| Method | | CIBERSORT proportion predict | | | RPC proportion predict | | | QP proportion predict | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | HCC | control | preg | HCC | control | preg | HCC | control | preg |
| Truth | HCC | 18 | 9 | 0 | 17 | 10 | 0 | 14 | 13 | 0 |
| | control | 7 | 25 | 0 | 7 | 25 | 0 | 3 | 29 | 0 |
| | preg | 0 | 1 | 16 | 0 | 1 | 16 | 0 | 0 | 17 |

Supplementary Table S1: Classification confusion matrices based on real data using different reference-based methods. HCC: hepatocellular carcinoma patients. control: healthy, unpregnant control people. preg: healthy pregnant women. Cibersort: using tissue proportions solved from Cibersort for prediction. RPC: using tissue proportions solved from Robust Partial Correlations for prediction. QP: using tissue proportions solved from Quadratic Programming procedure for prediction. Cibersort predicted accuracy: 0.78. RPC predicted accuracy: 0.76. QP predicted accuracy: 0.79.

Supplementary Figure S1: Boxplot of classification accuracies for NMF and QP under different noise level and sample size. NMF: Non-negative matrix factorization (NMF) approach. QP: using tissue proportions solved from Quadratic Programming procedure for prediction. *N* represent the total sample size used in simulation. 3-fold cross validation was conducted. A, low noise level; B, medium noise level; C, high noise level.

Supplementary Figure S2: Boxplot of classification accuracies for multiple methods in simulations. QP: using tissue proportions solved from Quadratic Programming procedure for prediction. OLS: using tissue proportions directly solved from Ordinary Least Square without constraint in QP. QP high var: using a 'high-noise reference' as the reference in the QP step to solve tissue proportions, then use the solved proportions for prediction. QP random: using a 'randomly shuffled reference' as the reference in the QP step to solve tissue proportions, then use the solved proportions for prediction. A, low noise level; B, medium noise level; C, high noise level.

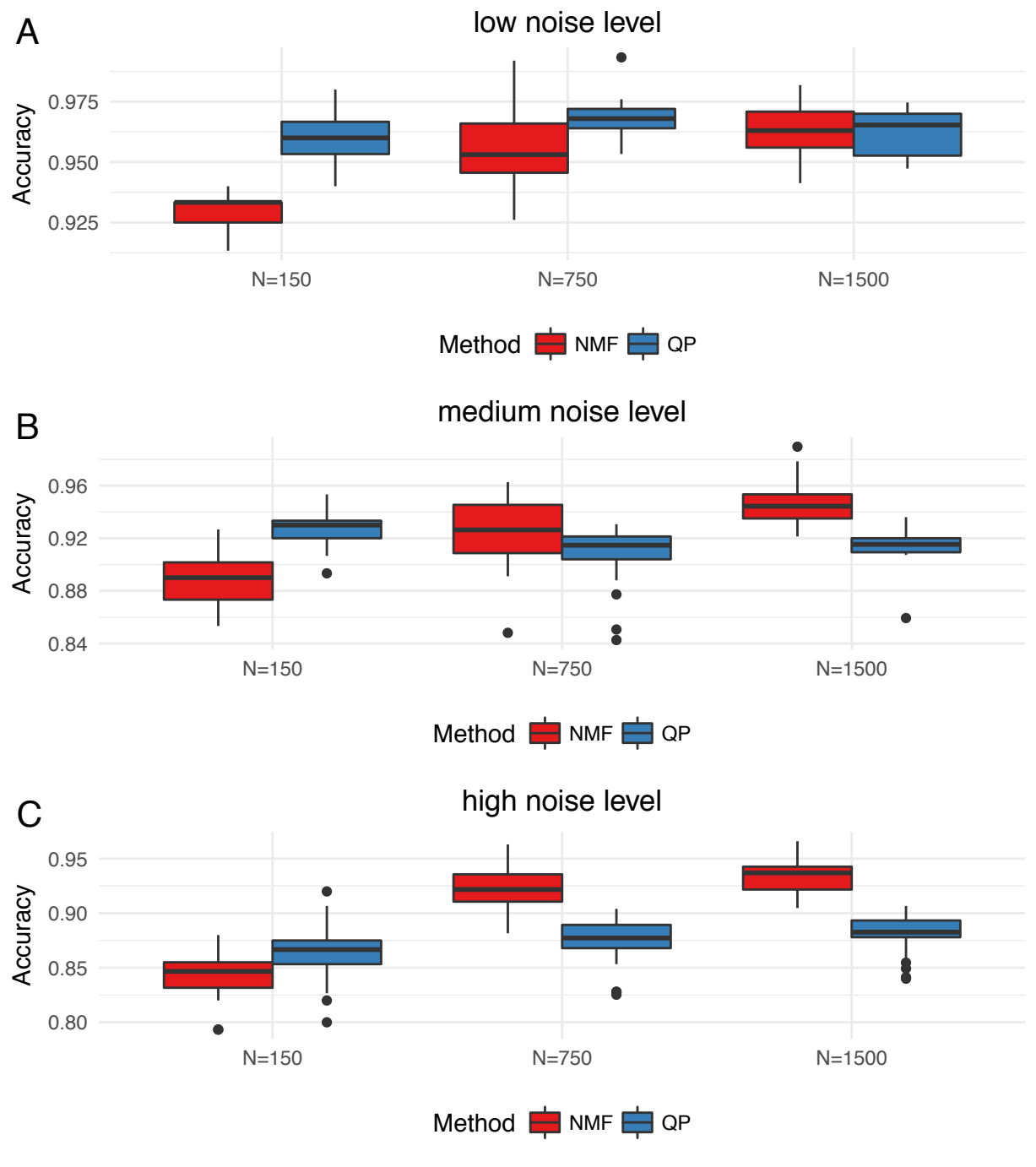
Supplementary Figure S3: Boxplot of classification accuracies for multiple reference-based methods in simulations. QP: using tissue proportions solved from Quadratic Programming procedure for prediction. RPC: using tissue proportions solved from Robust Partial Correlations for prediction. CBS: using tissue proportions solved from Cibersort for prediction. True prop: using true tissue proportions for prediction. A, low noise level; B, medium noise level; C, high noise level.

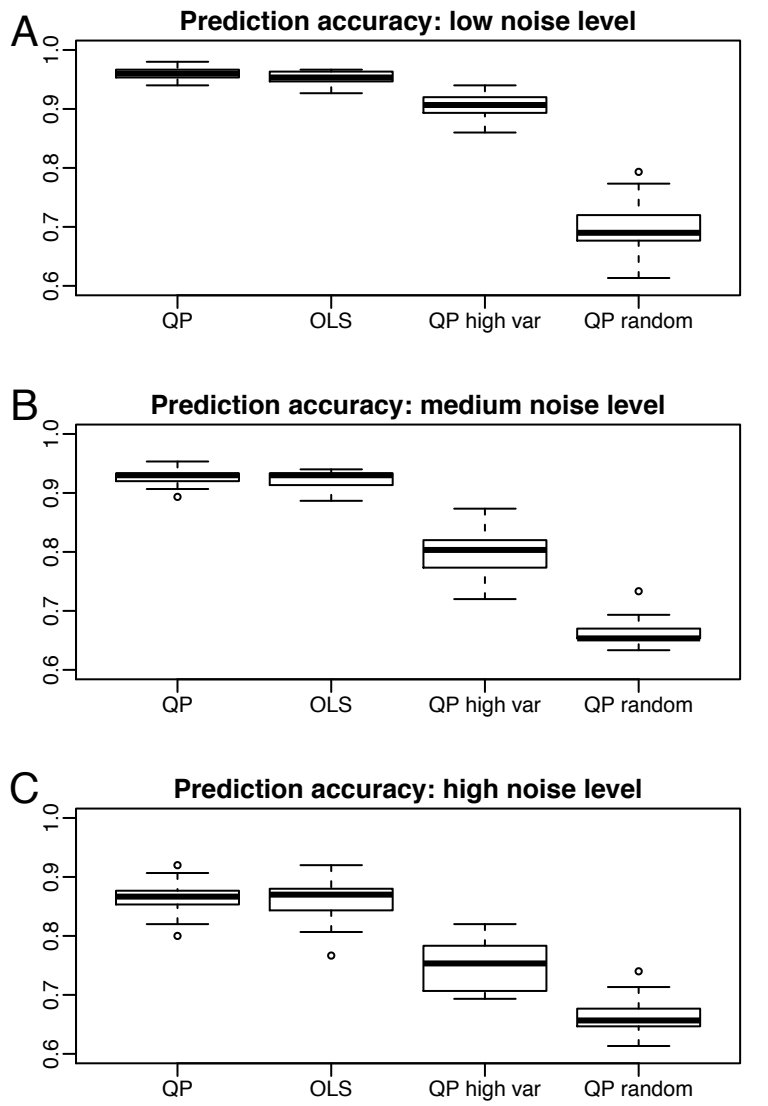
Supplementary Figure S4: Scatterplots of NMF estimated reference methylation levels versus true reference methylation levels in all 14 tissues in simulation. Spearman's correlation is shown in each panel.

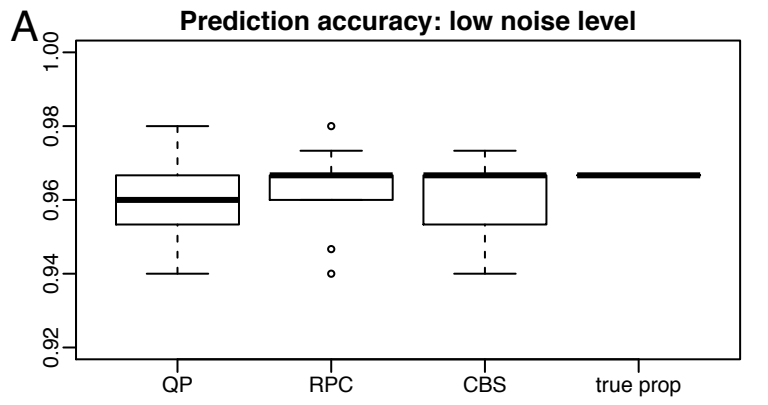
Supplementary Figure S5: Scatterplots of NMF estimated tissue proportions versus true tissue proportions in all 14 tissues in simulation. Spearman's correlation is shown in each panel.

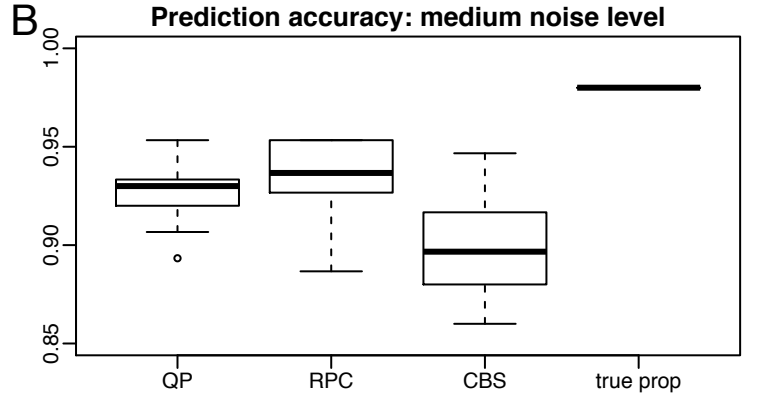
Supplementary Figure S6: Boxplot of real data solved tissue proportions for all 14 tissues, respectively, among 3 groups. One panel for each tissue.

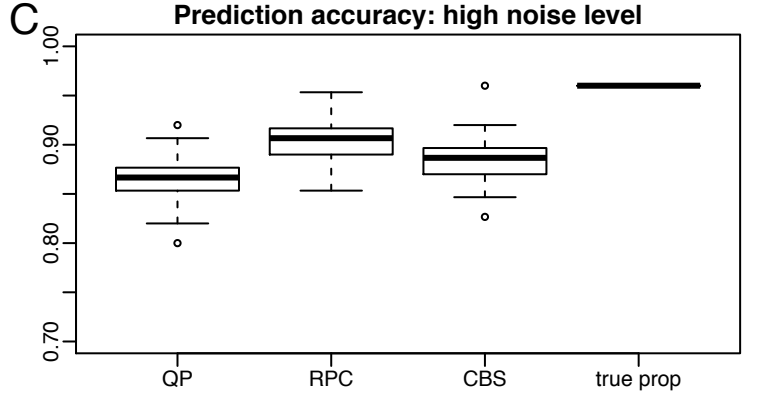
Supplementary Figure S7: Scatterplots of NMF estimated reference methylation levels versus true reference methylation levels in all 14 tissues in real data from Sun K et al. PNAS 2015. Spearman's correlation is shown in each panel.


A
low noise level
Accuracy
0.975
0.950
0.925
N=150
N=750
N=1500
Method
NMF
QP
B
medium noise level
Accuracy
0.96
0.92
0.88
0.84
N=150
N=750
N=1500
Method
NMF
QP
C
high noise level
Accuracy
0.95
0.90
0.85
0.80
N=150
N=750
N=1500
Method
NMF
QP

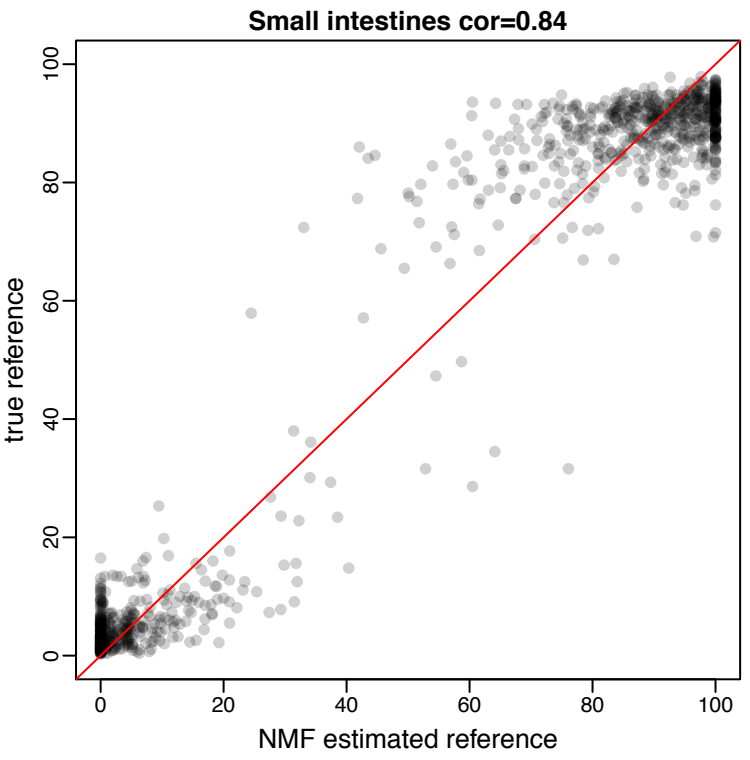

A
Prediction accuracy: low noise level
1.0
0.9
0.8
0.7
0.6
QP
OLS
QP high var
QP random
B
Prediction accuracy: medium noise level
1.0
0.9
0.8
0.7
0.6
QP
OLS
QP high var
QP random
C
Prediction accuracy: high noise level
1.0
0.9
0.8
0.7
0.6
QP
OLS
QP high var
QP random


A
Prediction accuracy: low noise level
1.00
0.98
0.96
0.94
0.92
QP
RPC
CBS
true prop

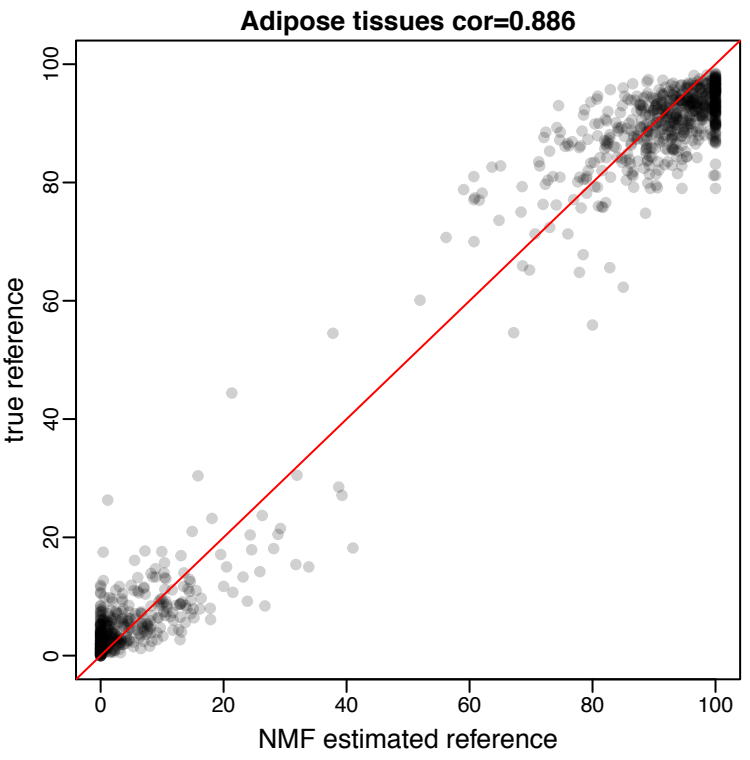

B
Prediction accuracy: medium noise level
1.00
0.95
0.90
0.85
QP
RPC
CBS
true prop


C
Prediction accuracy: high noise level
1.00
0.90
0.80
0.70
QP
RPC
CBS
true prop

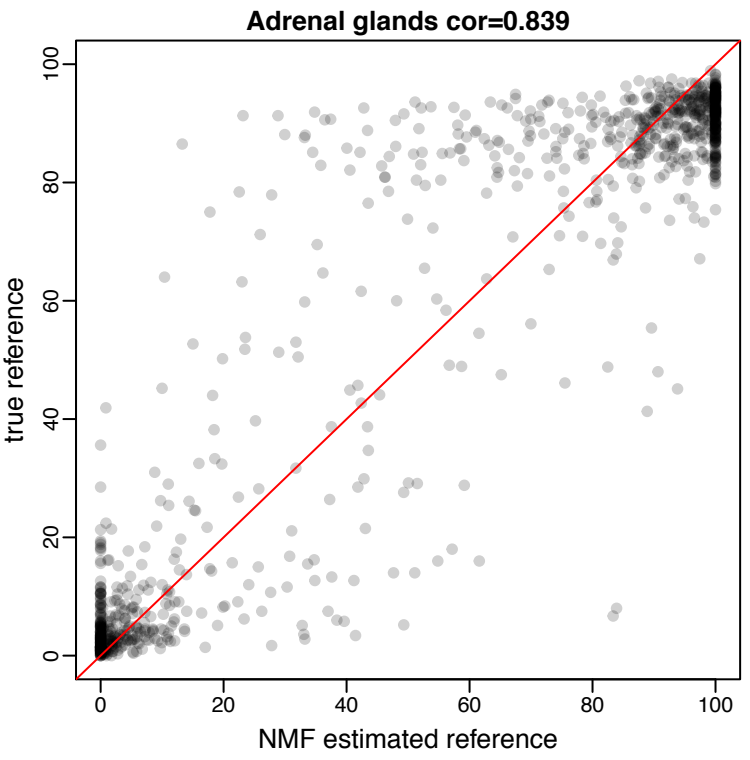
**Small intestines cor=0.84**



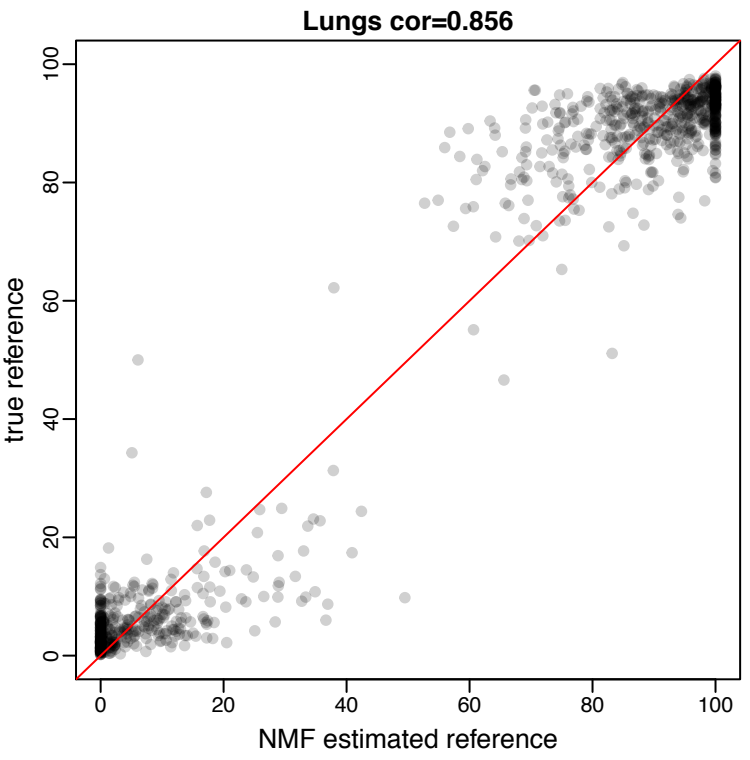

**Adipose tissues cor=0.886**



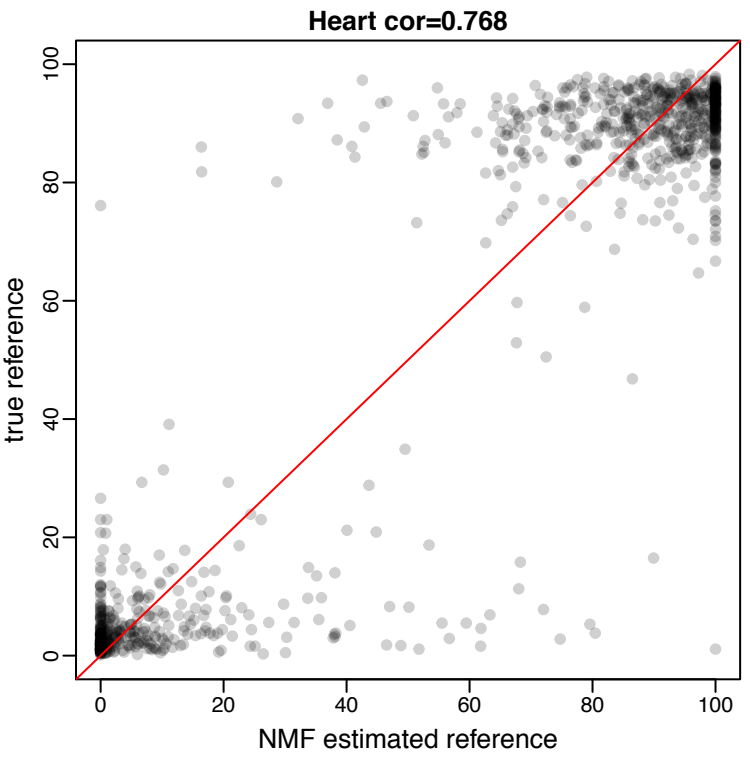

**Adrenal glands cor=0.839**



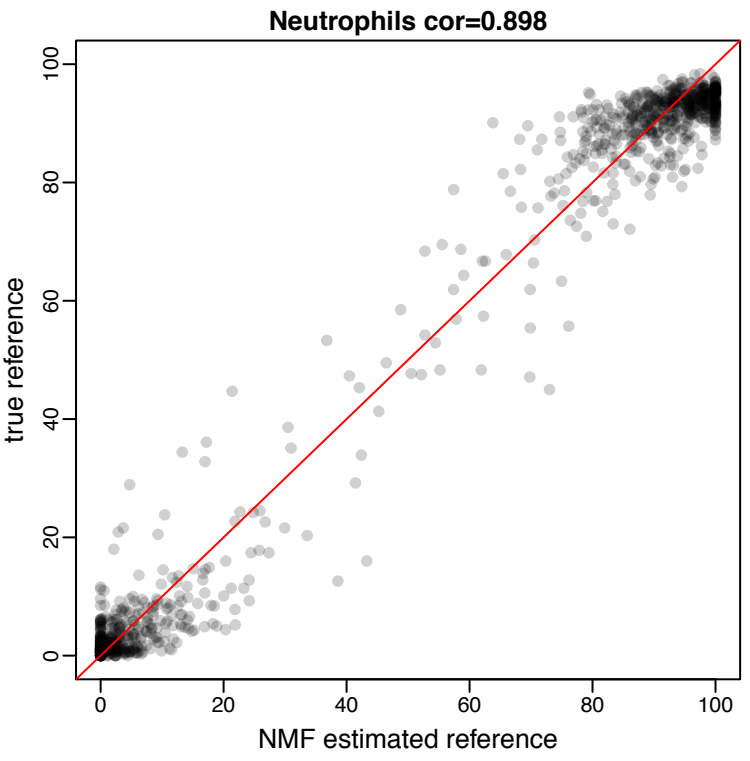

**Lungs cor=0.856**



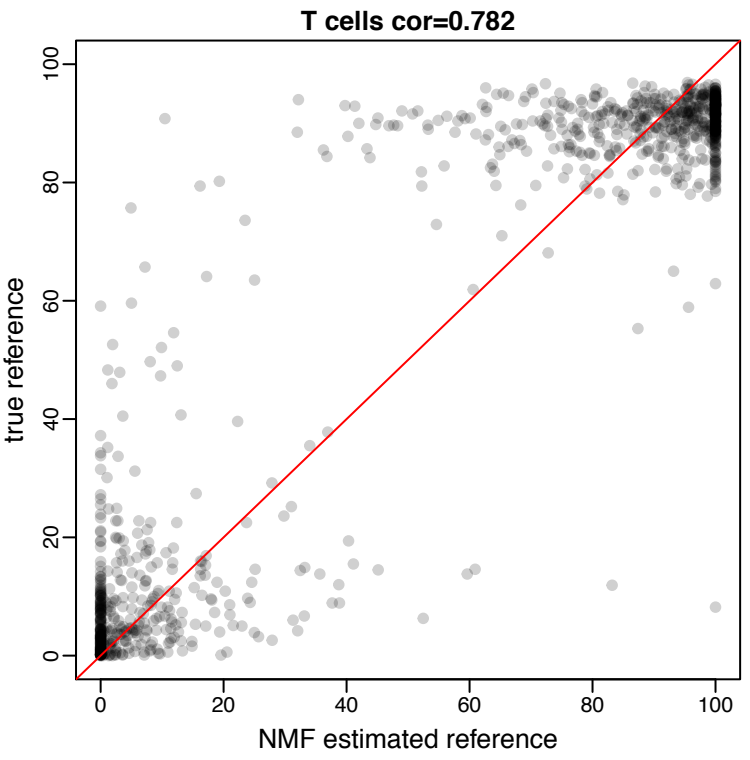

**Heart cor=0.768**



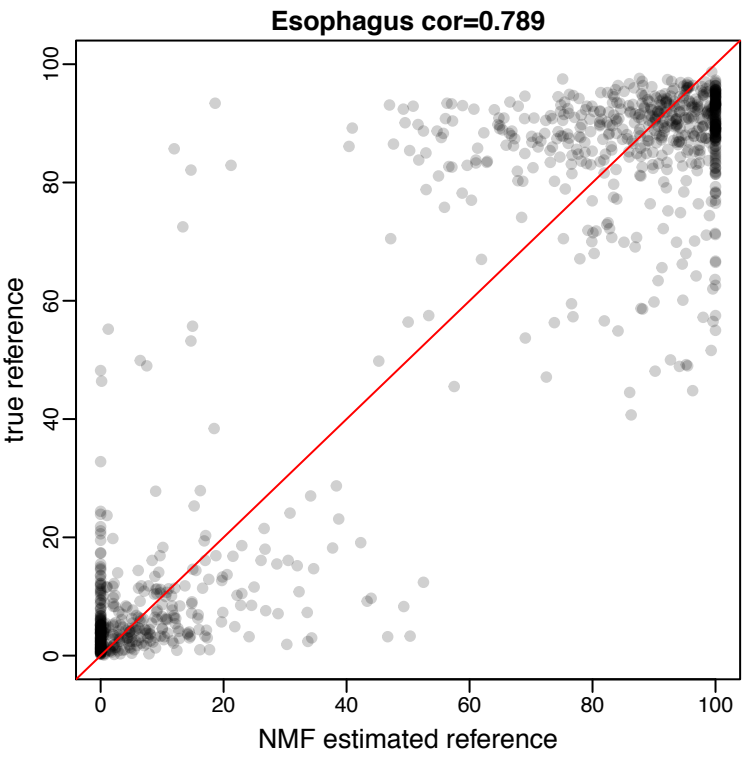

**Neutrophils cor=0.898**



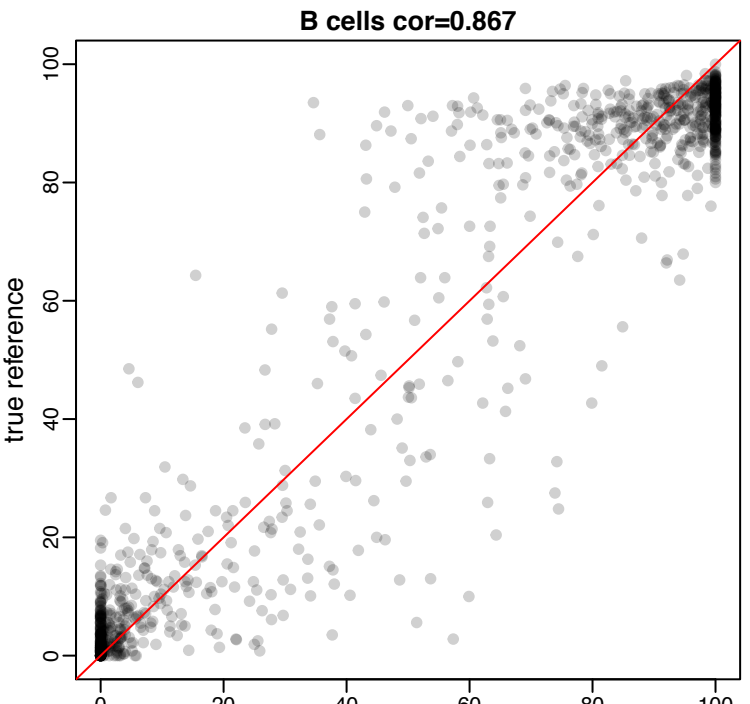

**T cells cor=0.782**



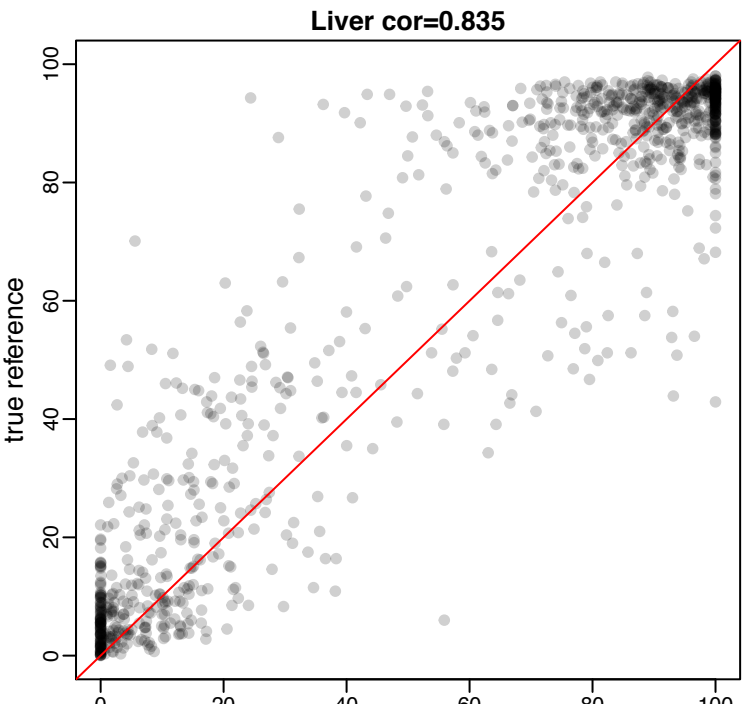

**Esophagus cor=0.789**



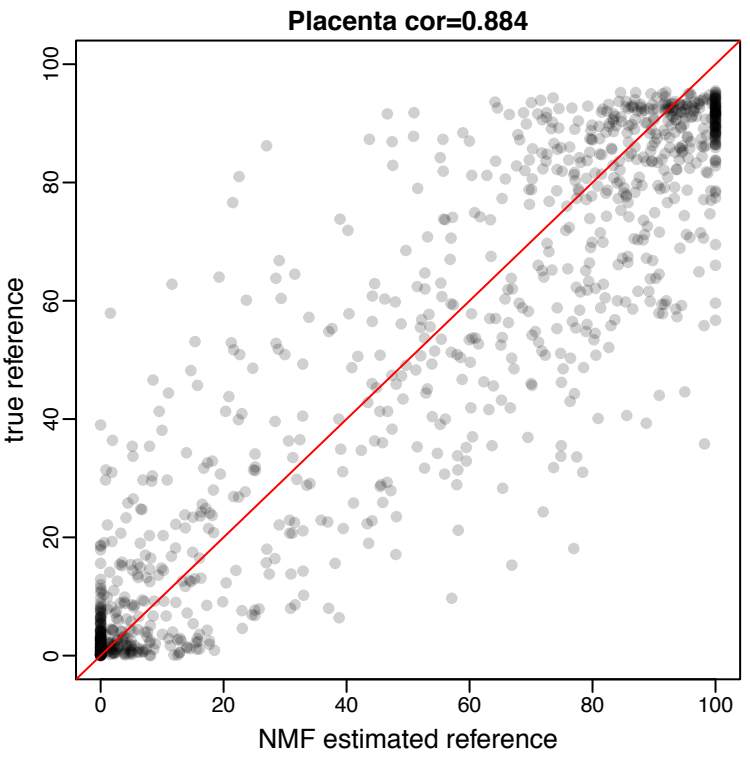

**B cells cor=0.867**



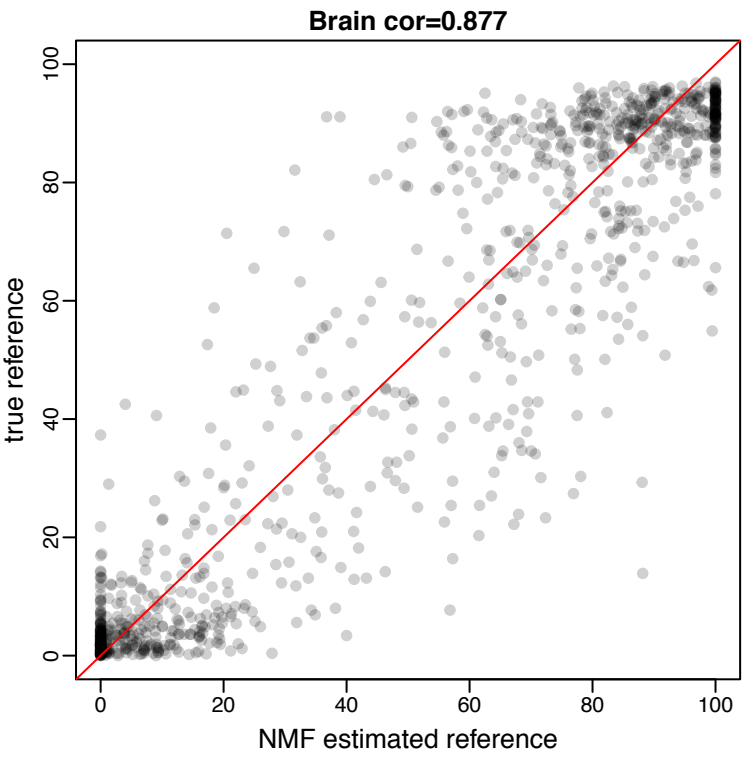

**Liver cor=0.835**



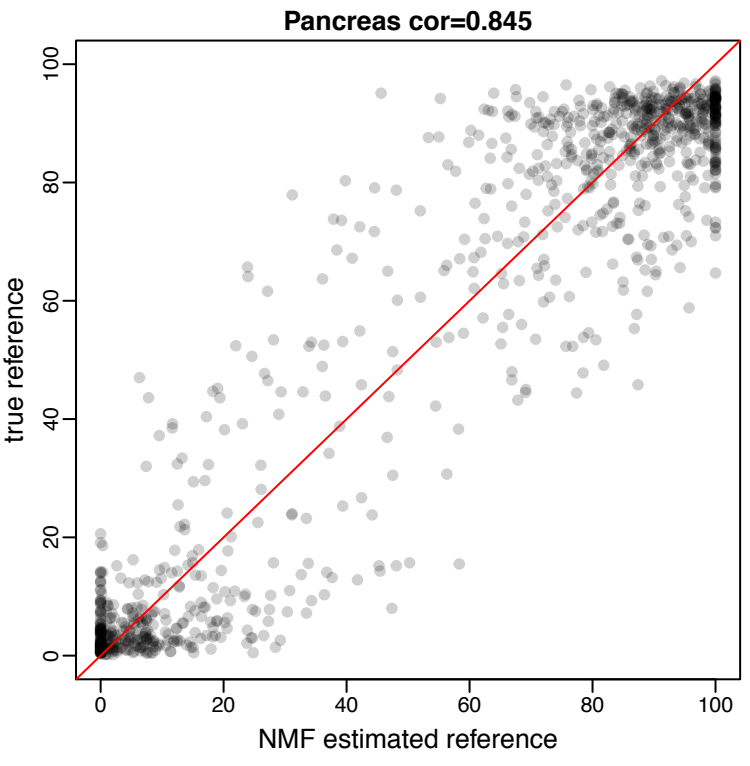

**Placenta cor=0.884**



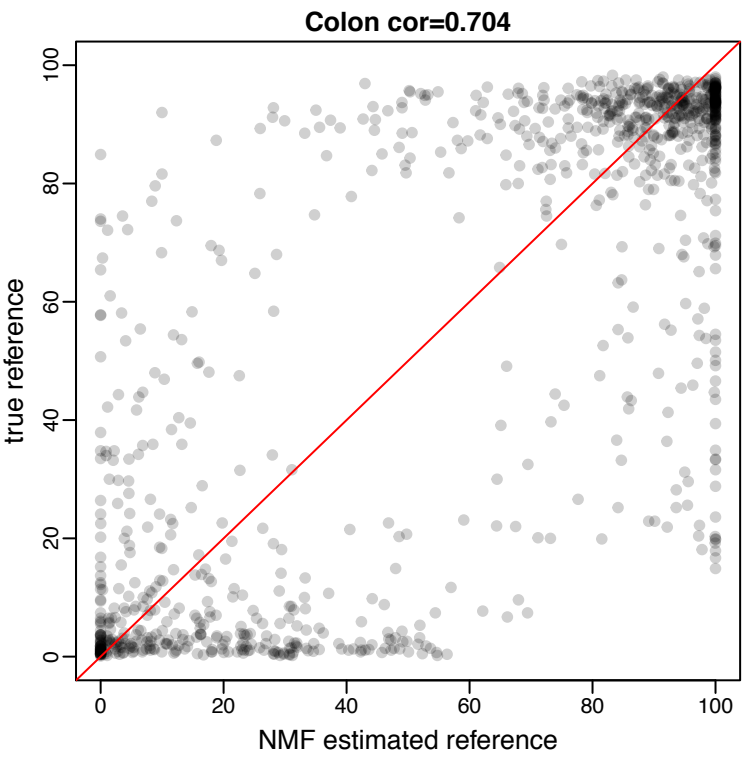

**Brain cor=0.877**



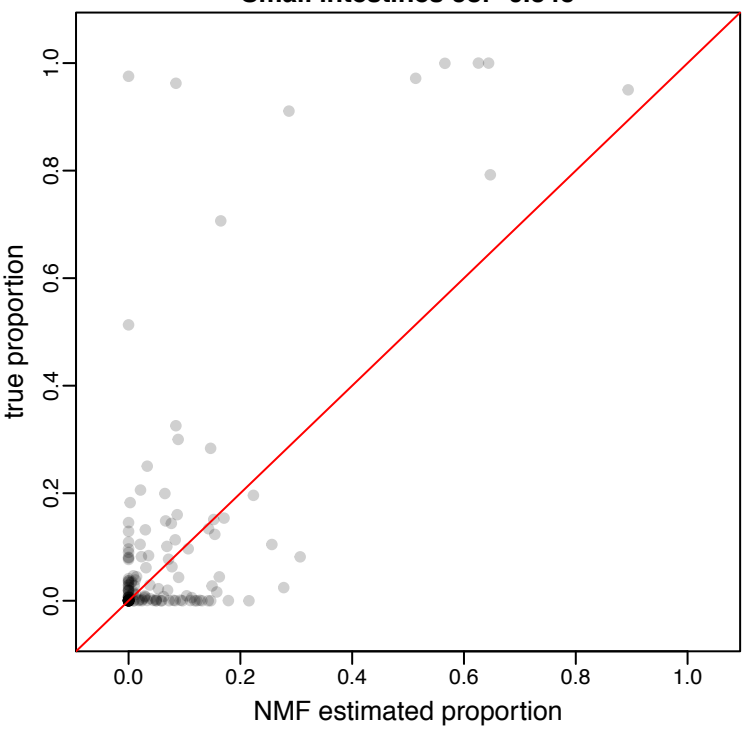

**Pancreas cor=0.845**



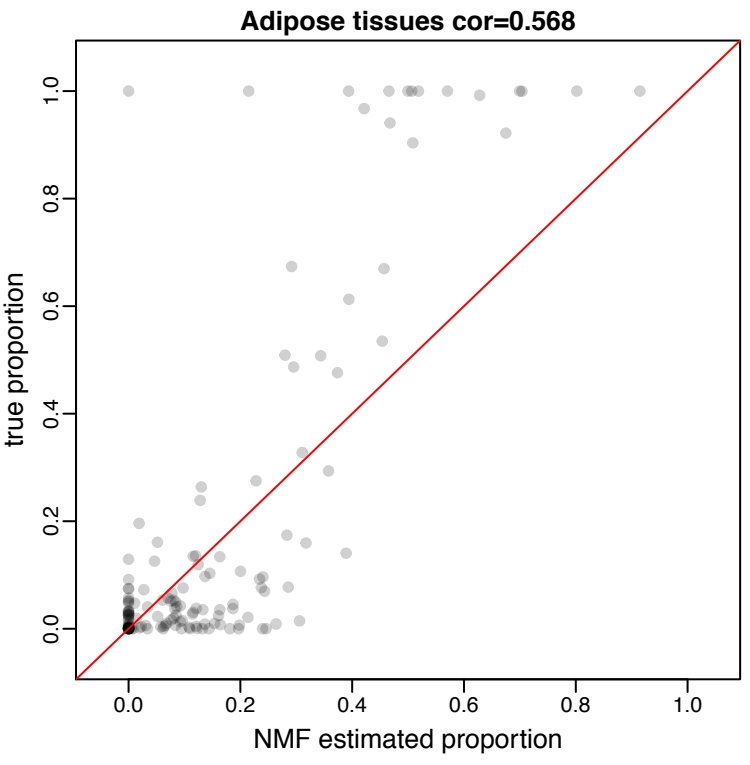

**Colon cor=0.704**



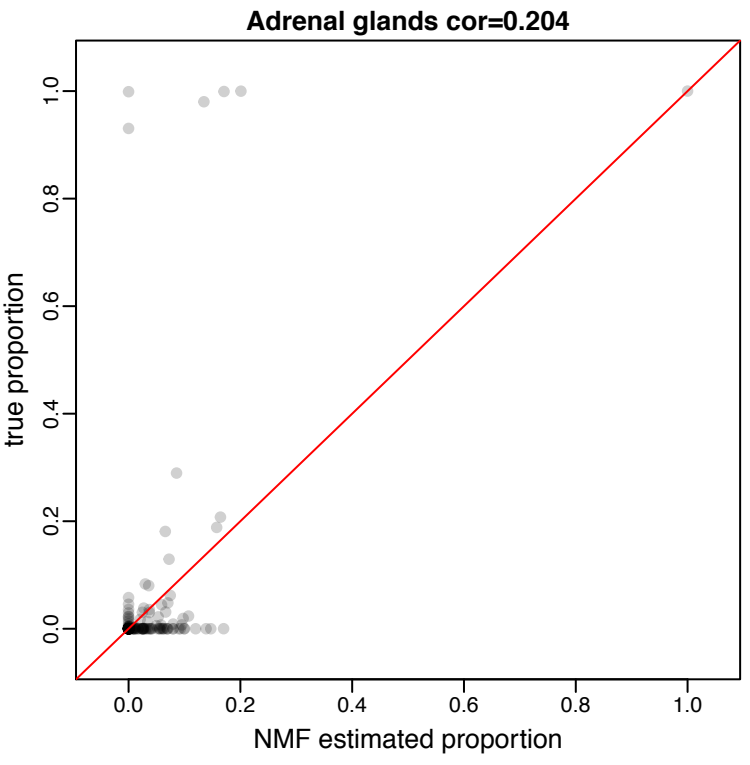
**Small intestines cor=0.345**




**Adipose tissues cor=0.568**




**Adrenal glands cor=0.204**

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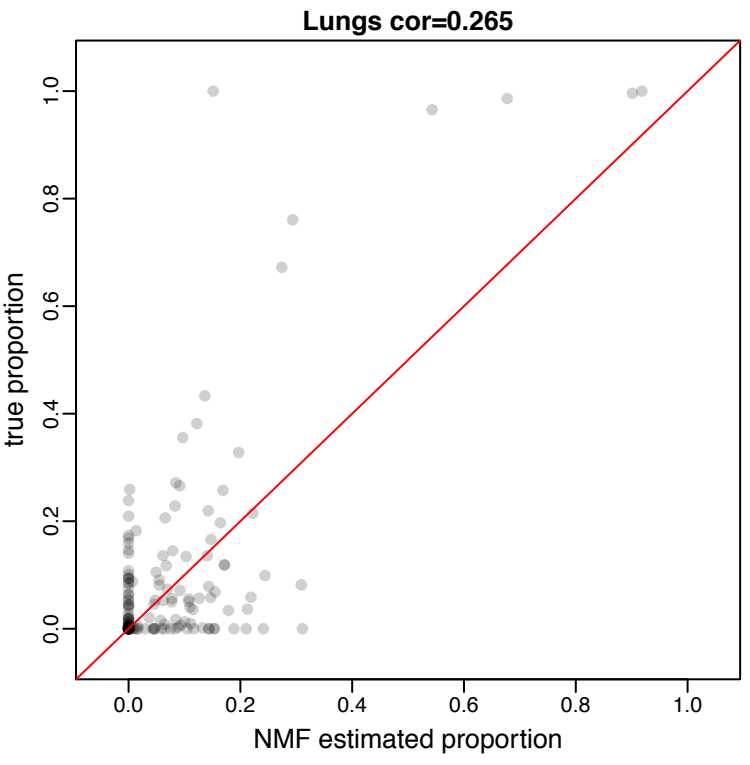
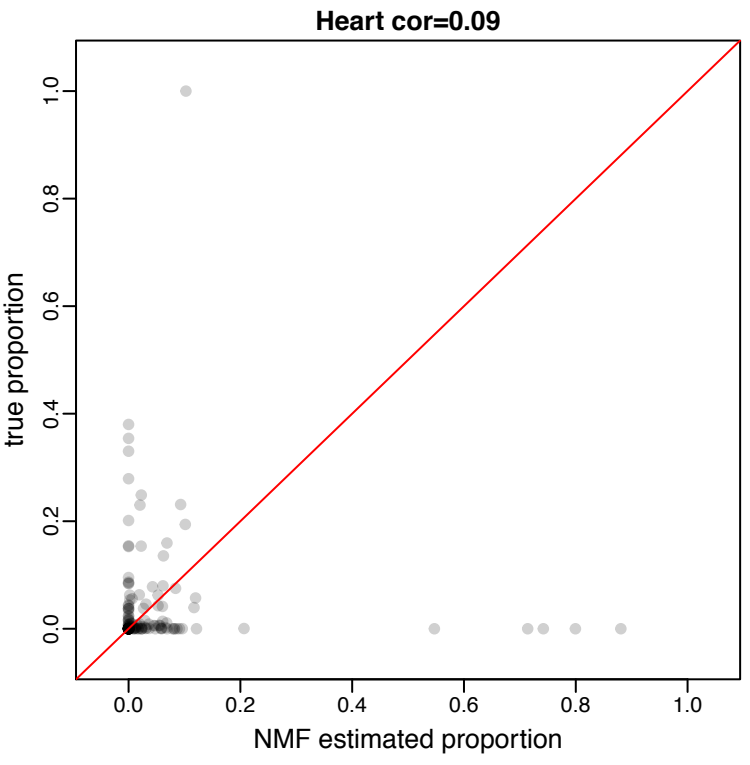
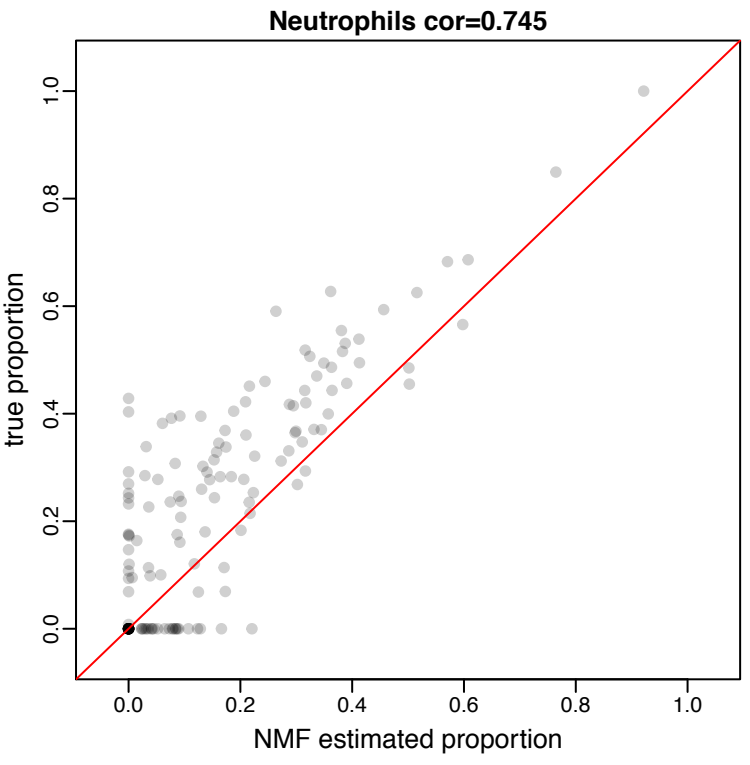


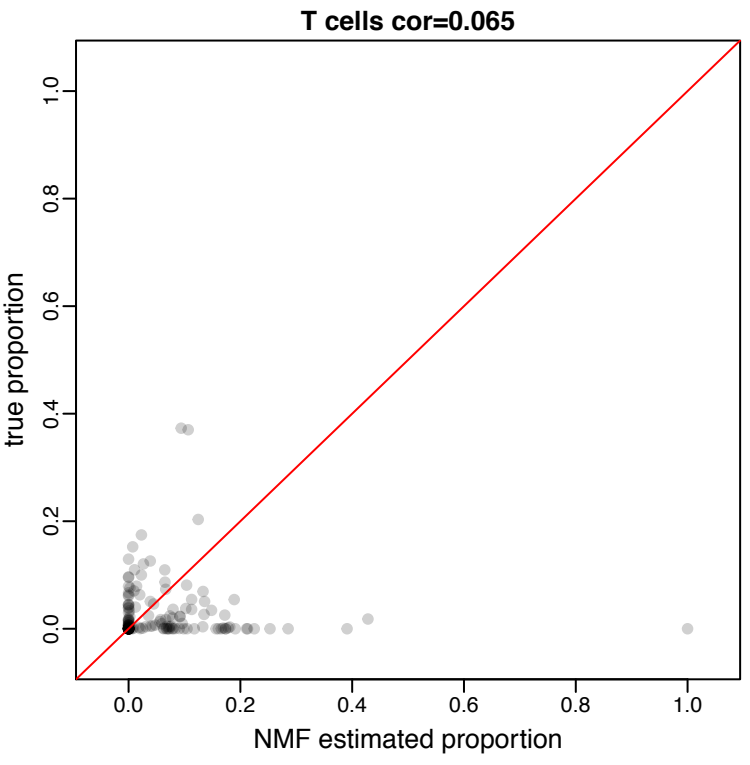

**Heart cor=0.09**



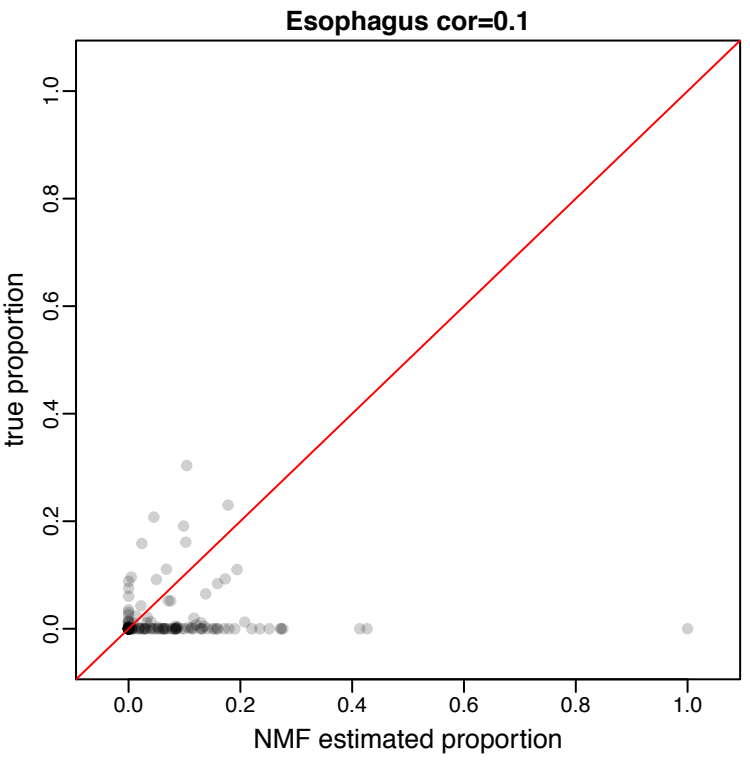

**Neutrophils cor=0.745**



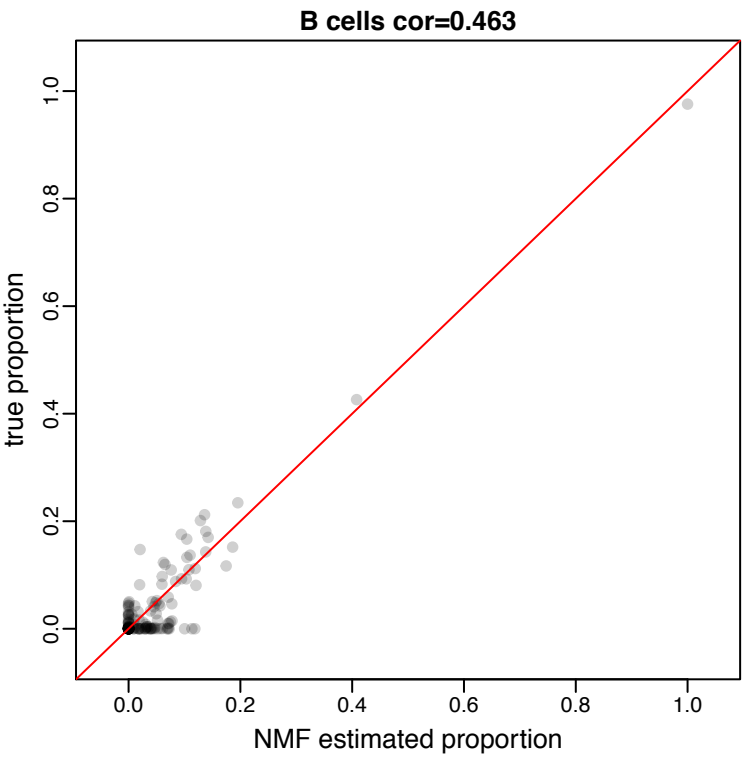

**T cells cor=0.065**



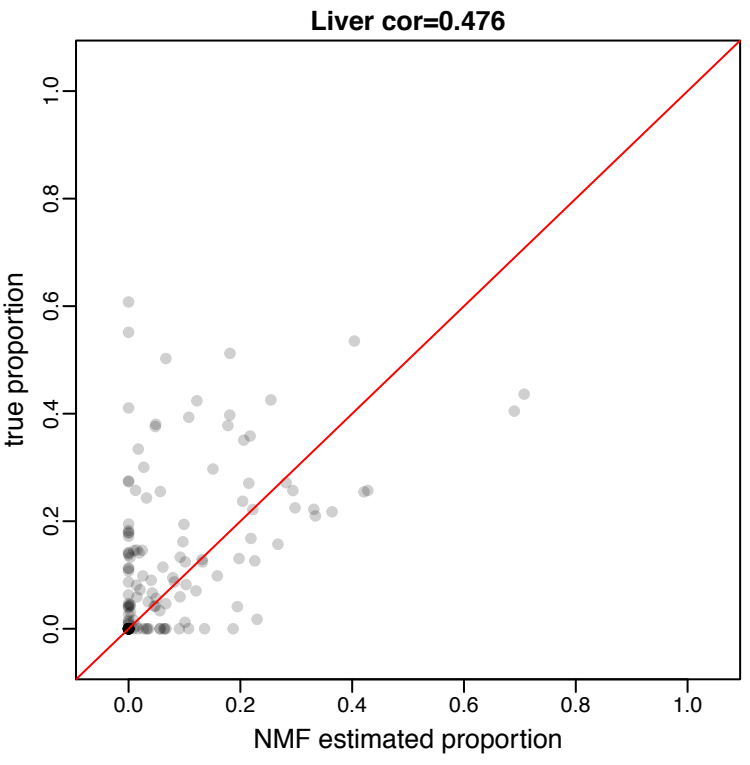

**Esophagus cor=0.1**



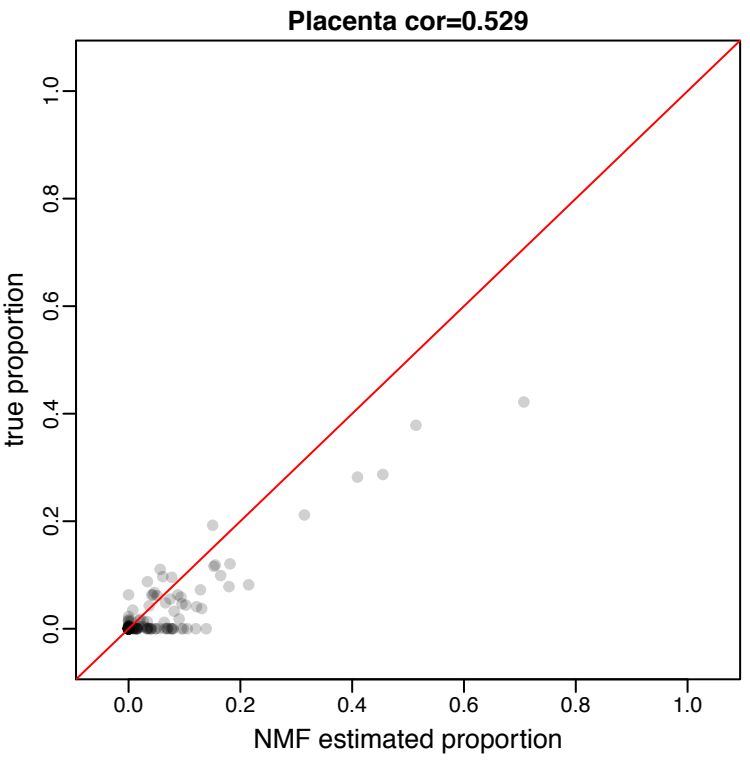

**B cells cor=0.463**



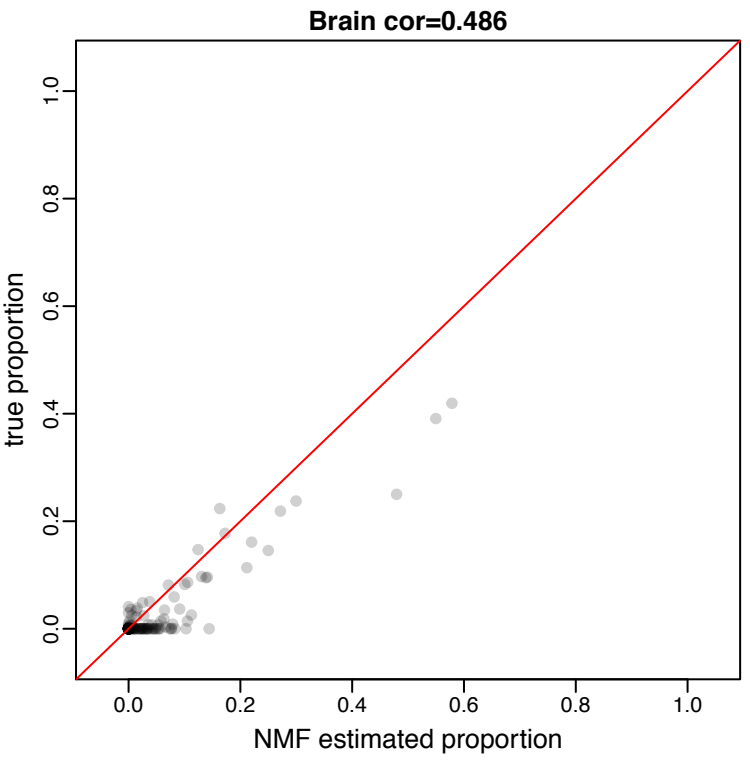

**Liver cor=0.476**



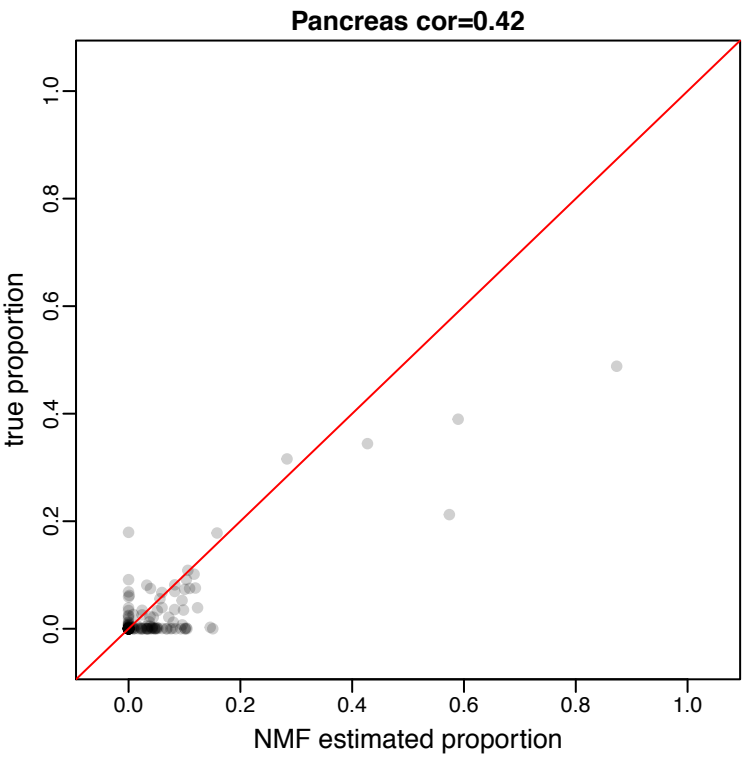

**Placenta cor=0.529**



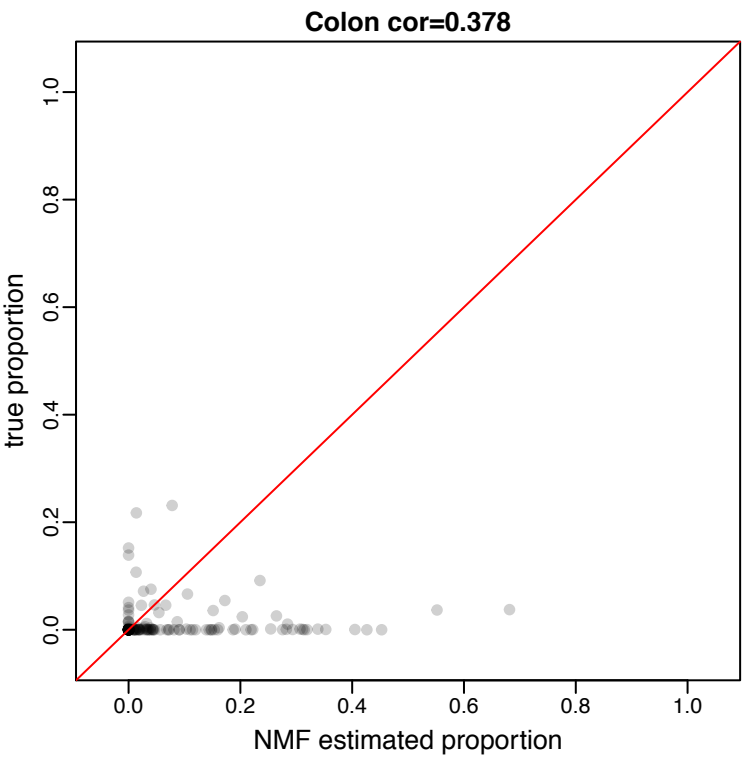

**Brain cor=0.486**

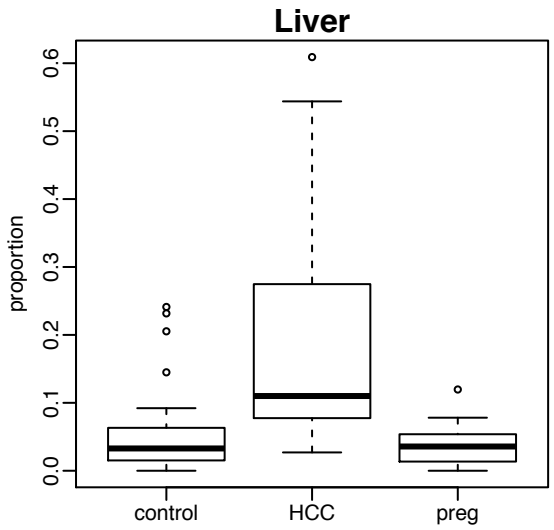


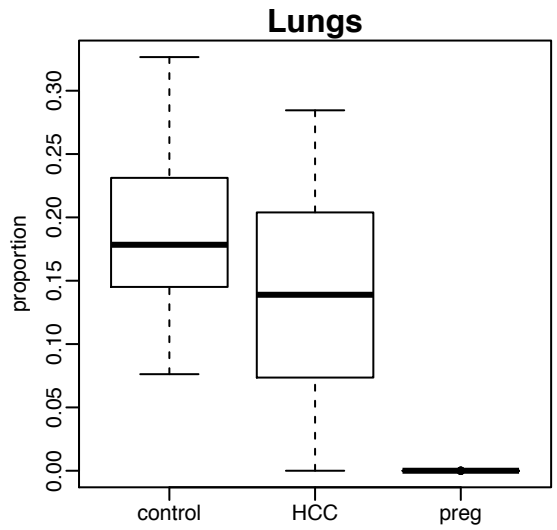

**Pancreas cor=0.42**




**Colon cor=0.378**




Liver
proportion
0.0
0.1
0.2
0.3
0.4
0.5
0.6
control
HCC
preg


Lungs
proportion
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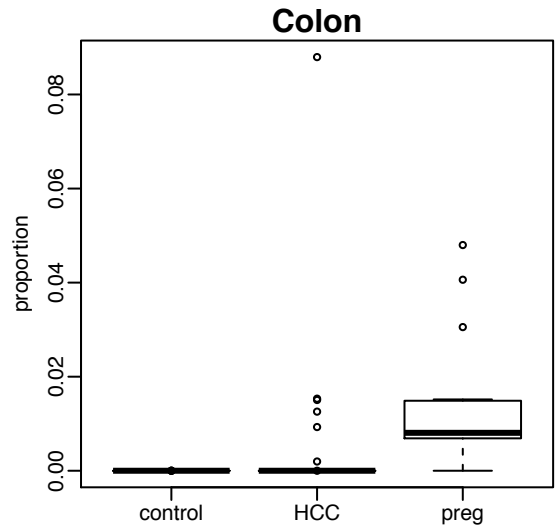
0.25
0.30
control
HCC
preg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control
HCC
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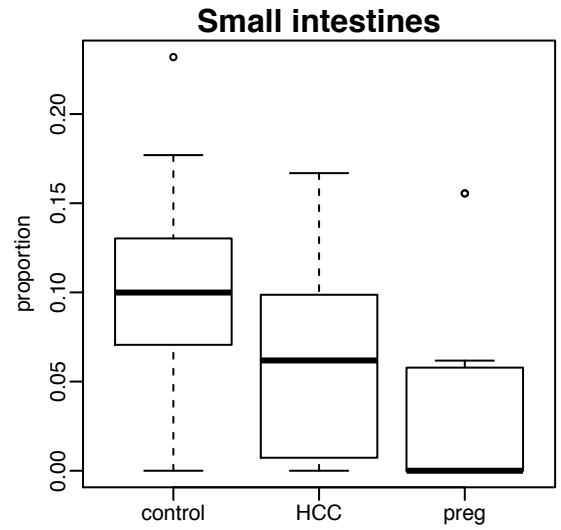
Small intestines
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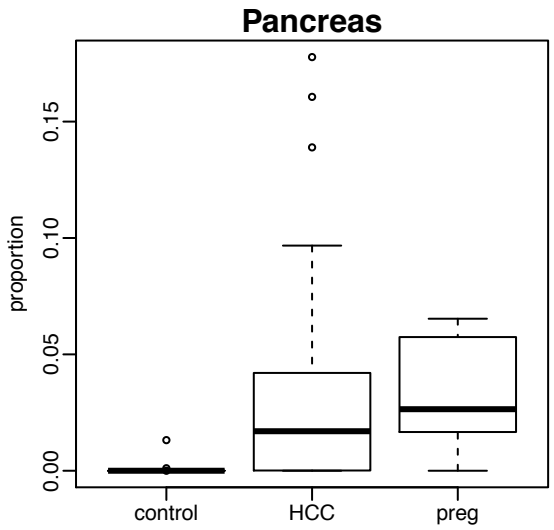
control
HCC
preg


Pancreas
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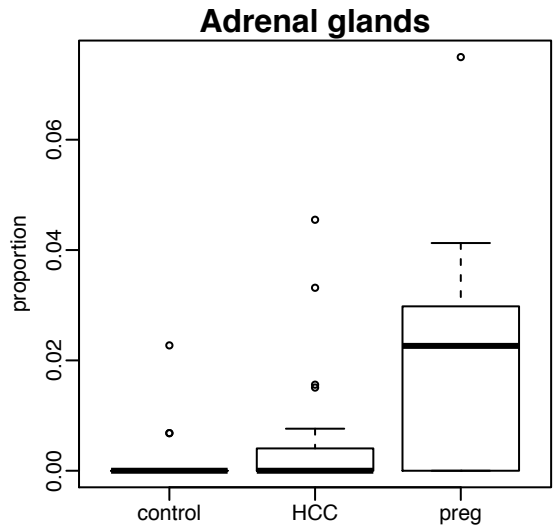
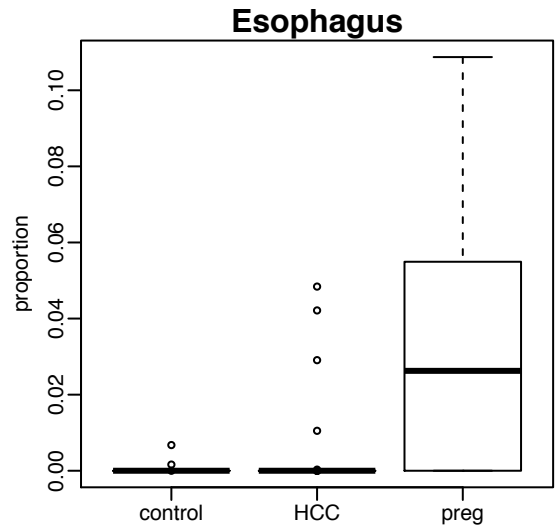
control
HCC
preg


Adrenal glands
proportion
0.00
0.02
0.04
0.06
control
HCC
preg


Esophagus
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0.02
0.04
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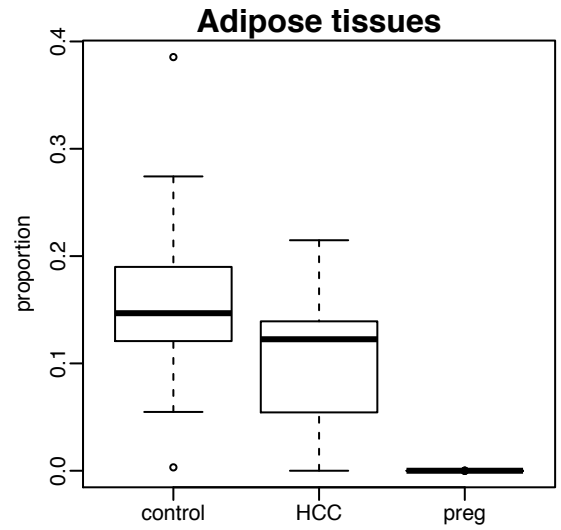
0.08
0.10
control
HCC
preg


Adipose tissues
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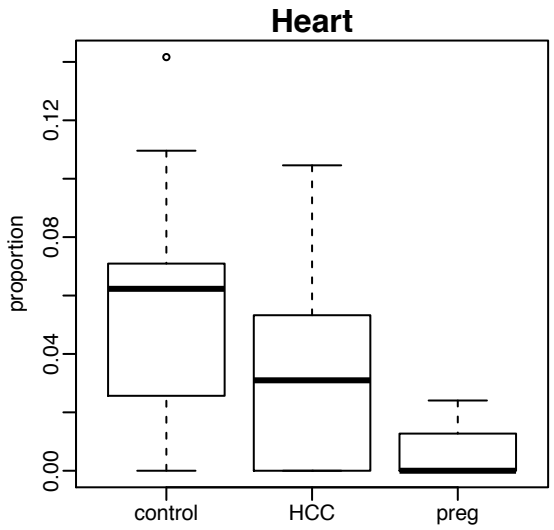
control
HCC
preg


Heart
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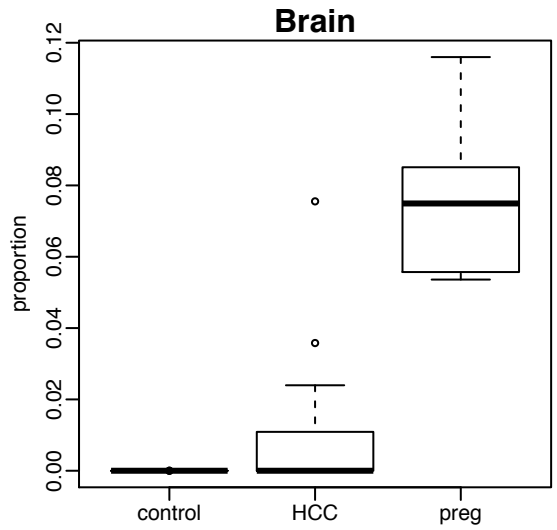
control
HCC
preg


Brain
proportion
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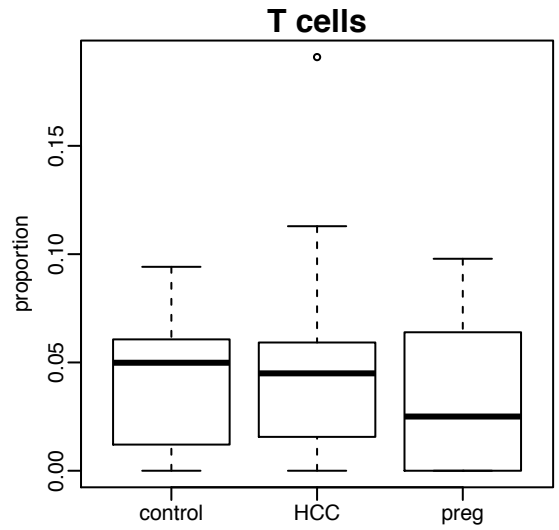
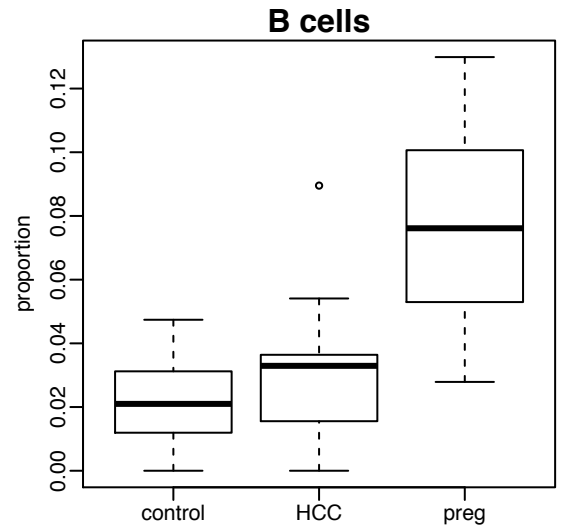
0.02
0.04
0.06
0.08
0.10
0.12
control
HCC
preg


T cells
proportion
0.00
0.05
0.10
0.15
control
HCC
preg


B cells
proportion
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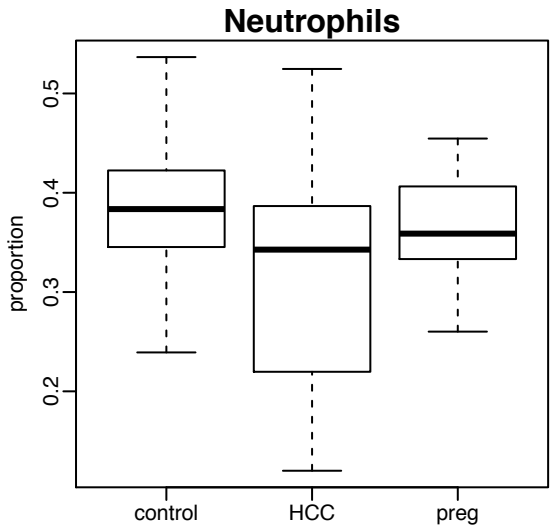
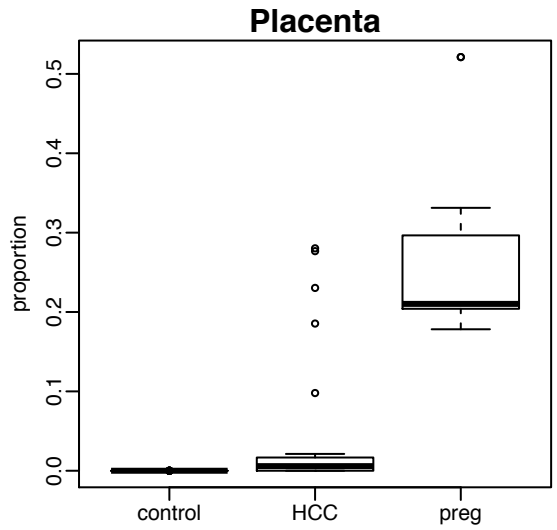
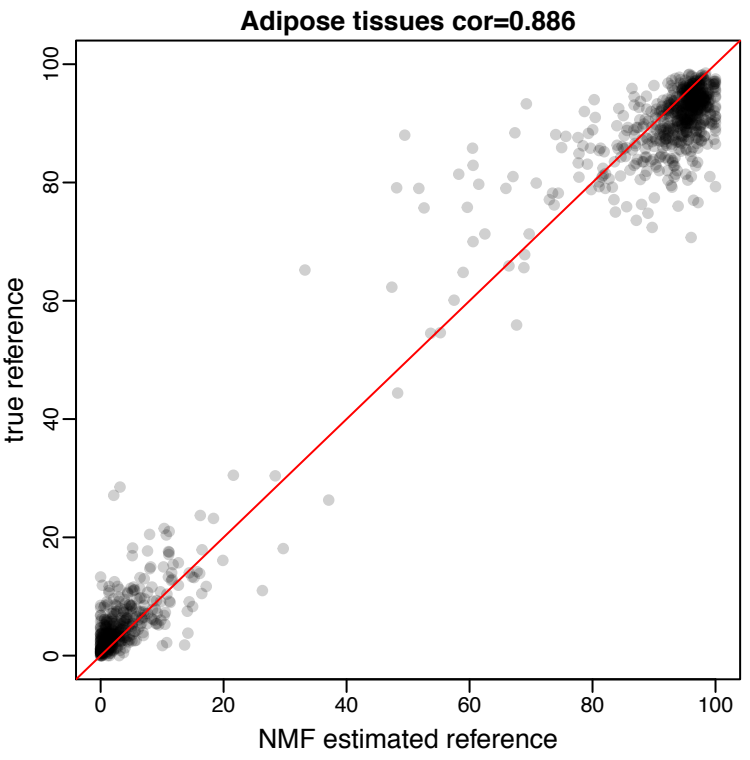
0.02
0.04
0.06
0.08
0.10
0.12
control
HCC
preg

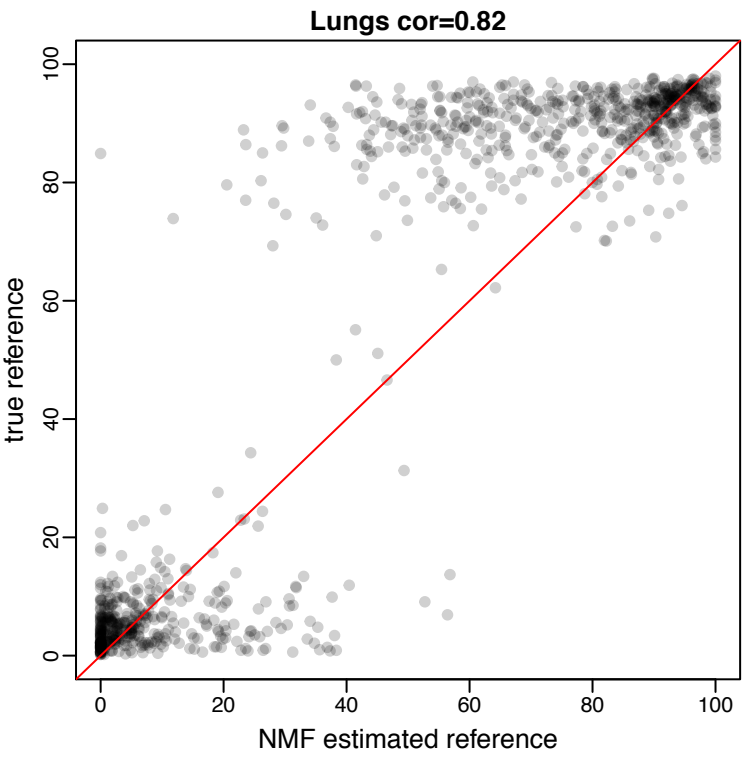

Neutrophils
proportion
0.2
0.3
0.4
0.5
control
HCC
preg


Placenta
proportion
0.0
0.1
0.2
0.3
0.4
0.5
control
HCC
preg

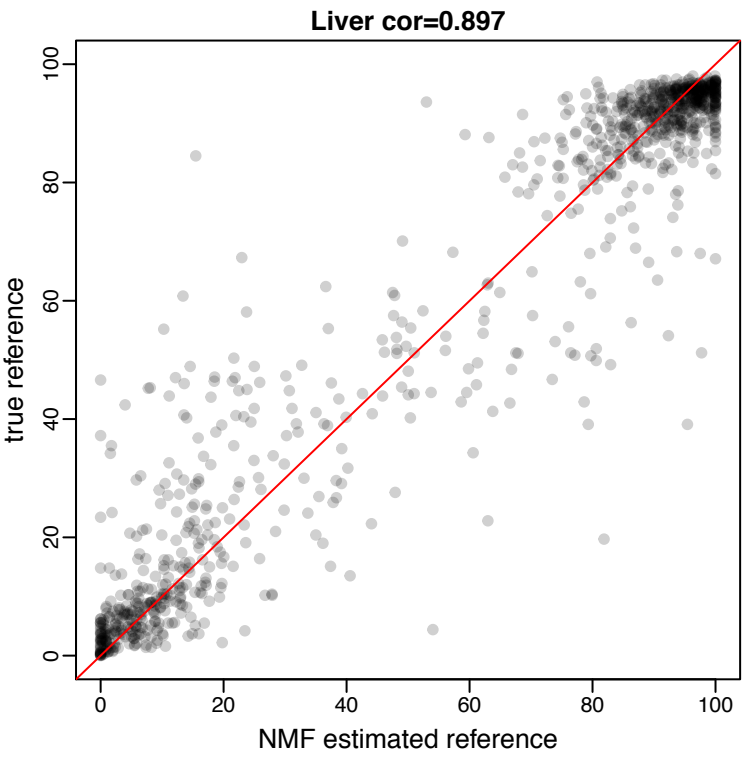
**Adipose tissues cor=0.886**



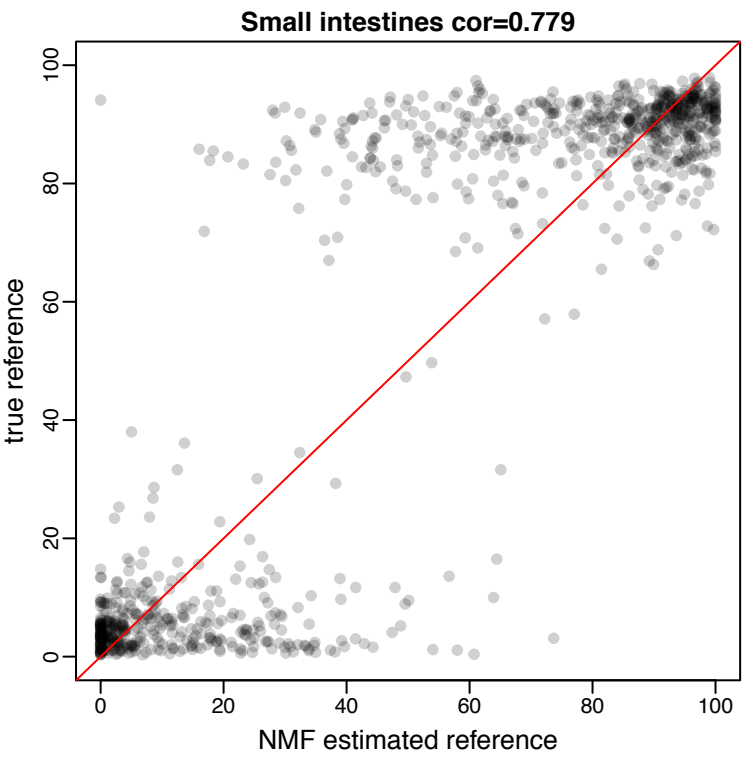

**Lungs cor=0.82**



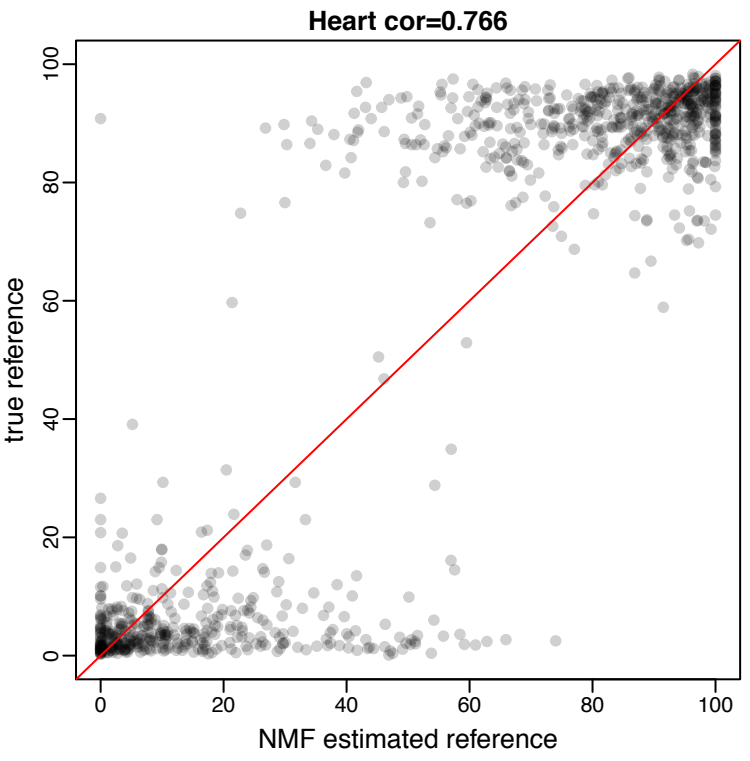

**Liver cor=0.897**



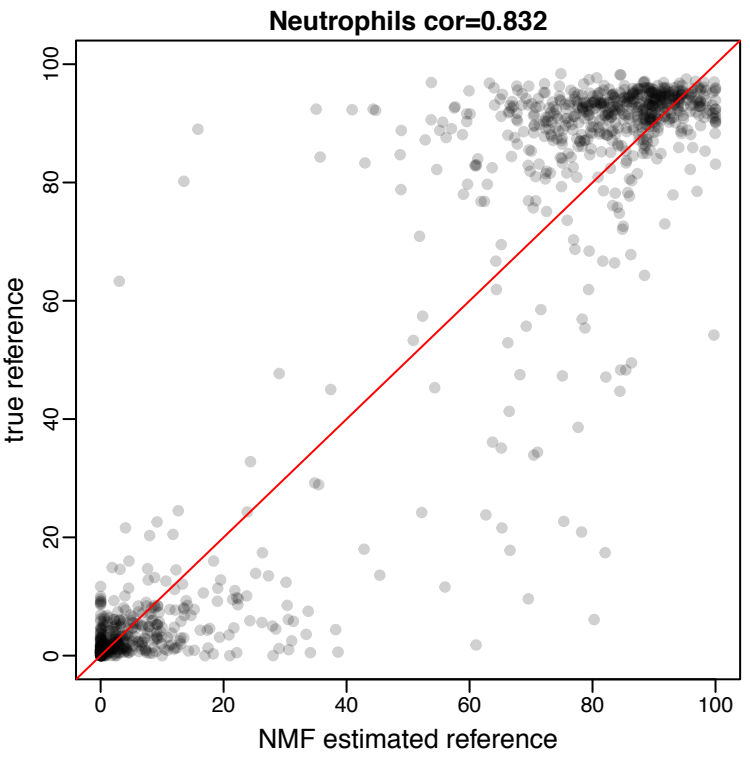

**Small intestines cor=0.779**



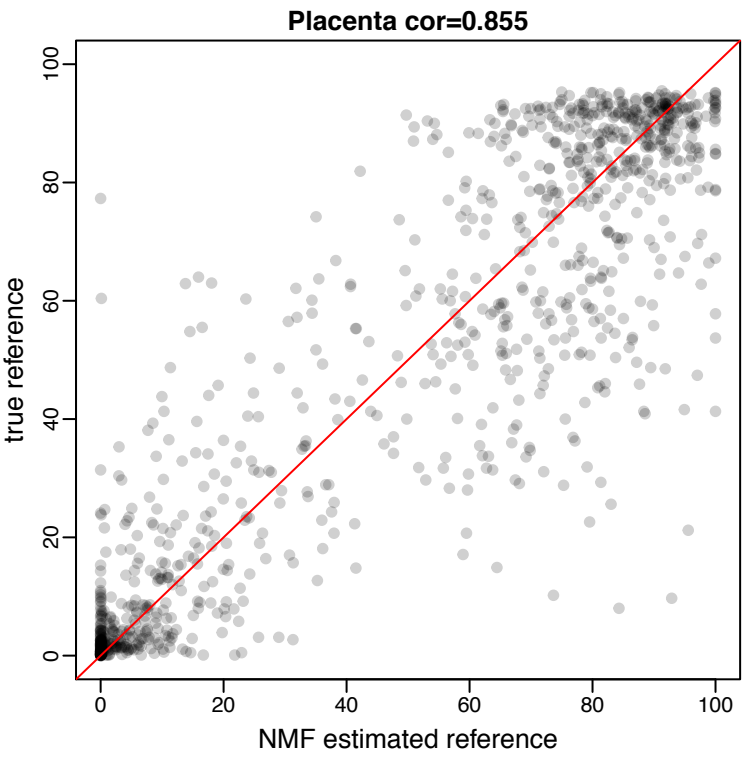

**Heart cor=0.766**



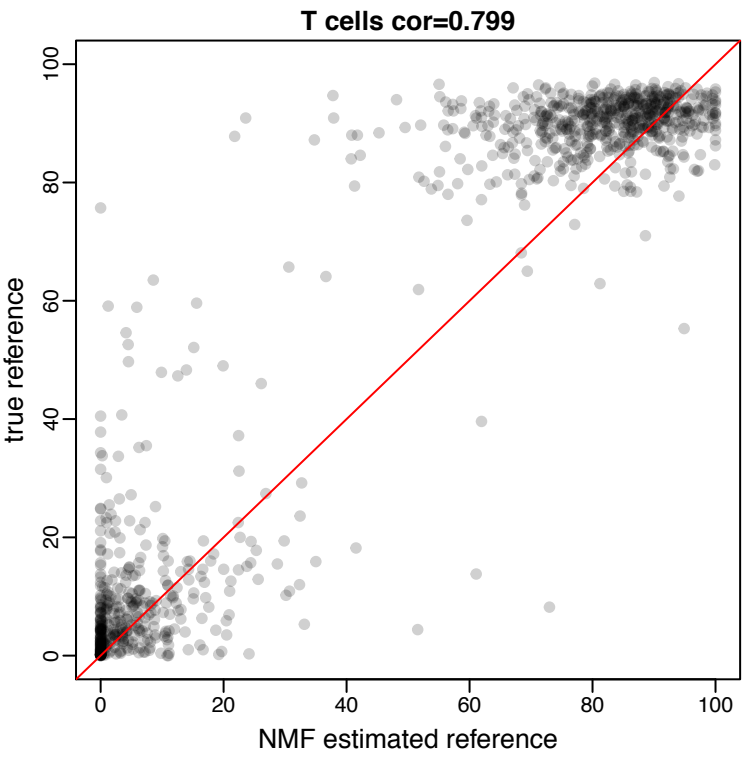

**Neutrophils cor=0.832**



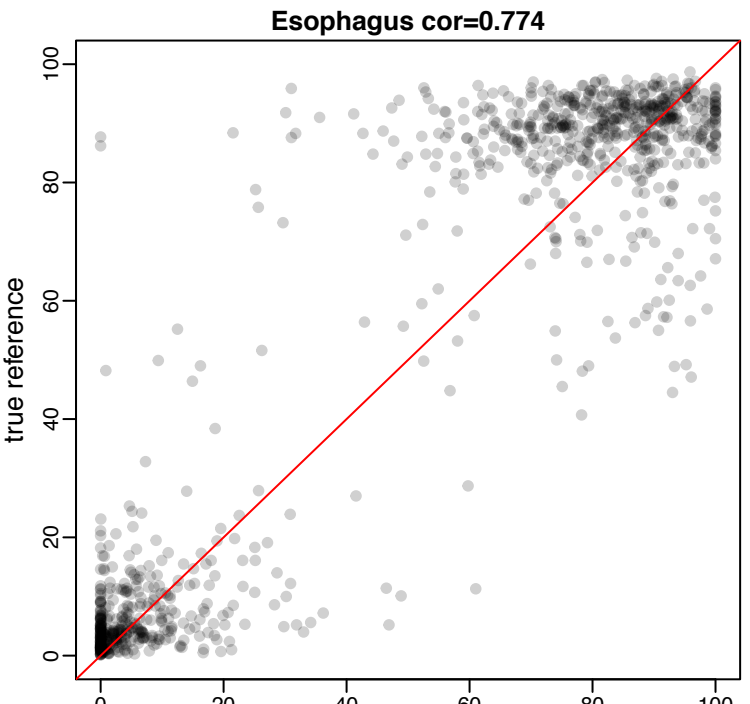

**Placenta cor=0.855**



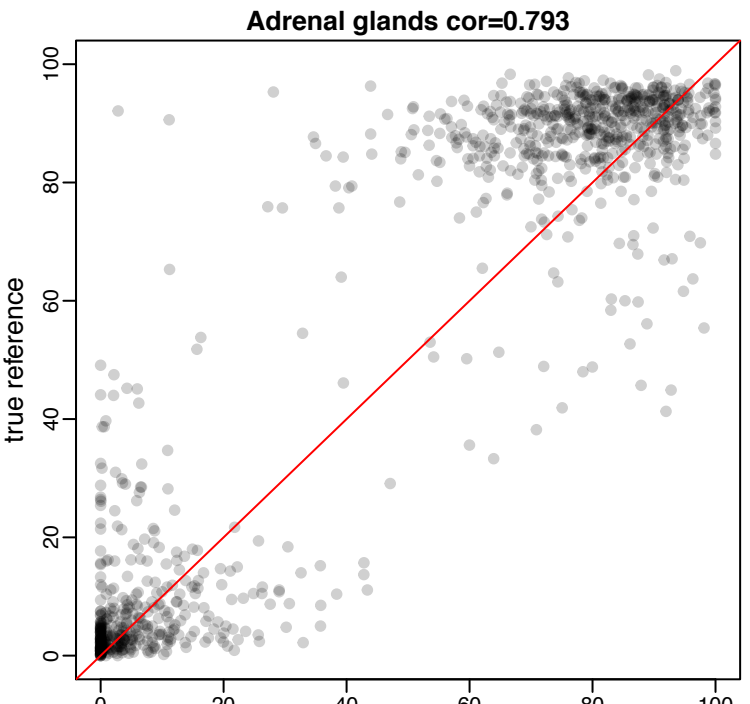

**T cells cor=0.799**



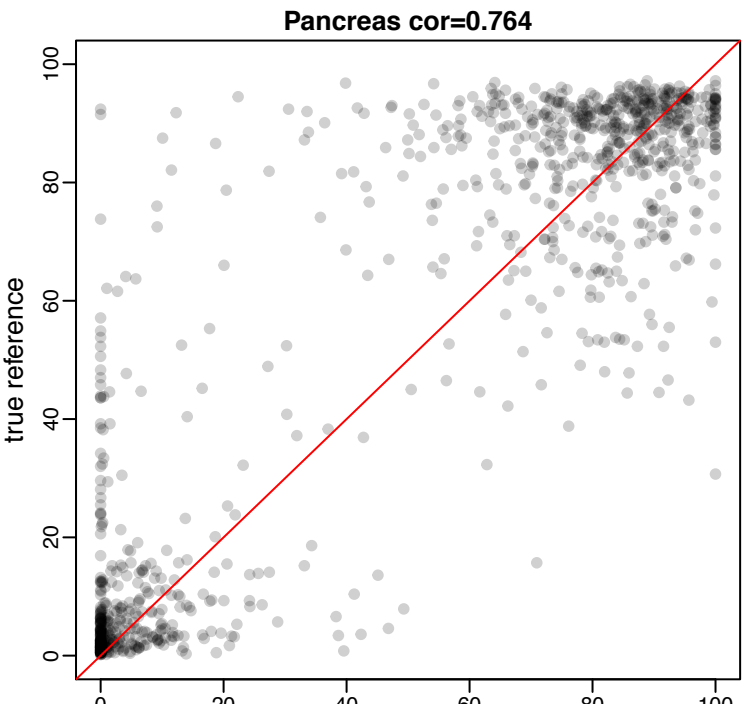

**Esophagus cor=0.774**



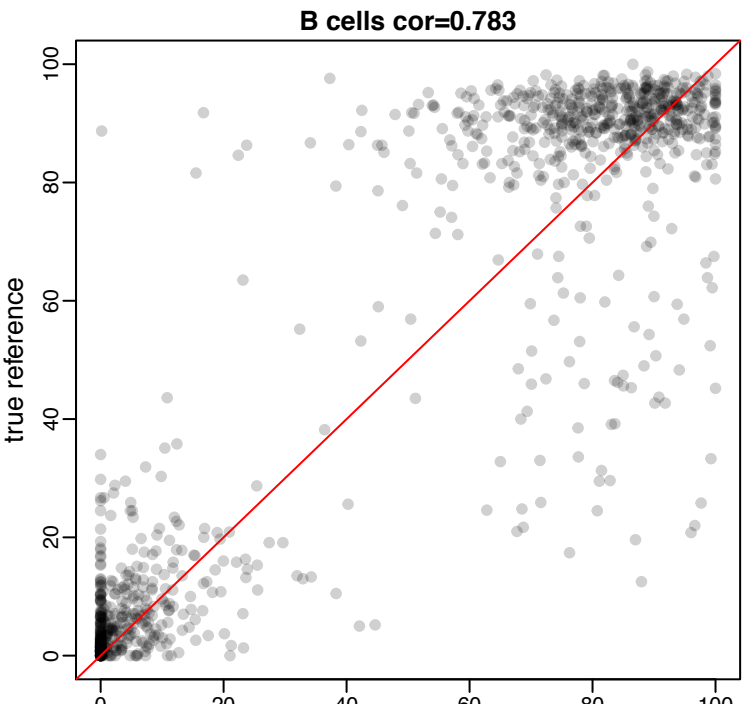

**Adrenal glands cor=0.793**



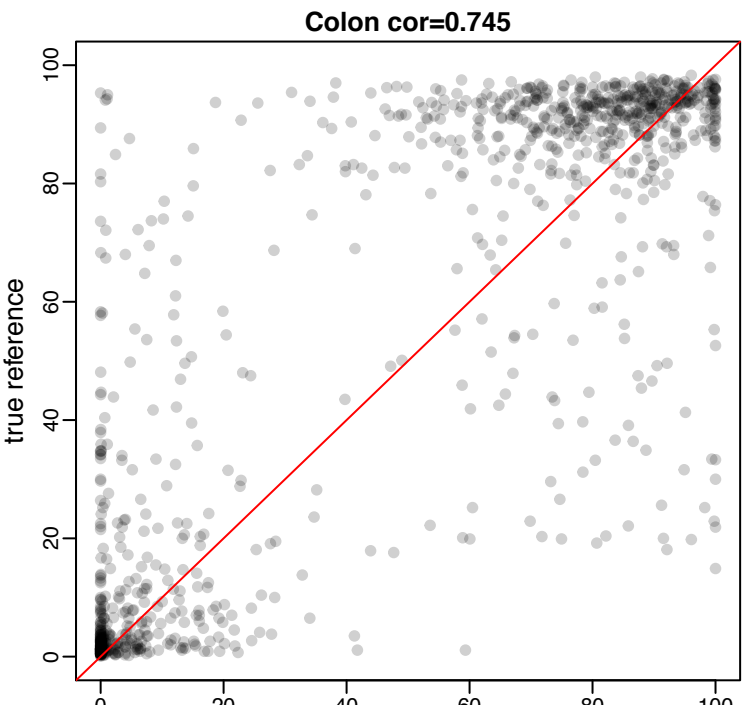

**Pancreas cor=0.764**

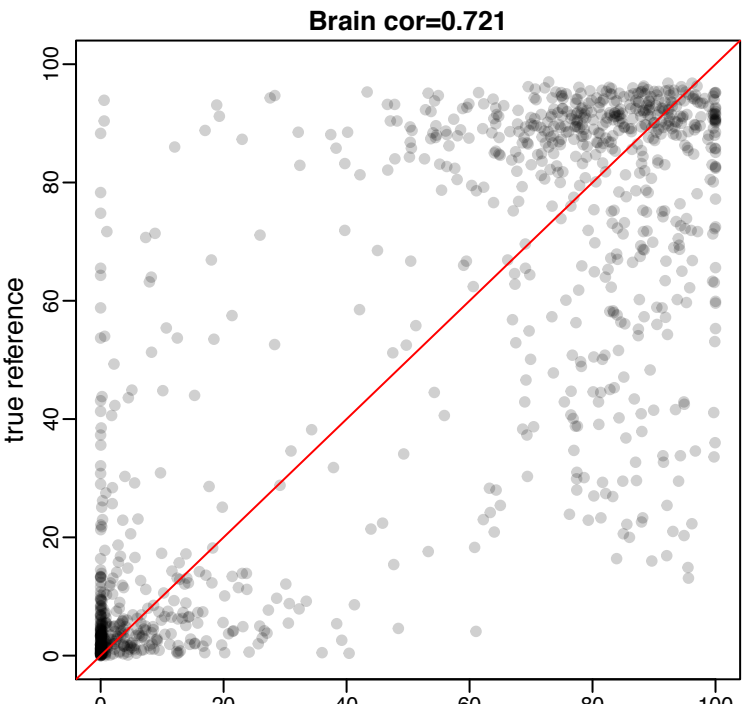



**B cells cor=0.783**




**Colon cor=0.745**




**Brain cor=0.721**