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Supplement: A tail-based test to detect differential expression in RNA-sequencing data

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Section A

In the third set of simulation studies, we generated raw counts of gene-level expression data. We fitted edgeR, DESeq2, and Limma+voom using raw count data and converted the gene-level measurements to exon-level Log2-RPKM measurement to fit our methods.

For a gene g, its mean expression level γ_g was generated from an exponential distribution with mean 100. We generated covariate C_i from a normal distribution $N(2.5, 0.5^2)$. Then we let the regulating factor $\delta_g = 1$ for the normal group. We generated the count data for N_{gj} of gene g for subject i from a negative binomial distribution.

We investigated the following two scenarios.
Scenario *DE-3* (null scenario): $\delta_g = 1$ for all genes in the cancer group.
Scenario *DE-4* (alternative scenario): For the cancer group, $\delta_g = 1 + X_g$ for 5% of the

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Table 1. FPRs at the nominal level of 5% for scenario *DE-3*. The values in the table are percentages.

Scenario *DE-3*	Nominal Level	5%			
Gene Length	Sample Size	TTS	$edgeR$	$DESeq2$	$Limma$
5	40	5.60	4.34	5.04	4.94
	60	5.38	4.30	5.00	5.06
	80	5.64	4.62	5.08	5.10
	100	5.34	4.50	5.40	4.88
10	40	5.48	4.50	5.08	4.96
	60	5.38	4.76	5.46	4.96
	80	5.16	4.52	5.02	5.00
	100	5.36	4.50	4.92	4.88
30	40	5.26	3.98	4.74	4.54
	60	5.60	4.22	5.04	4.94
	80	5.02	4.20	4.82	4.80
	100	4.50	3.96	4.34	4.52

expression data to simulate up-regulated DE genes and $\delta_g = (1 + X_g)^{-1}$ for 5% of the expression data to simulate down-regulated DE genes, where X_g follows an exponential distribution with rate=2. Let $\delta_g = 1$ for the remaining 90% of the expression data to simulate non-DE genes.

In each scenario, we ran $5,000$ Monte Carlo samples. For the quantile related test, we used $\tau = 0.5$ for testing both scenarios at a nominal level of 5%.
To convert the gene-level count data to exon-level count data, we allocated the count of gene g from subject i to m_i exon regions with probabilities p_1^g, ..., p_j^g and $\sum_{j=1}^{m_i} p_j^g = 1$. Following the allocation method of Lin and Sun [56], we generated p_j^g by $p_j^g = P_j^g / \sum_{j=1}^{m_i} P_j^g$, where P_j^g follows the standard exponential distribution. The majority of the reads were mapped to 1 or 2 exon regions when $k \leq 5$.

The results for scenario DE-3 are shown in Table 1. The FPRs of the four tests considered here are all around the nominal level.

The results for scenario DE-4 are shown in Table 2. All methods have correct FPRs at the appropriate level and achieve similar TPRs for various exon lengths and sample sizes. Such results demonstrate that the proposed test is robust and comparable with $edgeR$, $DESeq2$, and $Limma$ even when the data do not follow our assumed model.

Table 2. FPRs and TPRs at the nominal level of 5% for scenarios *DE-4*. The values in the table are percentages.

Scenario *DE-4*		FPR				TPR			
Gene Length	Sample Size	TTS	$edgeR$	$DESeq2$	$Limma$	TTS	$edgeR$	$DESeq$	$Limma$
5	40	5.60	4.29	5.53	5.60	60.80	60.20	61.80	60.40
	60	5.47	4.69	5.36	5.84	72.60	71.80	73.60	71.00
	80	5.49	4.73	5.33	5.00	75.80	76.60	76.80	75.40
	100	5.33	4.58	5.29	5.51	79.60	78.80	80.20	77.80
10	40	5.69	4.36	5.22	5.18	62.00	61.40	63.60	59.60
	60	4.93	4.09	4.71	5.02	71.60	72.00	72.00	70.60
	80	5.40	4.40	5.07	5.69	78.80	77.80	79.00	76.80
	100	5.53	4.87	5.38	5.73	80.20	80.20	80.40	79.80
30	40	5.47	4.33	5.18	5.07	65.40	63.00	65.00	61.60
	60	4.98	4.47	4.87	5.56	71.80	70.80	72.00	69.60
	80	5.00	4.51	4.87	5.18	77.00	75.40	76.80	76.40
	100	5.44	4.80	5.38	5.04	77.80	78.00	78.00	77.00

Section B

We list Lemma 1, proof of Lemma 1, and proof of Theorem 1 in this section.

Lemma 1. *If* $\lim_{n_1,n_0\to\infty}(n_1+n_0)^{-1}U_f$ *exists,* $E\|C_i\|_1^3<\infty$*, the number of exon region* m_i *is some fixed number, and* f_{ij} *are uniformly bounded away from 0 and infinity, then we have the Bahadur representation on* $\hat{\gamma}(\tau)$,

$$\hat{\boldsymbol{\gamma}}(\tau)-\boldsymbol{\gamma}(\tau)=U_f^{-1}\sum_i m_i^{-1}\sum_{j=1}^{m_i}\boldsymbol{C}_i^*\psi_\tau(e_{ij}(\tau))+o_p((n_0+n_1)^{-\frac{1}{2}}),$$

and the representation of $\bar{e}_\tau(d)$,

$$\bar{e}_\tau(d)=(\sum_{D_i=d}\sum_j^{m_i}e_{ij}^+(\tau))^{-1}\sum_{D_i=d}\sum_j^{m_i}e_{ij}(\tau)e_{ij}^+(\tau)+o_p((N_0+N_1)^{-\frac{1}{2}}).$$

Proof of Lemma 1 The Bahadur representation of the $(K+2)\times 1$ parameter estimator $\hat{\boldsymbol{\beta}}(\tau)$, according to Koenker [42] equation 4.4, can be written as

$$\hat{\boldsymbol{\beta}}(\tau)-\boldsymbol{\beta}(\tau)=D_\beta^{-1}(n_0+n_1)^{-1}\sum_i m_i^{-1}\sum_{j=1}^{m_i}\mathbf{x}_i{}^*\psi_\tau(e_{ij}(\tau))+(n_0+n_1)^{-1/2}R_n,$$

where diagonal matrix $D_\beta=\lim_{(n_0+n_1)\to\infty}(n_0+n_1)^{-1}\sum_i\hat{f}_{n(0)}\mathbf{x_i^*}\mathbf{x_i^*}^{\mathbf{T}}$, $\hat{f}_{n(0)}$ is the estimated conditional density function of e_{ij} given $(D_i,\boldsymbol{C}_i)$ evaluated at 0, $\mathbf{x}_i^*=(1,D_i^*,\mathbf{C_i}^*)$,$R_n=o_p(1)$, and $\psi_\tau(e_{ij}(\tau))=\tau-e_{ij}^-$.

Then, as $n_0,n_1\to\infty$, $\sum_i\hat{f}_{n(0)}\mathbf{x}_i^*\mathbf{x}_i^{*T}=\begin{pmatrix}\sum_i\hat{f}_{n(0)} & 0 & 0\\ 0 & \sum_i\hat{f}_{n(0)}D_i^{*2} & 0\\ 0 & 0 & \sum_i\hat{f}_{n(0)}\boldsymbol{C}_i^*\boldsymbol{C}_i^{*T}\end{pmatrix}$,

so the diagonal matrix $D_\beta=\begin{pmatrix}\frac{\sum_i\hat{f}_{n(0)}}{(n_0+n_1)} & 0 & 0\\ 0 & \frac{\sum_i\hat{f}_{n(0)}D_i^{*2}}{(n_0+n_1)} & 0\\ 0 & 0 & \frac{\sum_i\hat{f}_{n(0)}\boldsymbol{C}_i^*\boldsymbol{C}_i^{*T}}{(n_0+n_1)}\end{pmatrix}+o_p(1).$

Using the right bottom corner of D_β^{-1}, we can obtain the following,

$\hat{\boldsymbol{\gamma}}(\tau)-\boldsymbol{\gamma}(\tau)$

$=\left[\left\{\frac{\sum_i\hat{f}_{n(0)}\boldsymbol{C}_i^*\boldsymbol{C}_i^{*T}}{(n_0+n_1)}\right\}^{-1}+o_p(1)\right](n_0+n_1)^{-1}\sum_i m_i^{-1}\sum_{j=1}^{m_i}\boldsymbol{C}_i^*\psi_\tau(e_{ij}(\tau))+$

$o_p((n_0+n_1)^{-\frac{1}{2}})$.

$=\left(\sum_i\hat{f}_{n(0)}\boldsymbol{C}_i^*\boldsymbol{C}_i^{*T}\right)^{-1}\sum_i m_i^{-1}\sum_{j=1}^{m_i}\boldsymbol{C}_i^*\psi_\tau(e_{ij}(\tau))+o_p((n_0+n_1)^{-\frac{1}{2}})$.

The last equality follows from the central Limit Theorem for $\sum_i m_i^{-1}\sum_{j=1}^{m_i}\boldsymbol{C}_i^*\psi_\tau(e_{ij}(\tau))$

. The proof of the second part of Lemma 2.1 is equivalent to proving

$$\left\{\sum_{D_i=d} m_i^{-1}\sum_j^{m_i}\hat{e}_{ij}^{+}(\tau)\right\}^{-1}\sum_{D_i=d} m_i^{-1}\sum_j^{m_i} e_i(\tau)\hat{e}_{ij}^{+}(\tau)$$
$$-\{n_d(1-\tau)\}^{-1}\sum_{D_i=d} m_i^{-1}\sum_j^{m_i} e_{ij}(\tau)e_{ij}^{+}(\tau)$$
$$=o_p((n_0+n_1)^{-\frac{1}{2}})$$

Then, we need to verify the first and second equations below:

$$n_d^{-1}\sum_{D_i=d} m_i^{-1}\sum_j^{m_i}\hat{e}_{ij}^{+}(\tau)=1-\tau+o_p((n_0+n_1)^{-\frac{1}{2}})$$

$$n_d^{-1}\sum_{D_i=d} m_i^{-1}\sum_j^{m_i} e_{ij}(\tau)\left\{\hat{e}_{ij}^{+}(\tau)-e_{ij}^{+}(\tau)\right\}=o_p((n_0+n_1)^{-\frac{1}{2}}).$$

We can demonstrate the first equation by the second inequality in corollary 2.1 of Koenker[42], $n_d^{-1}\sum_{D_i=d} m_i^{-1}\sum_j^{m_i}\hat{e}_{ij}^{+}(\tau)\le 1-\tau\le n_d^{-1}\sum_{D_i=d} m_i^{-1}\sum_j^{m_i}\hat{e}_{ij}^{+}(\tau)+n_d^{-1}p$; hence, $n_d^{-1}\sum_{D_i=d} m_i^{-1}\sum_j^{m_i}\hat{e}_{ij}^{+}(\tau)=(1-\tau)+o_p(n_d^{-1})=(1-\tau)+o_p((n_1+n_0)^{-1/2})$.

To prove the second equation, we can use lemma 4.6 of He and Shao[33] and lemma 11.2 of Owen[71]. For more details, refer to Koenker[42] and He and Shao[33].

Proof of Theorem 1 According to Lemma 1, and $\delta(\tau)=0$, under the null hypothesis, we can write

$$T_\tau^{TTS}(n_1,n_0)=\left\{\sum_{D_i=1}\sum_{j=1}^{m_i} e_{ij}(\tau)e_{ij}^{+}(\tau)/N_1-\sum_{D_i=0}\sum_{j=1}^{m_i} e_{ij}(\tau)e_{ij}^{+}(\tau)/N_0\right\}(1-\tau)^{-1}$$
$$-\{\bar{\boldsymbol{C}}_\tau^T(1)-\bar{\boldsymbol{C}}_\tau^T(0)\}U_f^{-1}\sum_{i=1}^{n} m_i^{-1}\sum_{j=1}^{m_i}\boldsymbol{C}_i^{*}\psi_\tau(e_{ij}(\tau))$$
$$+o_p((n_0+n_1)^{-1/2})$$
$$=T_\tau^{*}(n_1,n_0)+o_p((n_0+n_1)^{-1/2}).$$

where

$$T^*_\tau(n_1,n_0) = \left\{\sum_{D_i=1}\sum_{j=1}^{m_i} e_{ij}(\tau)e^+_{ij}(\tau)/N_1 - \sum_{D_i=0}\sum_{j=1}^{m_i} e_{ij}(\tau)e^+_{ij}(\tau)/N_0\right\}(1-\tau)^{-1}$$
$$-\{\bar{\boldsymbol{C}}^T_\tau(1) - \bar{\boldsymbol{C}}^T_\tau(0)\}U_f^{-1}\sum_{i=1}^{n} m_i^{-1}\sum_{j=1}^{m_i}\boldsymbol{C}^*_i\psi_\tau(e_{ij}(\tau)).$$

Under the null hypothesis, the mean and variance of the test statistics are

$$E(T^*_\tau(n_1,n_0)) = \left\{\sum_{D_i=1}\sum_{j=1}^{m_i} E(e_{ij}(\tau)e^+_{ij})/N_1 - \sum_{D_i=0}\sum_{j=1}^{m_i} E(e_{ij}(\tau)e^+_{ij})/N_0\right\}(1-\tau)^{-1}$$
$$= (1-\tau)^{-1}E(e_{ij}(\tau)e^+_{ij})(1-1) = 0.$$

$$
\begin{aligned}
&Var(T_\tau^*(n_1,n_0)) = \\
&(1-\tau)^{-2}(V_1/N_1^2 + V_0/N_0^2) \\
&+\left\{\bar{\boldsymbol{C}}_\tau^T(1) - \bar{\boldsymbol{C}}_\tau^T(0)\right\} U_f^{-1} \left\{\sum_i m_i^{-2} \sum_{j=1}^{m_i} \boldsymbol{C}_i^* \boldsymbol{C}_i^{*T} \tau(1-\tau)\right\} U_f^{-1} \left\{\bar{\boldsymbol{C}}_\tau(1) - \bar{\boldsymbol{C}}_\tau(0)\right\} \\
&+\left\{\bar{\boldsymbol{C}}_\tau^T(1) - \bar{\boldsymbol{C}}_\tau^T(0)\right\} U_f^{-1} \left\{\sum_i m_i^{-2} \sum_{j\neq j'} \boldsymbol{C}_i^* \boldsymbol{C}_i^{*T} (\zeta-\tau^2)\right\} U_f^{-1} \left\{\bar{\boldsymbol{C}}_\tau(1) - \bar{\boldsymbol{C}}_\tau(0)\right\} \\
&+(1-\tau)^{-1} \left\{\sum_{D_i=1} \sum_{j=1}^{m_i} e_{ij}(\tau) e_{ij}^+(\tau)/N_1\right\} \left\{\bar{\boldsymbol{C}}_\tau^T(1) - \bar{\boldsymbol{C}}_\tau^T(0)\right\} \times \\
&U_f^{-1} \sum_{D_i=1}^{n} m_i^{-1} \sum_{j=1}^{m_i} \boldsymbol{C}_i^* \psi_\tau(e_{ij}(\tau)) \\
&-(1-\tau)^{-1} \left\{\sum_{D_i=0} \sum_{j=1}^{m_i} e_{ij}(\tau) e_{ij}^+(\tau)/N_0\right\} \left\{\bar{\boldsymbol{C}}_\tau^T(1) - \bar{\boldsymbol{C}}_\tau^T(0)\right\} \times \\
&U_f^{-1} \sum_{D_i=0}^{n} m_i^{-1} \sum_{j=1}^{m_i} \boldsymbol{C}_i^* \psi_\tau(e_{ij}(\tau)) \\
&-(1-\tau)^{-1} \left\{\bar{\boldsymbol{C}}_\tau^T(1) - \bar{\boldsymbol{C}}_\tau^T(0)\right\} U_f^{-1}/N_1 \sum_{D_i=1}^{n} \sum_{j=1}^{m_i} \boldsymbol{C}_i^* m_i^{-1} e_{ij} e_{ij}^+ \psi_\tau(e_{ij}(\tau)) \\
&+(1-\tau)^{-1} \left\{\bar{\boldsymbol{C}}_\tau^T(1) - \bar{\boldsymbol{C}}_\tau^T(0)\right\} U_f^{-1}/N_0 \sum_{D_i=0}^{n} \sum_{j=1}^{m_i} \boldsymbol{C}_i^* m_i^{-1} e_{ij} e_{ij}^+ \psi_\tau(e_{ij}(\tau)) \\
&= (1-\tau)^{-2}(V_1/N_1^2 + V_0/N_0^2) \\
&+\left\{\bar{\boldsymbol{C}}_\tau^T(1) - \bar{\boldsymbol{C}}_\tau^T(0)\right\} U_f^{-1} \left[\sum_i m_j^{-2} \left\{\sum_{k=1}^{m_j} \boldsymbol{C}_i^* \boldsymbol{C}_i^{*T} \tau(1-\tau) + \sum_{j\neq j'} \boldsymbol{C}_i^* \boldsymbol{C}_i^{*T} (\zeta-\tau^2)\right\}\right] \times \\
&U_f^{-1} \left\{\bar{\boldsymbol{C}}_\tau(1) - \bar{\boldsymbol{C}}_\tau(0)\right\} \\
&-(1-\tau)^{-1} \left\{\bar{\boldsymbol{C}}_\tau^T(1) - \bar{\boldsymbol{C}}_\tau^T(0)\right\} U_f^{-1}/N_1 \times \\
&\left\{\sum_{D_i=1}^{n} \sum_{j_1=1}^{m_i} \sum_{j_2=1}^{m_i} \boldsymbol{C}_i^* m_i^{-1} e_{ij_1} e_{ij_1}^+ \psi_\tau(e_{ij_2}(\tau)) - \sum_{D_i=1}^{n} \sum_{j_1=1}^{m_i} e_{ij_1} e_{ij_1}^+ \sum_{j_2=1}^{m_i} m_i^{-1} \boldsymbol{C}_i^* \psi_\tau(e_{ij_2}(\tau))\right\} \\
&+(1-\tau)^{-1} \left\{\bar{\boldsymbol{C}}_\tau^T(1) - \bar{\boldsymbol{C}}_\tau^T(0)\right\} U_f^{-1}/N_0 \times \\
&\left\{\sum_{D_i=0}^{n} \sum_{j_1=1}^{m_i} \sum_{j_2=1}^{m_i} \boldsymbol{C}_i^* m_i^{-1} e_{ij_1} e_{ij_1}^+ \psi_\tau(e_{ij_2}(\tau)) - \sum_{D_i=0}^{n} \sum_{j_1=1}^{m_i} e_{ij_1} e_{ij_1}^+ \sum_{j_2=1}^{m_i} m_i^{-1} \boldsymbol{C}_i^* \psi_\tau(e_{ij_2}(\tau))\right\}
\end{aligned}
$$

where

$$V_d = \sum_{D_i=d} \sum_{j=1}^{m_i} var(e_{ij}e_{ij}^{+}) + \sum_{D_i=d} \sum_{j \neq j'} cov(e_{ij}e_{ij}^{+}, e_{ij'}e_{ij'}^{+}),$$

which can be estimated by s_{n_0,n_1}^2.

$$\begin{aligned}
s_{n_0,n_1}^2 &= (1-\tau)^{-2} \left\{ V_1 / \left(\sum_{D_i=1} m_i \right)^2 + V_0 / \left(\sum_{D_i=0} m_i \right)^2 \right\} \\
&+ \left\{ \bar{\boldsymbol{C}}_\tau^T(1) - \bar{\boldsymbol{C}}_\tau^T(0) \right\} U_f^{-1} \left[\sum_i m_j^{-2} \left\{ \sum_{k=1}^{m_j} \boldsymbol{C}_i^* \boldsymbol{C}_i^{*T} \tau(1-\tau) + \sum_{j \neq j'} \boldsymbol{C}_i^* \boldsymbol{C}_i^{*T} (\zeta - \tau^2) \right\} \right] \\
&\times U_f^{-1} \left\{ \bar{\boldsymbol{C}}_\tau(1) - \bar{\boldsymbol{C}}_\tau(0) \right\} \\
&-(1-\tau)^{-1} \left\{ \bar{\boldsymbol{C}}_\tau^T(1) - \bar{\boldsymbol{C}}_\tau^T(0) \right\} U_f^{-1} / N_1 \\
&\times \left\{ \sum_{D_i=1}^{n} \sum_{j_1=1}^{m_i} \sum_{j_2=1}^{m_i} \boldsymbol{C}_i^* m_i^{-1} \hat{e}_{ij_1} \hat{e}_{ij_1}^{+} \tau - \sum_{D_i=1}^{n} \sum_{j_1=1}^{m_i} \hat{e}_{ij_1} \hat{e}_{ij_1}^{+} \sum_{j_2=1}^{m_i} m_i^{-1} \boldsymbol{C}_i^* \psi_\tau(\hat{e}_{ij_2}(\tau)) \right\} \\
&+(1-\tau)^{-1} \left\{ \bar{\boldsymbol{C}}_\tau^T(1) - \bar{\boldsymbol{C}}_\tau^T(0) \right\} U_f^{-1} / N_0 \\
&\times \left\{ \sum_{D_i=0}^{n} \sum_{j_1=1}^{m_i} \sum_{j_2=1}^{m_i} \boldsymbol{C}_i^* m_i^{-1} \hat{e}_{ij_1} \hat{e}_{ij_1}^{+} \tau - \sum_{D_i=0}^{n} \sum_{j_1=1}^{m_i} \hat{e}_{ij_1} \hat{e}_{ij_1}^{+} \sum_{j_2=1}^{m_i} m_i^{-1} \boldsymbol{C}_i^* \psi_\tau(\hat{e}_{ij_2}(\tau)) \right\}
\end{aligned}$$

By the central limit theorem, $T_\tau^*(n_1, n_0)$ is asymptotically normal with mean 0 and variance. Thus, by Lemma 1 and $T_\tau(n_1, n_0) - T_\tau^*(n_1, n_0) = o_p((n_0 + n_1)^{-1/2})$, we prove the asymptotic normality of the test statistic $T_\tau(n_1, n_0)$.

Section C

Tables 3, 4, 5, 6, 7, 8 list genes that are detected by TTS but not by the other methods, with the supporting medical literature.

Table 3. List of genes detected by TTS but missed by QRS_c

Test method	Gene list
QRS_c	$ADAMTS9$, $C3ORF21$, $MBD4$, $ZMAT3$, $FOXP1$, $GSK3B$ $PLD1$, $SIAH2$, $C3orf33$, $EHHADH$, $IQCB1$, $RPL14$ $BTLA$, $CCR5$, $DOCK3$, $CTNNB1$, $IGF2BP2$, $MYD88$ $PFKFB4$, $PIK3CB$, $VPRBP$, $TLR9$, VHL, $LRRN1$ $PAK2$, $EAF2$,TF, $VGLL4$, $RASSF1$, $FHIT$, $FLNB$
Reference	27,44,89,112,129,131 16,19,21,35,63,90 3,17,20,88,99,134 4,24,60,106,109,132 1,40,74,79,118,126,135

Table 4. List of genes detected by TTS but missed by LME

Test method	Gene list
LME	$ADAMTS9$, $C3orf33$, $CCR5$, $CTNNB1$, $EHHADH$, $FHIT$ $FLNB$, $GSK3B$, $IGF2BP2$, $IQCB1$, $PAK2$, $RPL14$ $SENP2$, $SIAH2$, $UBA3$, $VPRBP$, $VGLL4$
Reference	17,19,35,44,88,135 1,3,21,40,90,131 50,63,106,108,126

Table 5. List of genes detected by TTS but missed by $Limma$ and $edgeR$

Test method	Gene list
$Limma$	$ADAMTS9$, $C3orf33$, $CCR5$, $FHIT$, $GSK3B$, $IGF2BP2$ $PAK2$, $RABL3$, $RBM5$, $SETD2$, TF
Reference	3,17,35,44,131,135 40,79,93,105,127
$edgeR$	$CACNA2D3$, $CAMK1$, $CCR5$, $FBXL2$, $GSK3B$, $SETD2$ $SLC6A20$
Reference	15,17,52,54,105,131 101

Table 6. List of genes detected by TTS but missed by $DESeq2$, part 1

Gene list	$ABCC5$, $ABHD5$, $ACTL6A$, $AGTR1$ $ALDH1L1$, $ATP11B$, $ATP1B3$, ATR $B3GALNT1$, $BAP1$, $BCHE$, $BTLA$ $C3orf1$, $C3orf21$, $C3orf33$, $CACNA2D2$ $CACNA2D3$, $CAMK1$, $CBLB$, $CCDC37$ $CCR5$, $CD86$, $CDC25A$, $CDCP1$ $CHL1$, $CLDN18$, $COPB2$, $CSTA$ $CTDSPL$, $CTNNB1$, $CX3CR1$, $DCBLD2$ $DCUN1D1$, $DLEC1$, $DOCK3$, $DTX3L$, $DVL3$, $EAF2$, $EHHADH$, $EIF2A$ $EIF4A2$, $EIF4G1$, $EIF5A2$, $EPHB3$ $ETV5$, $FAM107A$, $FBXL2$, $FGD5$
Reference	19,34,110,118 29,66,70,92 5,58,68,77 7,19,99,103 12,35,116,129 51,52,54,96 17,18,31,114 9,25,59,84 9,81,83,88 47,98,122,134 11,37,85,120 15,24,73,130

Table 7. List of genes detected by TTS but missed by $DESeq2$, part 2

Gene list	$FHIT$, $FLNB$, $FNDC3B$, $FOXP1$ $FXR1$, $GATA2$, $GORASP1$, $GSK3B$ $HDAC11$, $HES1$, $HYAL1$, $HYAL2$ $IGF2BP2$, $IL17RD$, $IL17RE$, $IQCB1$ $IQSEC1$, $KIAA1524$, $LEPREL1$, $LIMD1$ $LMCD1$, LPP, $LRIG1$ $LRRN1$, LTF, $LZTFL1$, $MAGI1$, $MASP1$, $MBD4$, $MCM2$, $METTL6$ $MINA$, MME, $MYD88$, $MYLK$, $NEK10$ $NEK4$, $NISCH$, $NPRL2$ $OPA1$, $P2RY14$, $PAK2$, $PDCD6IP$ $PFKFB4$, $PIK3CB$, $PLD1$, $PLS1$
Reference	1,10,27,135 19,24,43,131 2,41,107 3,21,115 22,24,86,87 14,45,46 13,24,36,111 39,78,89,94 20,49,95,97 61,64,69,102 40,53,60,80,117 16,25,109 62,72,113

Table 8. List of genes detected by TTS but missed by $DESeq2$, part 3

Gene list	$POLQ$, $PTH1R$, $PTPRG$
	$RABL3$, $RAP2B$, $RASSF1$, $RFC4$
	$RNF7$, $RPL14$, $RPL22L1$, $RUVBL1$
	$RYBP$, $SATB1$, $SEMA3B$, $SENP2$
	$SETD2$, $SIAH2$, $SLC4A7$, $SLC6A20$
	$SLCO2A1$, $SMARCC1$, $SPCS1$, $TBL1XR1$, TF
	$TFRC$, $TGFBR2$,$THPO$, $THRB$, $TIGIT$
	TKT, $TLR9$, $TNFSF10$
	$TRAIP$, $TRIM59$, $UBA3$, $UBE2E2$
	$VGLL4$, VHL, $VPRBP$, $WWTR1$
	XPC, $ZMAT3$, $ZMYND10$
Reference	25,74,75,127
	48,67,90,123
	57,82,104,108
	28,63,101,105
	23,55,79,100,133
	8,38,48,121,125
	4,32,119
	24,50,91,124
	65,106,126,132
	29,112,128

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