

Outline

1. Genes expressed differently between diagnostic groups (CTRL vs. SCZ/BD)?
 - ▶ mRNA samples from whole blood
 - ▶ n=1298
 - ▶ ~47,000 probes
 - ▶ also tested: significance of age, gender, tobacco use, waist size, cannabis use
2. Protein levels different between diagnostic groups?
 - ▶ n=2306
 - ▶ Linear regression and Mann–Whitney U test
3. Relation of mRNA and protein levels?
 - ▶ n=870
 - ▶ Linear regression and Pearson correlation

proteins
Alcam
BDNF
CatS
CRP
CXCL16
DKK1
Gal3
gp130
IGFBP4
IL1RA
MIF
MPO
OPG
sCD14
sIL2R
sTNFR1
vWF
YKL40

Outline

mRNA levels

- Demographic data

- Differently expressed genes

- Covariates

Protein levels

- QC

- Linear regression

- Mann-Whitney U test

mRNA vs. protein levels

mRNA probes on Illumina chip

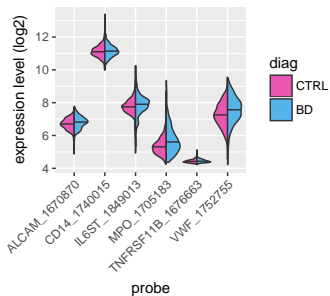
protein	mRNA probe ID
Alcam	ALCAM (1670870)
BDNF	BDNF (1706644)
BDNF	BDNF (1712712)
BDNF	BDNF (1719820)
BDNF	BDNF (1751276)
BDNF	BDNF (1761910)
BDNF	BDNF (1793988)
BDNF	BDNF (1809543)
CatS	CTSS (1743032)
CRP	CRP (1780575)
CXCL16	CXCL16 (1672278)
CXCL16	CXCL16 (1728478)
DKK1	DKK1 (1773337)
DKK1	DKK1 (2174189)
Gal3	LGALS3 (1803788)
Gal3	LGALS3 (1730660)
Gal3	LGALS3BP (1659688)

protein	mRNA probe ID
gp130	IL6ST (1748753)
gp130	IL6ST (1849013)
gp130	IL6ST (1797861)
gp130	IL6ST (1746604)
IGFBP4	IGFBP4 (1665865)
IL1RA	IL1RN (1689734)
MIF	MIF (1807074)
MPO	MPO (1705183)
OPG	TNFRSF11B (1676663)
sCD14	CD14 (2396444)
sCD14	CD14 (1740015)
sIL2R	IL2RA (1683774)
sIL2R	IL2RA (2108699)
sTNFR1	TNFRSF1A (1685005)
vWF	VWF (1752755)
YKL40	CHI3L1 (1772289)
YKL40	CHI3L1 (3307868)

Demographic data, mRNA, (n=1298)

	Schizophrenia	Bipolar Disorder	Healthy Controls
Participants, n	493	300	505
Schizophrenia, n (%)	361 (73.2)		
Schizoaffective, n (%)	90 (18.3)		
Schizophreniform, n (%)	42 (8.5)		
Bipolar I, n (%)		215 (71.7)	
Bipolar II, n (%)		67 (22.3)	
BipolarNOS, n (%)		18 (6.0)	
Male, n (%)	297 (60.2)	124 (41.3)	295 (58.4)
Female, n (%)	196 (39.8)	176 (58.7)	210 (41.6)
Age (years), mean (SD)	30.5 (SD)	34.2 (11.73)	
Waist (cm), mean (SD)	91.75 (15.02)	89.6 (12.90)	
Tobacco daily use, n (%)	279 (56.6)	169 (56.3)	
Non-smokers, n (%)	201 (40.8)	128 (42.7)	
Cannabis use within last 14 days	25 (5.2)	22 (7.3)	
Not used within last 14 days	454 (92.1)	272 (90.7)	

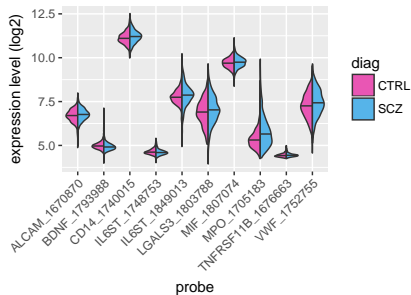
Results mRNA BD



linear model: $\text{expr} \sim \text{diag} + \text{age} + \text{sex}$

probe	logFC	p-value
MPO	0.441	7.85E-018
VWF	0.288	6.96E-007
ALCAM	0.090	0.0007
IL6ST	0.075	0.0638
CD14	0.056	0.0428
TNFRSF11B	0.017	0.0318

Results mRNA SCZ



linear model: $\text{expr} \sim \text{diag} + \text{age} + \text{sex}$

probe	logFC	p-value
MPO	0.414	2.40E-018
VWF	0.173	0.0003
LGALS3	0.146	0.0036
CD14	0.106	5.54E-006
IL6ST	0.073	0.0508
ALCAM	0.071	0.0022
MIF	0.052	0.0082
BDNF	-0.046	0.0012
IL6ST	-0.024	0.0276
TNFRSF11B	0.018	0.0057

Selected mRNA probes

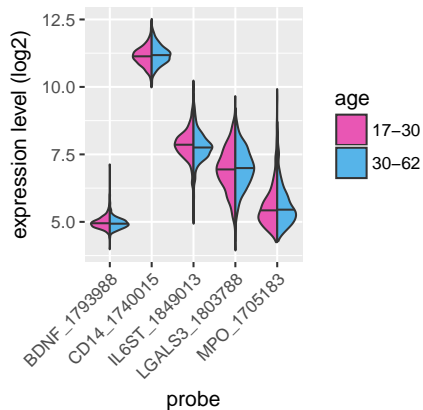
protein	mRNA probe ID
Alcam	ILMN_1670870_ALCAM
Gal3	ILMN_1803788_LGALS3
gp130	ILMN_1849013_IL6ST
MIF	ILMN_1807074_MIF
MPO	ILMN_1705183_MPO
sCD14	ILMN_1740015_CD14
vWF	ILMN_1752755_VWF

Covariates SCZ

Age

linear model: $\text{expr} \sim \text{diag} + \text{age} + \text{sex}$

probe	p-value
ILMN_1740015_CD14	2.22E-05
ILMN_1849013_IL6ST	0.0196
ILMN_1705183_MPO	0.0240
ILMN_1803788_LGALS3	0.0681
ILMN_1793988_BDNF	0.0958
ILMN_1748753_IL6ST	0.4639
ILMN_1807074_MIF	0.4680
ILMN_1752755_VWF	0.4807
ILMN_1676663_TNFRSF11B	0.5755
ILMN_1670870_ALCAM	0.8399

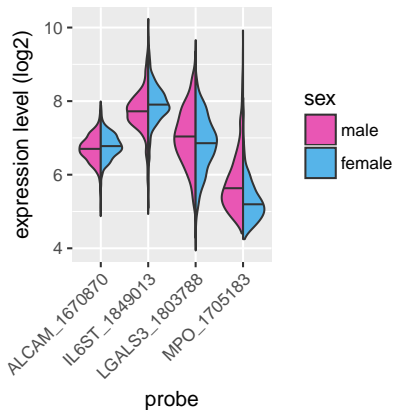


Covariates SCZ

Sex

linear model: $\text{expr} \sim \text{diag} + \text{age} + \text{sex}$

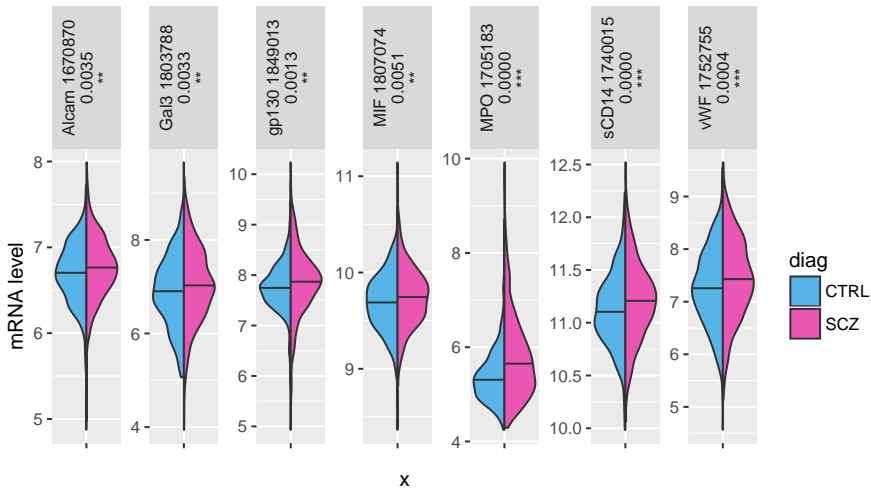
probe	p-value
ILMN_1705183_MPO	8.10E-26
ILMN_1849013_IL6ST	2.77E-07
ILMN_1803788_LGALS3	2.11E-05
ILMN_1670870_ALCAM	0.0022
ILMN_1740015_CD14	0.4276
ILMN_1748753_IL6ST	0.4605
ILMN_1807074_MIF	0.5387
ILMN_1752755_VWF	0.6273
ILMN_1676663_TNFRSF11B	0.6346
ILMN_1793988_BDNF	0.7669



Covariates SCZ

Sex

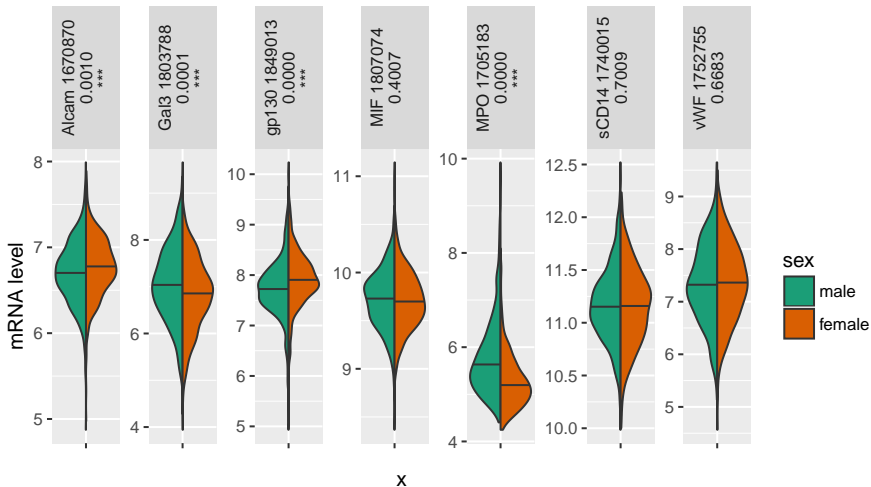
CTRL vs. SCZ (n=998)



Covariates SCZ

Sex

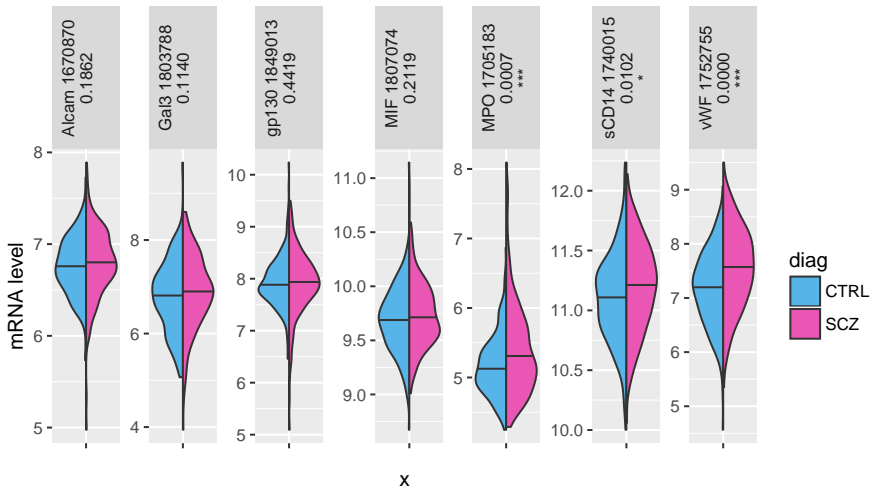
male vs. female (n=998)



Covariates SCZ

Sex

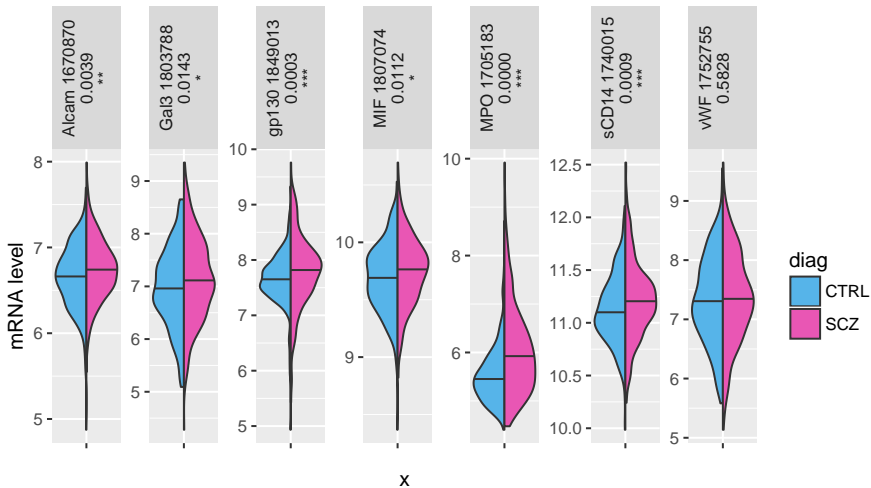
female only: CTRL vs. SCZ (n=406)



Covariates SCZ

Sex

male only: CTRL vs. SCZ (n=592)



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mRNA levels

- Demographic data

- Differently expressed genes

- Covariates

Protein levels

- QC

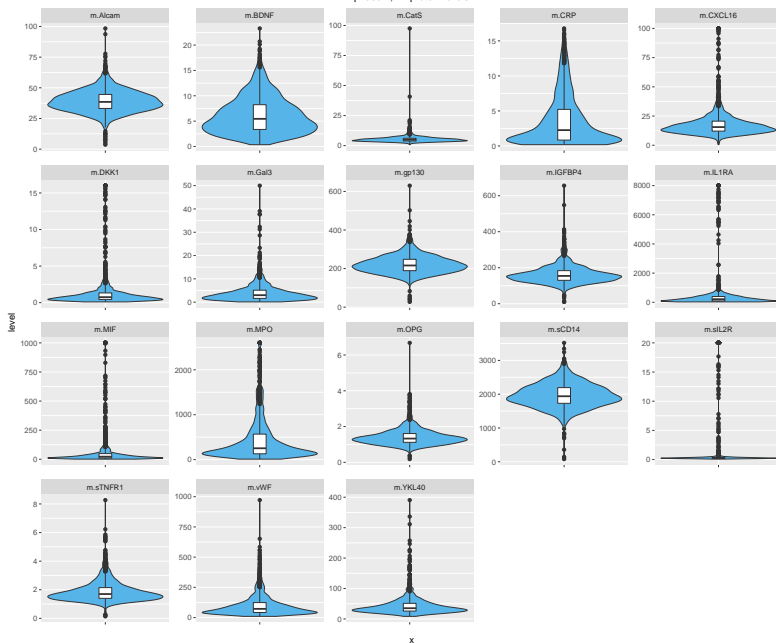
- Linear regression

- Mann-Whitney U test

mRNA vs. protein levels

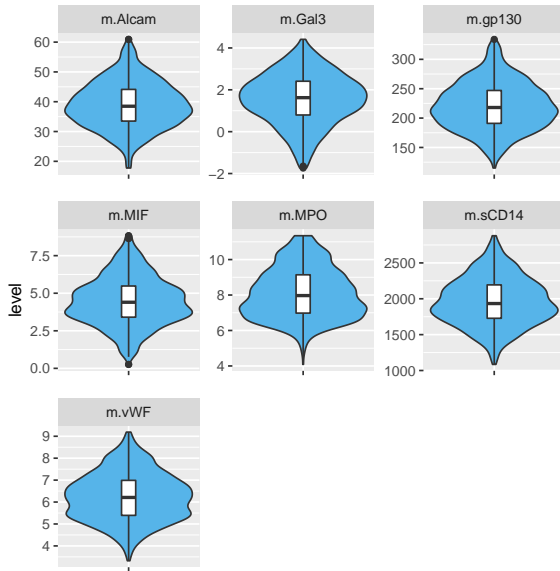
Protein levels - QC

mRNA phase 1,2 - protein levels



Protein levels - QC

mRNA phase 1,2 – protein levels – filtered/transformed



Results Protein levels

linear regression

linear model: $\text{prot.lvl} \sim \text{diag} + \text{age} + \text{sex}$

BD:

protein	p-value
m.Alcam	0.1564
m.Gal3	0.0001
m.gp130	0.0044
m.MIF	0.1829
m.MPO	0.9690
m.sCD14	0.0927
m.vWF	0.3567

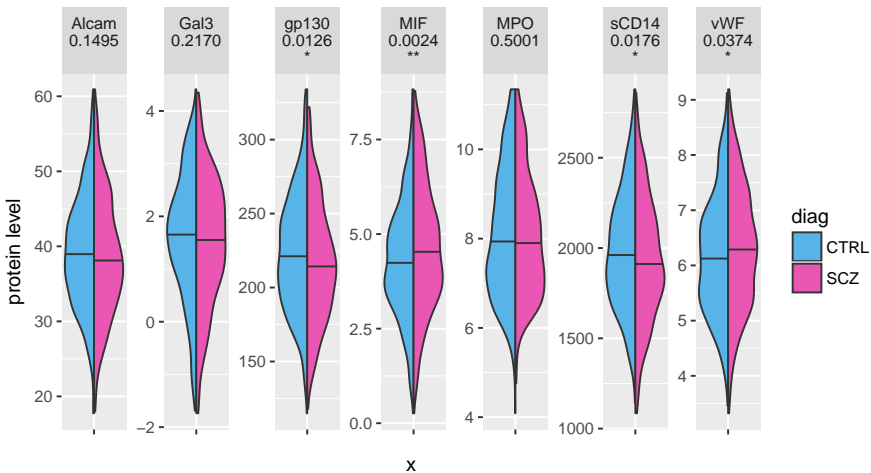
SCZ:

protein	p-value
m.Alcam	0.3883
m.Gal3	0.2034
m.gp130	0.0051
m.MIF	0.0018
m.MPO	0.3835
m.sCD14	0.0296
m.vWF	0.0525

Protein levels

Mann-Whitney U test

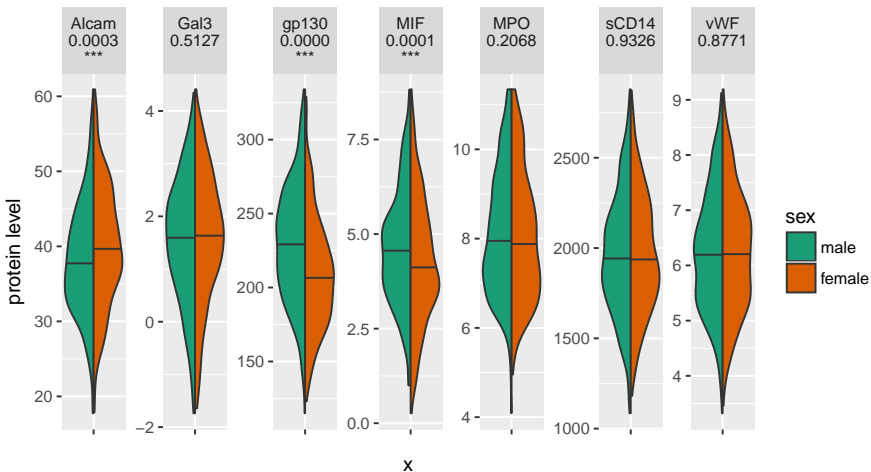
CTRL vs. SCZ (n=1818)



Protein levels

Mann-Whitney U test

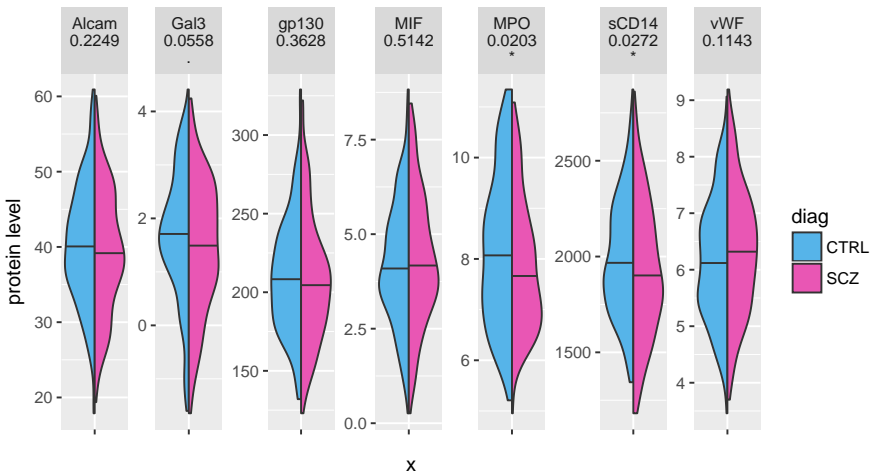
male vs. female (n=1818)



Protein levels

Mann-Whitney U test

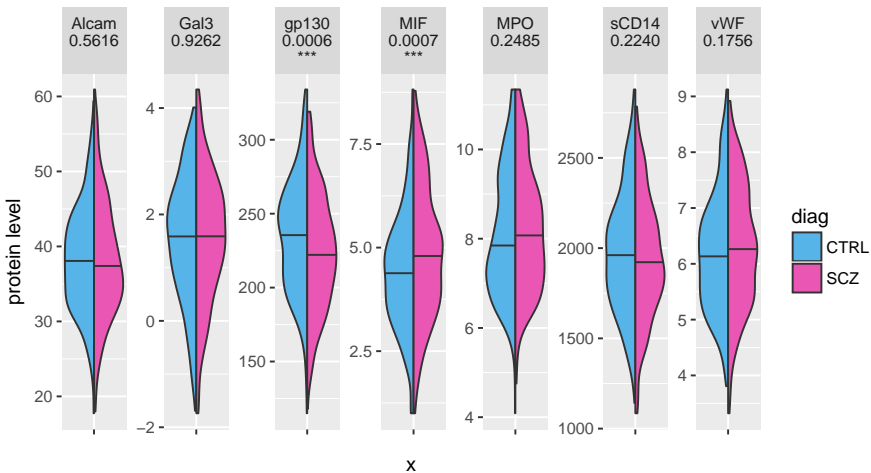
female only: CTRL vs. SCZ (n=798)



Protein levels

Mann-Whitney U test

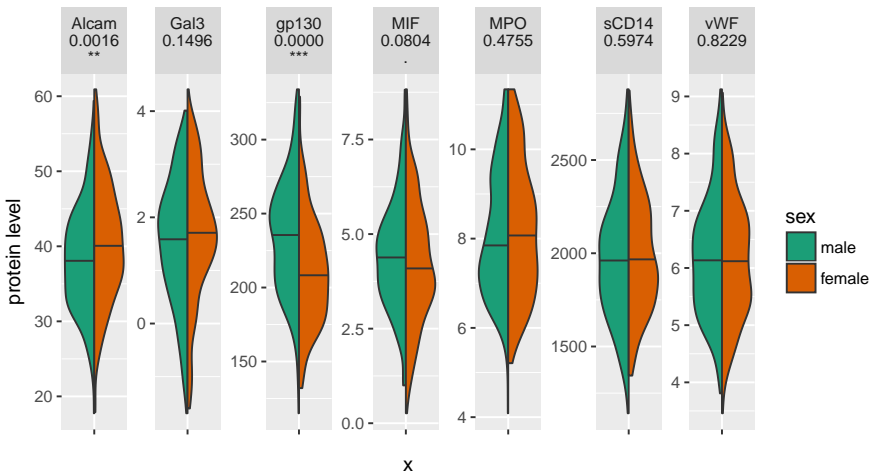
male only: CTRL vs. SCZ (n=1020)



Protein levels

Mann-Whitney U test

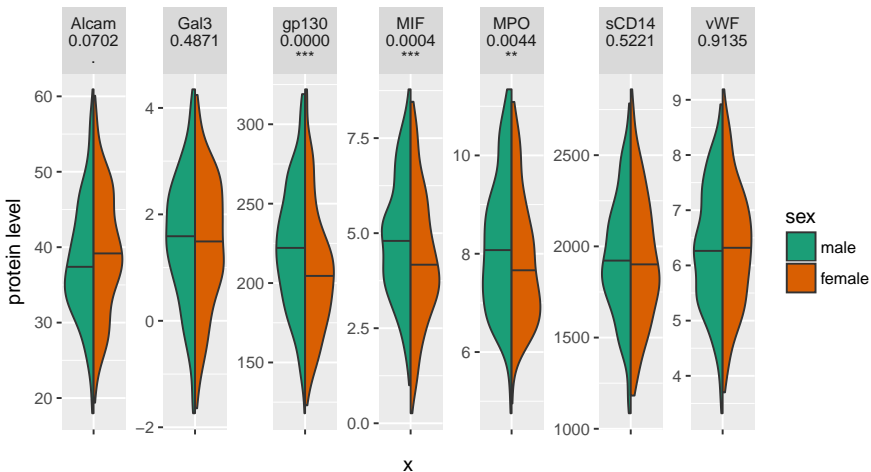
CTRL: male vs. female (n=1012)



Protein levels

Mann-Whitney U test

SCZ: male vs. female (n=806)



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Protein levels

- QC

- Linear regression

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mRNA vs. protein levels

probeid	cor_pearson	pval_pearson	proteinid
ILMN_1807074_MIF	-0.1262	0.0002	m.MIF
ILMN_1705183_MPO	0.0706	0.0382	m.MPO
ILMN_1740015_CD14	0.0546	0.1120	m.sCD14
ILMN_1670870_ALCAM	-0.0489	0.1550	m.Alcam
ILMN_1752755_VWF	0.0473	0.1650	m.vWF
ILMN_1849013_IL6ST	-0.0182	0.5971	m.gp130
ILMN_1803788_LGALS3	0.0171	0.6165	m.Gal3