(sel_Primaire,which(VAR_List$PAM50_CL %in% "CLDNlow")))

 Disease-free survival

Call: survfit(formula = Surv(EvtDel, Evt) ~ rep(1, length(Evt)), subset = Subset)

   330 observations deleted due to missingness
records   n.max n.start  events  median 0.95LCL 0.95UCL
    343     343     343     120     141     140      NA

N=343,
5-Year  survival = 67%  (95CI = [0.62-0.73])
```

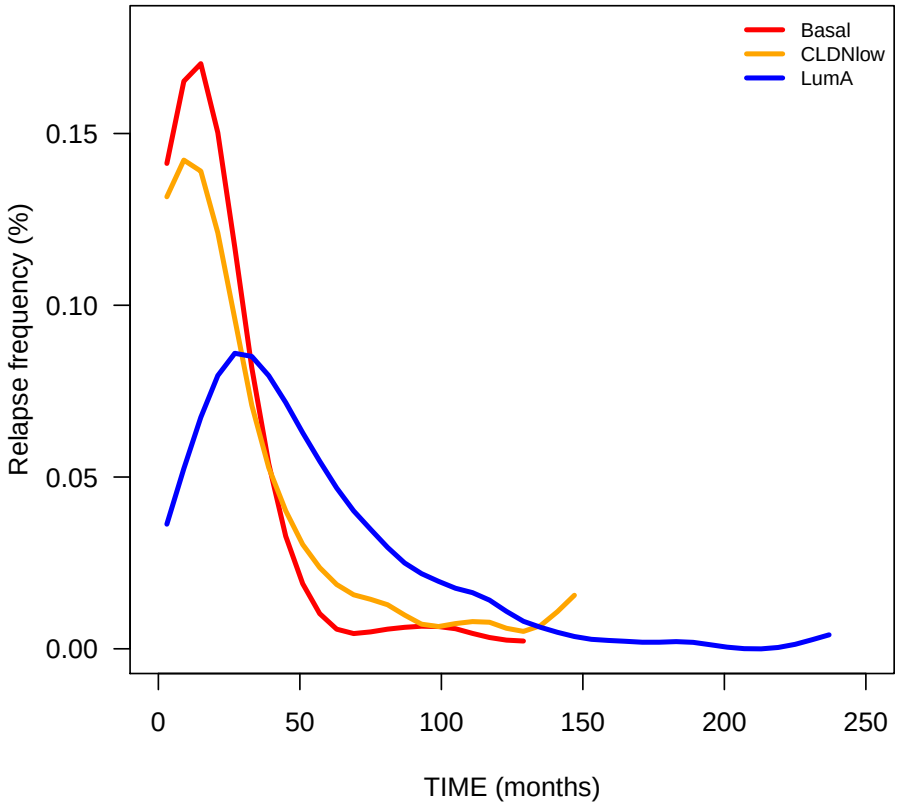
```
50% survival time (month) : 141
Follow-up median (months) : 72.24
```

```
> #### DFS PAM50/CLDNlow
> KM_DFS_PAM50CL <- Surv.PF(VAR_List$PAM50_CL, VAR_ListSurv$DFS$Evt, VAR_ListSurv$DFS$Del,
+                           "Disease-free", Subset=sel_Primaire)

 Disease-free survival

Call:
survdiff(formula = Surv(EvtDel, Evt) ~ Grpe, subset = Subset)

n=3355, 2092 observations deleted due to missingness.

               N Observed Expected (O-E)^2/E (O-E)^2/V
Grpe=Basal   641      245      186    18.487    22.084
Grpe=CLDNlow 343      120      111     0.777     0.861
Grpe=ERBB2   427      205      133    38.432    43.504
Grpe=LumA    982      246      381    48.072    71.685
Grpe=LumB    663      268      231     5.999     7.500
Grpe=Normal  299       81      122    13.986    15.679

 Chisq= 126  on 5 degrees of freedom, p= 0

Grp 1 : Basal N=641, 5-Year survival = 60%, 95%CI = [0.56-0.64]
Grp 2 : CLDNlow N=343, 5-Year survival = 67%, 95%CI = [0.62-0.73]
Grp 3 : ERBB2 N=427, 5-Year survival = 55%, 95%CI = [0.5-0.6]
Grp 4 : LumA N=982, 5-Year survival = 80%, 95%CI = [0.77-0.83]
Grp 5 : LumB N=663, 5-Year survival = 64%, 95%CI = [0.6-0.68]
Grp 6 : Normal N=299, 5-Year survival = 79%, 95%CI = [0.75-0.84]
```

```
> #### Kaplan-Meier plot, DFS PAM50/CL
> col_PAM50CL <- c("red","orange","magenta","blue","cyan","green")
> PlotSurv.PF(KM_DFS_PAM50CL, limit=c(0,120), mark=FALSE, style=1,
+             color = col_PAM50CL, texte = FALSE, pVal = FALSE)
> legend("bottomleft", sort(unique(VAR_List$PAM50_CL)), col=col_PAM50CL, lwd=3, box.col=0, cex=0.75)
```




```
> #### Freq. relapse f(t), Claudin-low, Basal & LuminalA BC
> source("g:/Ori Tools/Prog/Rwork/Script/survie.PF/Survival.PF/R/FreqRelapse.PF.r")
> Freq_3KPAM50CLDN <-FreqSurv_PF(VAR_List$PAM50_CL,
+                                VAR_ListSurv$DFS$Evt,
+                                VAR_ListSurv$DFS$Del,
+                                Subset=intersect(sel_Primaire,
+                                                 which(VAR_List$PAM50_CL %in%
+                                                         c("Basal", "CLDNlow", "LumA"))))
> #### Plot Freq. relapse f(t), 3 moleclar subtypes
> Plot_FreqRelapse.PF(Freq_3KPAM50CLDN,
+                     col= col_PAM50CL[c(1,2,4)], xlim=c(0,250),
+                     ylim=c(0,0.18), lwd=3)
> legend("topright", sort(unique(VAR_List$PAM50_CL))[c(1,2,4)],
+        col=col_PAM50CL[c(1,2,4)],
+        lwd=3, box.col=0, cex=0.75)
```



3.2 Pronostic associations

Variables evaluation, univariate DFS

```
> ###### coxph regression for batch run (use of survival R package)
> source("g:/Ori Tools/Prog/Rwork/Script/20121008_UV.batch.r")
> #### All primary BC
> UV_DFS_AllBC <- Batch.UV.PF(List.Grpe = list(Age=VAR_List$age.g,
+                                              Histo_type=VAR_List$Histo_OK,
+                                              Histo_grade=VAR_List$Grade2K,
+                                              pT=VAR_List$pT2K,
+                                              pN=VAR_List$pN,
+                                              ESR1_groups=VAR_List$mRNA_ESR1,
+                                              PGR_groups=VAR_List$mRNA_PGR,
+                                              ERBB2_groups=VAR_List$mRNA_ERBB2,
+                                              TN_exp=VAR_List$TN,
+                                              Amst70g=VAR_List$GES_Prog70g_Grp,
+                                              GGI=VAR_List$GES_GGI_Grp,
+                                              RS=VAR_List$GES_RSPaik_Grp,
+                                              ROR_P=VAR_List$GES_PAM50_ROR_P_Grp,
+                                              IR=VAR_List$GES_IR_Caldas_IR_GrpERdep,
+                                              LCK=VAR_List$GES_LCK_Rody_LCK_Grp,
+                                              ImmuneKin28g = VAR_List$GES_K.Imm28g_Grp,
+                                              B_cellK = VAR_List$GES_StromaBianchini_metagene_Terc),
+                         Evt = VAR_ListSurv$DFS$Evt, EvtDel = VAR_ListSurv$DFS$Del,
+                         Subset = sel_Primaire, PRINT = FALSE)
> # Print global UV table
```

```
> print(xtable(UV_DFS_AllBC$Res.Batch,
+              caption="univariate DFS, all BC", table.placement="top"),
+       size="footnotesize")
```

	VAR	MODTEST	n	HR.95CI.	p
1	Age	>50	2366	1.01 [0.87-1.16]	0.922
2	Histo_type	ILC	624	1.09 [0.71-1.67]	0.269
3		MED		0.53 [0.20-1.42]	
4		MIX		0.44 [0.18-1.06]	
5		other		1.04 [0.57-1.92]	
6	Histo_grade	2-3	2552	2.36 [1.86-3.01]	2.84e-12
7	pT	pT2-3	1744	1.52 [1.29-1.8]	6.86e-07
8	pN	1	2366	1.37 [1.18-1.58]	2.28e-05
9	ESR1_groups	1	3355	0.56 [0.5-0.63]	0
10	PGR_groups	1	3353	0.7 [0.63-0.79]	2.25e-09
11	ERBB2_groups	1	3355	1.4 [1.18-1.65]	7.32e-05
12	TN_exp	yes	3354	1.7 [1.49-1.94]	1.11e-15
13	Amst70g	Poor	3355	1.83 [1.57-2.12]	3e-15
14	GGI	High	2655	2.1 [1.82-2.43]	0
15	RS	High	3355	2.15 [1.87-2.47]	0
16		Intermediate		1.63 [1.38-1.93]	
17	ROR_P	High	3355	2.11 [1.85-2.41]	0
18		Median		1.75 [1.45-2.10]	
19	IR	Poor	3354	1.19 [1.06-1.34]	0.00292
20	LCK	High	3355	0.91 [0.79-1.04]	0.151
21	ImmuneKin28g	Poor	3355	1.04 [0.88-1.24]	0.615
22	B_cellK	2_Int	3353	0.87 [0.76-1.00]	3.94e-05
23		3_High		0.72 [0.63-0.83]	

univariate DFS, all BC

```
> #### PAM50/CL BC
> Subtype <- sort(unique(VAR_List$PAM50_CL))
> UV_DFS_PAM50CL <- list()
> for (i in seq_along(Subtype)){
+   UV_DFS_PAM50CL[[i]] <- Batch.UV.PF(List.Grpe = list(Age=VAR_List$age.g,
+                                          Histo_type=VAR_List$Histo_OK,
+                                          Histo_grade=VAR_List$Grade2K,
+                                          pT=VAR_List$pT2K,
+                                          pN=VAR_List$pN,
+                                          ESR1_groups=VAR_List$mRNA_ESR1,
+                                          PGR_groups=VAR_List$mRNA_PGR,
+                                          ERBB2_groups=VAR_List$mRNA_ERBB2,
+                                          TN_exp=VAR_List$TN,
+                                          Amst70g=VAR_List$GES_Prog70g_Grp,
+                                          GGI=VAR_List$GES_GGI_Grp,
+                                          RS=VAR_List$GES_RSPaik_Grp,
+                                          ROR_P=VAR_List$GES_PAM50_ROR_P_Grp,
+                                          IR=VAR_List$GES_IR_Caldas_IR_GrpERdep,
+                                          LCK=VAR_List$GES_LCK_Rody_LCK_Grp,
+                                          ImmuneKin28g = VAR_List$GES_K.Imm28g_Grp,
+                                          B_cellK = VAR_List$GES_StromaBianchini_metagene_Terc),
+                       Evt = VAR_ListSurv$DFS$Evt, EvtDel = VAR_ListSurv$DFS$Del,
+                       Subset = intersect(sel_Primaire, which(VAR_List$PAM50_CL %in% Subtype[i])),
+                       PRINT = FALSE)
+   names(UV_DFS_PAM50CL)[i] <- Subtype[i]
+ }
> # Print CLDN UV table
> print(xtable(UV_DFS_PAM50CL$CLDNlow$Res.Batch,
+              caption="univariate DFS, CLDN-low", table.placement="top"),
+       size="footnotesize")
```

	VAR	MODTEST	n	HR.95CI.	p
1	Age	>50	237	0.9 [0.57-1.4]	0.636
2	Histo_type	ILC	59	0.00 [0.00- Inf]	0.837
3		MED		0.45 [0.06-3.35]	
4		MIX		0.00 [0.00- Inf]	
5		other		1.90 [0.44-8.10]	
6	Histo_grade	2-3	270	3.63 [1.32-9.92]	0.0122
7	pT	pT2-3	155	2.33 [1.27-4.26]	0.00601
8	pN	1	194	2.23 [1.34-3.72]	0.00201
9	ESR1_groups	1	343	0.38 [0.25-0.58]	5.02e-06
10	PGR_groups	1	343	0.56 [0.38-0.83]	0.00386
11	ERBB2_groups	1	343	1.98 [0.92-4.26]	0.079
12	TN_exp	yes	343	2.19 [1.51-3.18]	3.82e-05
13	Amst70g	Poor	343	1.22 [0.74-2.02]	0.435
14	GGI	High	283	1.42 [0.92-2.2]	0.113
15	RS	High	343	3.03 [1.68-5.46]	0.00109
16		Intermediate		2.73 [1.40-5.31]	
17	ROR_P	High	343	1.85 [1.24-2.75]	0.00874
18		Median		1.28 [0.69-2.36]	
19	IR	Poor	343	1.17 [0.82-1.68]	0.387
20	LCK	High	343	0.89 [0.62-1.28]	0.541
21	ImmuneKin28g	Poor	343	1.14 [0.78-1.65]	0.507
22	B_cellK	2_Int	343	0.70 [0.44-1.11]	0.0692
23		3_High		0.61 [0.40-0.93]	

univariate DFS, CLDN-low

3.3 Pathological response associations

Evaluation pCR and clinicopathological&molecular features

```
> #### All primary BC
> TabpCR_AllBC <- Table_PF(VAR_List$response.CT.pCR.no.invasive.cancer.,
+                          Var = list(Age=VAR_List$age.g, pT=VAR_List$pT2K,
+                                     Histo_grade=VAR_List$Grade2K, Histo_type=VAR_List$Histo_OK,
+                                     ESR1_groups=VAR_List$mRNA_ESR1, PGR_groups=VAR_List$mRNA_PGR,
+                                     ERBB2_groups=VAR_List$mRNA_ERBB2, TN_exp=VAR_List$TN,
+                                     DLDA30=VAR_List$GES_DLDA30Hess_GrpTxt,
+                                     Stromal=VAR_List$GES_DCNFarmer_grp,
+                                     A_Score=VAR_List$GES_A_ScoreDesmedt_grp,
+                                     RBloss=VAR_List$GES_RBloss_Ertel_RB_Grp2K),
+                          Subset = sel_Primaire, Print = FALSE)
> # Print global pCR table
> print(xtable(TabpCR_AllBC, caption="pCR, all BC", table.placement="!h"),
+       size="scriptsize")
```

	Var	Mod	X3	nPCR	pCR	p..NonParam	Statistic
1	Age					0.0868	0.8
2		<=50	697	521(53%)	176(58%)		[0.61-1.04]
3		>50	595	469(47%)	126(42%)		
4	pT					0.859	1.1
5		pT1	44	32(14%)	12(13%)		[0.53-2.53]
6		pT2-3	279	196(86%)	83(87%)		
7	Histo_grade					0.000168	8.1
8		1	53	51(6%)	2(1%)		[2.11-69.38]
9		2-3	1126	854(94%)	272(99%)		
10	Histo_type					0.752	
11		IDC	468	337(82%)	131(85%)		
12		ILC	15	10(2%)	5(3%)		
13		MIX	37	29(7%)	8(5%)		
14		other	47	36(9%)	11(7%)		
15	ESR1_groups					7.21e-18	0.3
16		0	697	470(47%)	227(75%)		[0.22-0.4]
17		1	597	522(53%)	75(25%)		
18	PGR_groups					4.24e-08	0.38
19		0	979	716(72%)	263(87%)		[0.26-0.56]
20		1	315	276(28%)	39(13%)		
21	ERBB2_groups					0.00059	1.9
22		0	1125	881(89%)	244(81%)		[1.31-2.7]
23		1	169	111(11%)	58(19%)		
24	TN_exp					8.16e-10	2.3
25		no	777	642(65%)	135(45%)		[1.73-2.97]
26		yes	517	350(35%)	167(55%)		
27	DLDA30					7.53e-23	0.26
28		pCR_like	439	264(27%)	175(58%)		[0.2-0.35]
29		RD_like	855	728(73%)	127(42%)		
30	Stromal					0.115	0.81
31		pCR_Like	642	480(48%)	162(54%)		[0.62-1.06]
32		RD_Like	652	512(52%)	140(46%)		
33	A_Score					0.000148	2
34		nonpCR_Like	258	196(46%)	62(30%)		[1.36-2.85]
35		pCR_Like	378	233(54%)	145(70%)		
36	RBloss					0.00652	1.7
37		Low	1150	895(90%)	255(84%)		[1.14-2.51]
38		High	144	97(10%)	47(16%)		

pCR, all BC

```
> #### PAM50/CL BC
> TabpCR_PAM50CL <- list()
> for (i in seq_along(Subtype)){
+   TabpCR_PAM50CL[[i]] <- Table_PF(VAR_List$response.CT.pCR.no.invasive.cancer.,
+                          Var = list(Age=VAR_List$age.g, pT=VAR_List$pT2K,
+                                     Histo_grade=VAR_List$Grade2K, Histo_type=VAR_List$Histo_OK,
+                                     ESR1_groups=VAR_List$mRNA_ESR1, PGR_groups=VAR_List$mRNA_PGR,
+                                     ERBB2_groups=VAR_List$mRNA_ERBB2, TN_exp=VAR_List$TN,
+                                     DLDA30=VAR_List$GES_DLDA30Hess_GrpTxt,
+                                     Stromal=VAR_List$GES_DCNFarmer_grp,
```

```
+                                     A_Score=VAR_List$GES_A_ScoreDesmedt_grp,
+                                     RBloss=VAR_List$GES_RBloss_Ertel_RB_Grp2K),
+                          Subset = intersect(sel_Primaire, which(VAR_List$PAM50_CL %in% Subtype[i])),
+                          Print = FALSE)
+   names(TabpCR_PAM50CL)[i] <- Subtype[i]
+ }
> # Print CLDN UV table
> print(xtable(TabpCR_PAM50CL$CLDNlow, caption="pCR, CLDN-low", table.placement="!h"),
+       size="scriptsize")
```

	Var	Mod	X3	nPCR	pCR	p..NonParam	Statistic
1	Age					0.392	0.76
2		<=50	123	80(52%)	43(59%)		[0.41-1.37]
3		>50	104	74(48%)	30(41%)		
4	pT					1	0.93
5		pT1	5	3(8%)	2(9%)		[0.1-11.96]
6		pT2-3	55	34(92%)	21(91%)		
7	Histo_grade					0.0569	Inf
8		1	8	8(6%)	0(0%)		[0.82-Inf]
9		2-3	204	136(94%)	68(100%)		
10	Histo_type					0.125	
11		IDC	77	45(67%)	32(84%)		
12		ILC	5	3(4%)	2(5%)		
13		MIX	6	6(9%)	0(0%)		
14		other	17	13(19%)	4(11%)		
15	ESR1_groups					0.0735	0.47
16		0	183	119(77%)	64(88%)		[0.19-1.07]
17		1	45	36(23%)	9(12%)		
18	PGR_groups					0.42	0.64
19		0	195	130(84%)	65(89%)		[0.24-1.57]
20		1	33	25(16%)	8(11%)		
21	ERBB2_groups					0.472	1.7
22		0	219	150(97%)	69(95%)		[0.33-8.34]
23		1	9	5(3%)	4(5%)		
24	TN_exp					0.285	1.4
25		no	71	52(34%)	19(26%)		[0.74-2.83]
26		yes	157	103(66%)	54(74%)		
27	DLDA30					0.0161	0.49
28		pCR_like	120	73(47%)	47(64%)		[0.27-0.91]
29		RD_like	108	82(53%)	26(36%)		
30	Stromal					0.623	1.2
31		pCR_Like	55	39(25%)	16(22%)		[0.59-2.5]
32		RD_Like	173	116(75%)	57(78%)		
33	A_Score					0.00315	3.9
34		nonpCR_Like	37	31(32%)	6(11%)		[1.46-12.32]
35		pCR_Like	118	67(68%)	51(89%)		
36	RBloss					1	0.96
37		Low	212	144(93%)	68(93%)		[0.25-3.15]
38		High	16	11(7%)	5(7%)		

pCR, CLDN-low

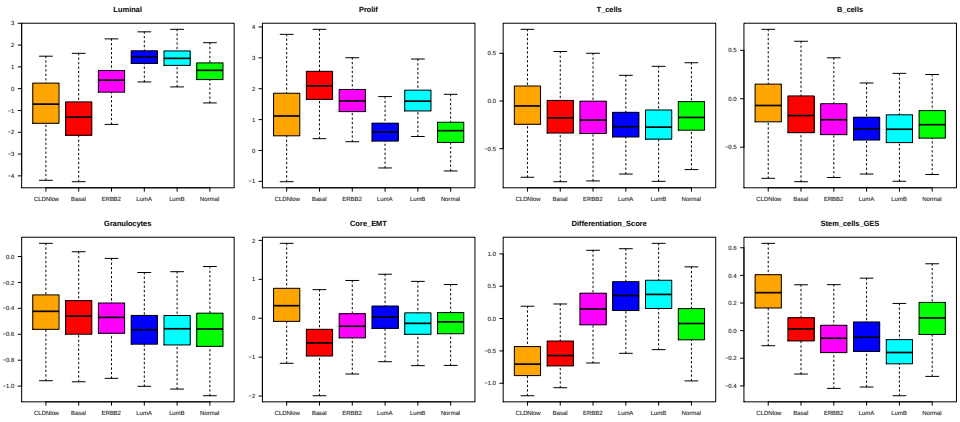
3.4 Correlation PAM50/CLDN-low and metagenes

List of metagenes

```
> MetaG_List <- list(Luminal=VAR_List$GES_MetaG_Lum_CH353IPC,
+       Prolif=VAR_List$GES_MetaG_Prolif_CH353IPC,
+       T_cells=VAR_List$GES_Palmer_T_Module,
+       B_cells=VAR_List$GES_Palmer_B_Module,
+       Granulocytes=VAR_List$GES_Palmer_GRANS_Module,
+       Core_EMT=VAR_List$GES_Taube_EMTMetaG_Score,
+       Differentiation_Score=VAR_List$GES_DiffPrat_Score,
+       Stem_cells_GES=VAR_List$GES_Creighton_CD44pCD24m_Score)
```

Plot Metagene ~ PAM50/CLDNlow

```
> VAR_List$PAM50_CL[which(VAR_List$PAM50_CL %in% "CLDNlow")] <- " CLDNlow"
> par(mfrow=c(2,4), mar=c(3,3,4,1))
> for (i in seq_along(MetaG_List)){
+   boxplot(MetaG_List[[i]]~VAR_List$PAM50_CL,
+             subset=sel_Primaire,
+             col=col_PAM50CL[c(2,1,3:6)], las=1,
+             main=names(MetaG_List)[i], outline=FALSE)
+ }
```



Metagenes : evaluation CLDNlow vs. others (TukeyHSD, ANOVA lm models)

```
> #### script format output aov(lm x ~ y) & TukeyHSD
> ## x : metagene x
> ## y : PAM50/CLDN-low
> source("G:\\Ori Tools\\Prog\\Rwork\\Script\\20130925_UVMV_glm.batch.r")
> UVGLM_PAM50CL <- list()
> for (i in seq_along(MetaG_List)){
+     UVGLM_PAM50CL[[i]] <- TukeyHSD_PF(lm(MetaG_List[[i]] ~ VAR_List$PAM50_CL,
+                                          subset=sel_Primaire), Ref="CLDNlow")
+     names(UVGLM_PAM50CL)[i] <- names(MetaG_List)[i]
+     xtmp <- xtable(UVGLM_PAM50CL[[i]],
+                    caption=gsub("_", "-", names(UVGLM_PAM50CL)[i]),
+                    table.placement="!h",
+                    display=c("f", "d", "f", "E", "E"))
+     print(xtmp, size="footnotesize", caption.placement="top")
+ }
```

Luminal

	N	OddsRatio[CI95]	pvalue	p.adj
Basal vs CLDNlow	5447	0.58[0.54-0.62]	1.95E-43	5.85E-43
ERBB2 vs CLDNlow	5447	2.86[2.67-3.06]	5.88E-133	3.53E-132
LumA vs CLDNlow	5447	8.73[8.23-9.27]	0.00E+00	0.00E+00
LumB vs CLDNlow	5447	8.34[7.83-8.89]	0.00E+00	0.00E+00
Normal vs CLDNlow	5447	4.27[3.95-4.62]	2.89E-188	2.31E-187

Prolif

	N	OddsRatio[CI95]	pvalue	p.adj
Basal vs CLDNlow	5447	2.65[2.52-2.79]	7.48E-195	8.23E-194
ERBB2 vs CLDNlow	5447	1.59[1.5-1.68]	9.35E-43	2.81E-42
LumA vs CLDNlow	5447	0.54[0.52-0.57]	2.86E-94	2.29E-93
LumB vs CLDNlow	5447	1.62[1.54-1.71]	6.29E-54	2.51E-53
Normal vs CLDNlow	5447	0.55[0.51-0.58]	3.64E-55	1.82E-54

T-cells

	N	OddsRatio[CI95]	pvalue	p.adj
Basal vs CLDNlow	5447	0.86[0.84-0.88]	1.60E-27	2.08E-26
ERBB2 vs CLDNlow	5447	0.86[0.84-0.88]	4.11E-26	4.93E-25
LumA vs CLDNlow	5447	0.8[0.78-0.81]	5.62E-72	8.43E-71
LumB vs CLDNlow	5447	0.8[0.78-0.82]	2.73E-61	3.82E-60
Normal vs CLDNlow	5447	0.87[0.85-0.89]	3.09E-17	3.40E-16

B-cells

	N	OddsRatio[CI95]	pvalue	p.adj
Basal vs CLDNlow	5447	0.87[0.85-0.89]	2.97E-25	2.67E-24
ERBB2 vs CLDNlow	5447	0.84[0.82-0.86]	7.29E-36	8.01E-35
LumA vs CLDNlow	5447	0.75[0.74-0.77]	2.29E-113	3.44E-112
LumB vs CLDNlow	5447	0.77[0.75-0.78]	7.26E-91	1.02E-89
Normal vs CLDNlow	5447	0.79[0.77-0.81]	1.04E-50	1.35E-49

Granulocytes

	N	OddsRatio[CI95]	pvalue	p.adj
Basal vs CLDNlow	5447	0.94[0.93-0.96]	6.10E-09	3.05E-08
ERBB2 vs CLDNlow	5447	0.94[0.92-0.95]	5.53E-10	3.32E-09
LumA vs CLDNlow	5447	0.86[0.85-0.87]	1.70E-56	2.55E-55
LumB vs CLDNlow	5447	0.86[0.84-0.87]	1.04E-53	1.46E-52
Normal vs CLDNlow	5447	0.85[0.83-0.87]	1.47E-39	1.91E-38

Core-EMT

	N	OddsRatio[CI95]	pvalue	p.adj
Basal vs CLDNlow	5447	0.37[0.36-0.39]	0.00E+00	0.00E+00
ERBB2 vs CLDNlow	5447	0.57[0.55-0.6]	3.00E-99	3.60E-98
LumA vs CLDNlow	5447	0.71[0.68-0.74]	7.29E-50	5.10E-49
LumB vs CLDNlow	5447	0.61[0.59-0.64]	8.22E-89	9.04E-88
Normal vs CLDNlow	5447	0.61[0.58-0.64]	1.02E-60	8.15E-60

Differentiation-Score

	N	OddsRatio[CI95]	pvalue	p.adj
Basal vs CLDNlow	5447	1.13[1.1-1.16]	5.54E-14	1.11E-13
ERBB2 vs CLDNlow	5447	2.17[2.11-2.23]	0.00E+00	0.00E+00
LumA vs CLDNlow	5447	2.62[2.56-2.69]	0.00E+00	0.00E+00
LumB vs CLDNlow	5447	2.69[2.63-2.77]	0.00E+00	0.00E+00
Normal vs CLDNlow	5447	1.71[1.66-1.77]	5.50E-155	4.95E-154

Stem-cells-GES

	N	OddsRatio[CI95]	pvalue	p.adj
Basal vs CLDNlow	5447	0.76[0.75-0.77]	2.23E-263	2.67E-262
ERBB2 vs CLDNlow	5447	0.71[0.71-0.72]	0.00E+00	0.00E+00
LumA vs CLDNlow	5447	0.72[0.72-0.73]	0.00E+00	0.00E+00
LumB vs CLDNlow	5447	0.65[0.64-0.66]	0.00E+00	0.00E+00
Normal vs CLDNlow	5447	0.82[0.81-0.83]	1.77E-103	1.60E-102