Supplementary Information

RNA sequence and structure determinants of Pol III transcriptional termination in human cells

Matthew S. Verosloff[1,2], William K. Corcoran[1,2], Taylor B. Dolberg[2,3], David Z. Bushhouse[1,2], Joshua N. Leonard[2,3,*], Julius B. Lucks[2,3,*]

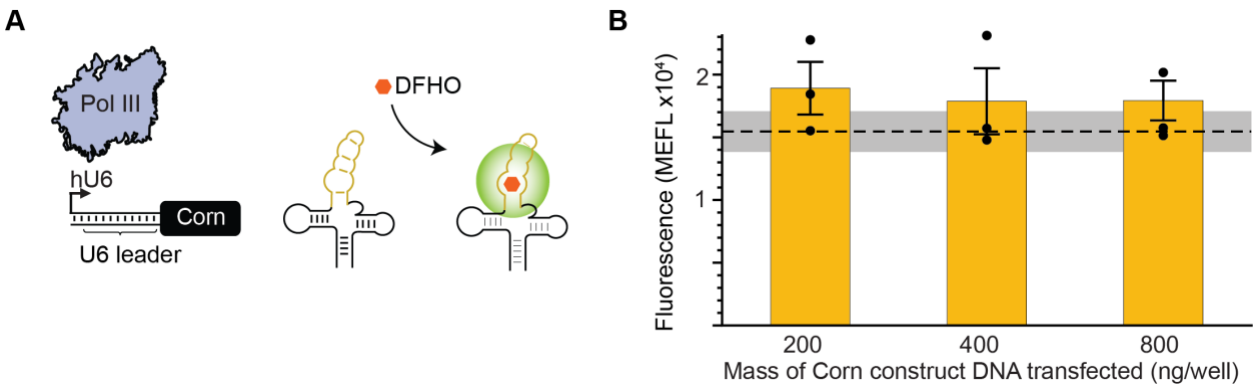
1 – Interdisciplinary Biological Sciences Graduate Program, Northwestern University, 2204 Tech Drive, Evanston, IL, 60208, USA

2 – Center for Synthetic Biology, Northwestern University, 2145 Sheridan Rd, Evanston, IL, 60208, USA

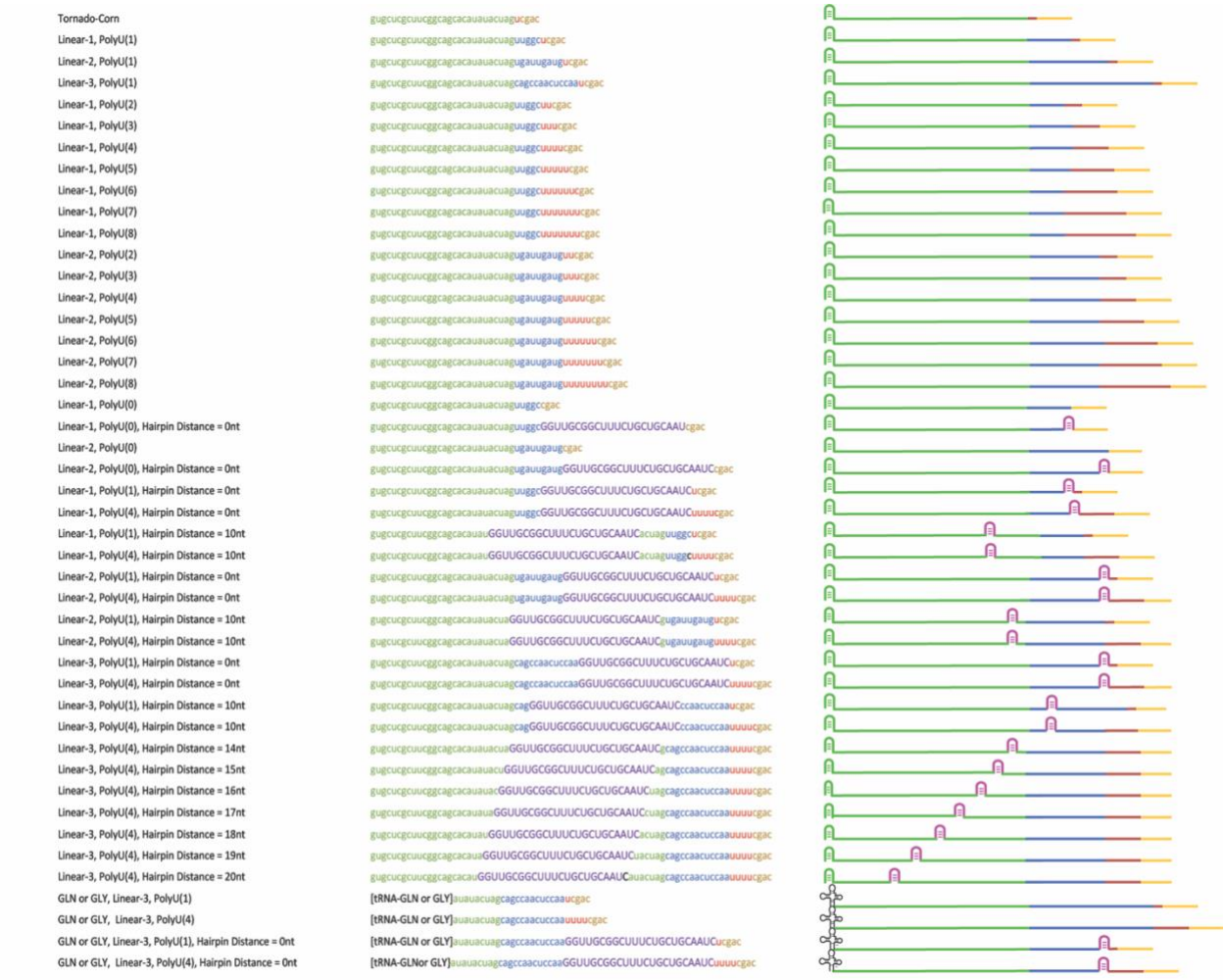
3 – Department of Chemical and Biological Engineering, Northwestern University, 2145 Sheridan Rd, Evanston, IL, 60208, USA

*Corresponding authors: Joshua N. Leonard, 2145 Sheridan Rd Evanston IL 60208 USA, (847) 491-7455 & Julius B. Lucks, 2145 Sheridan Rd Evanston IL 60208 USA, (847)-467-2943

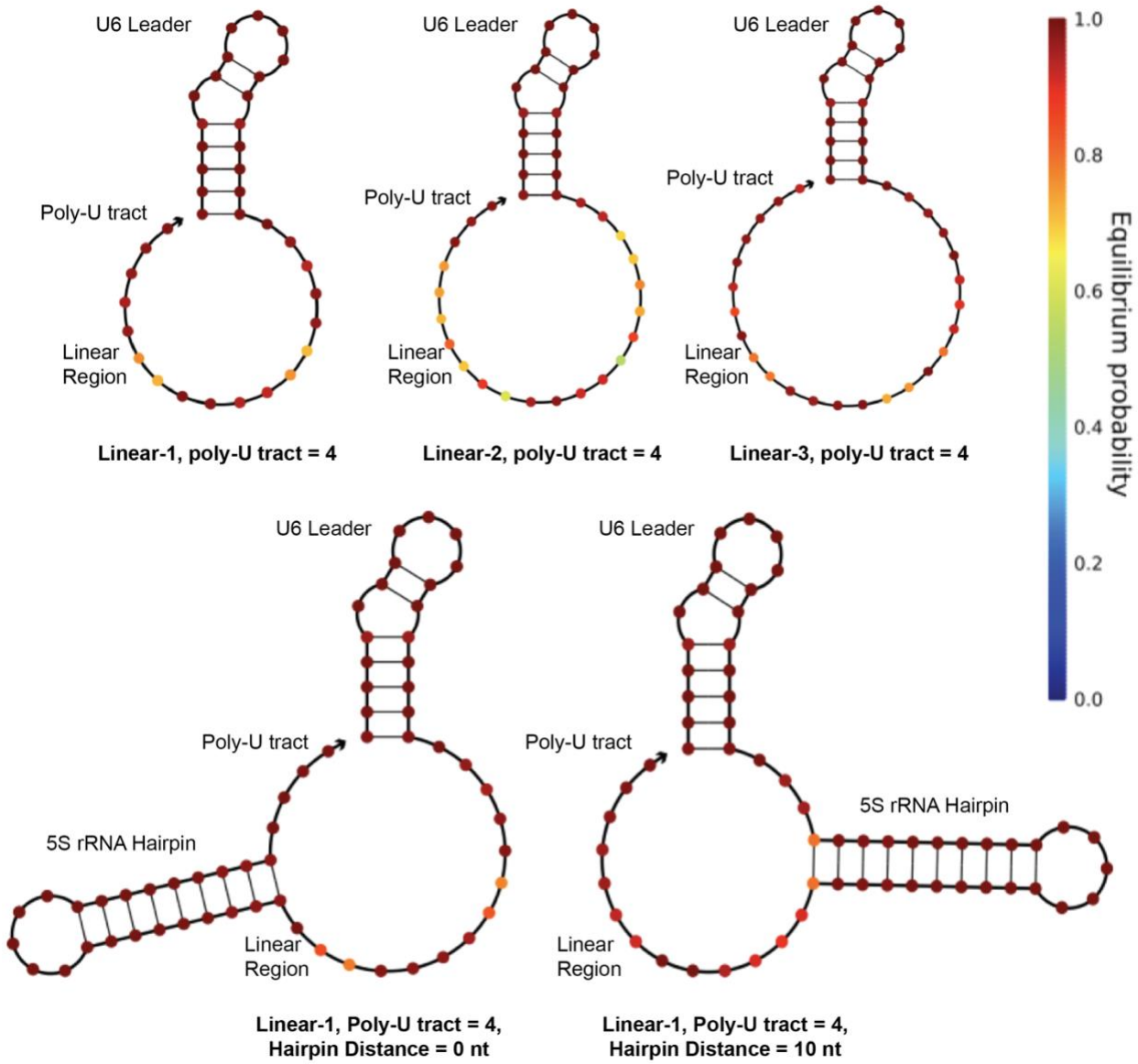
Table of Contents



Supplementary Figure 1: Evaluating Corn aptamer detection in the context of linear RNA transcripts. A) A schematic overview of an expression cassette for evaluating observed signal from the fluorescent aptamer Corn expressed as a Pol III-driven transcript. The system comprises a human U6 promoter driving transcription of a Corn aptamer (yellow line) placed within a tRNA scaffold. **B)** Various doses of a construct bearing this expression cassette were transfected into HEK293FT cells, holding total DNA dose constant using empty vector DNA. Then, 48 h later, DFHO was added to the culture medium, and cells were harvested for analysis by flow cytometry. The resulting signal was compared to that observed for a vector-only control. None of these cases differed substantially from the vector-only control as measured by a 1-sided heteroscedastic Welch's t-test followed by the Benjamini-Hochberg procedure with a false discovery rate cutoff of 0.05 (**Supplementary Table 2**). Colored bars represent the average of 3 biological replicates with individual points plotted as circles. Error bars represent the S.E.M. The dashed line represents the average of three replicates for the vector-only control (v) and the grey horizontal bar represents the S.E.M. of the vector-only control.

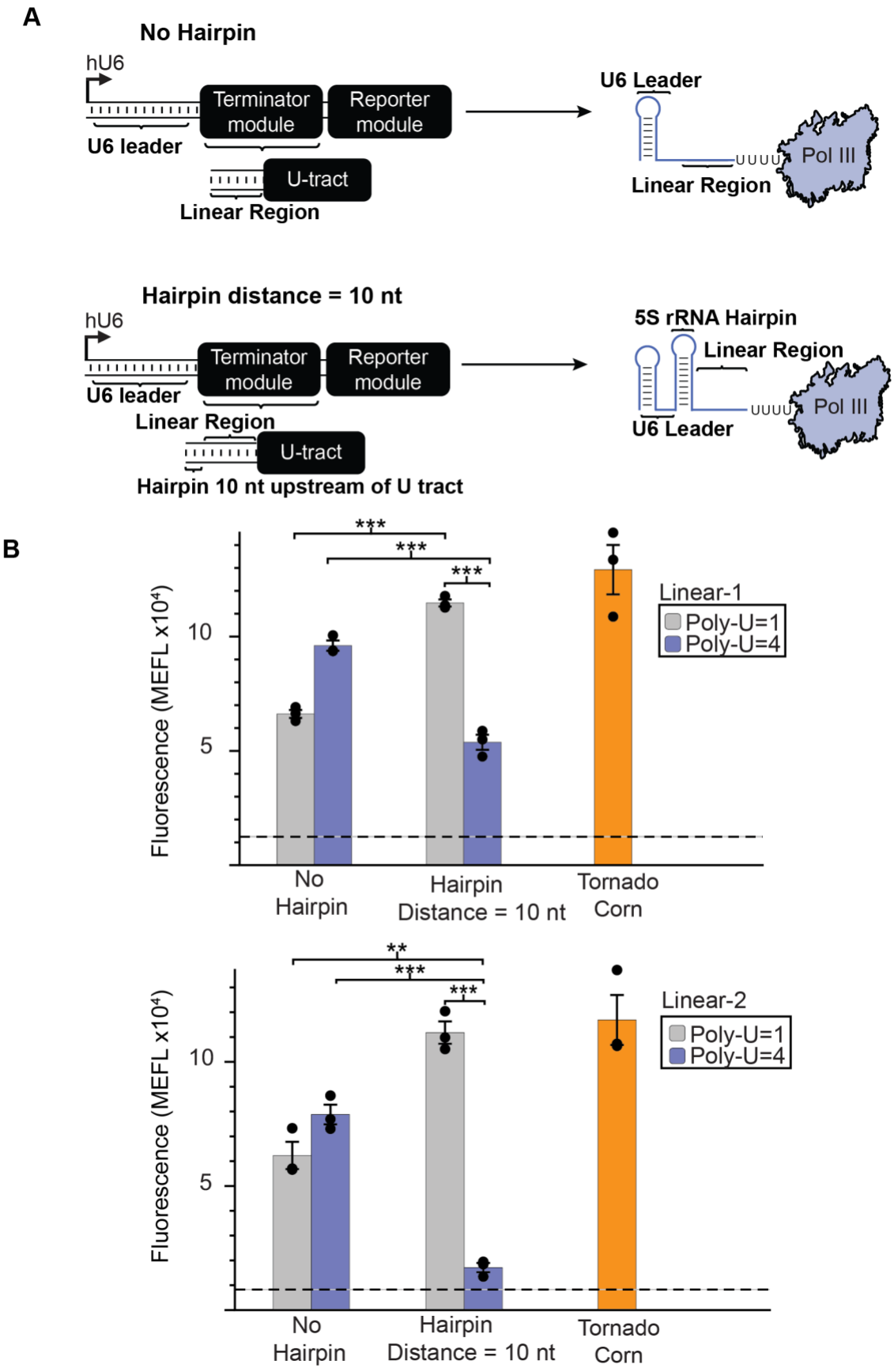


Supplementary Figure 2: Sequence and predicted structure of employed linear transcripts. This figure summarizes all the sequences that occur between the U6 promoter and reporter module for all transcripts designed to include linear tracts. Transcripts consisted of a 27 bp leader U6 leader sequence (green), a poly-U tract (red), linear tracts (blue), a hairpin from the 5S ribosomal RNA (purple), and a consistent 3' region (yellow). When applicable, tRNA are denoted in black. Locations of predicted secondary structure are annotated as the respective hairpins (right column).

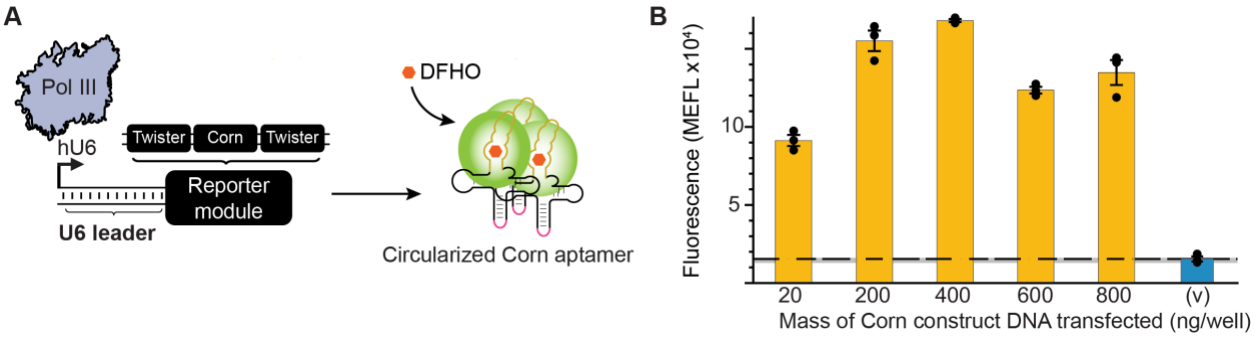


Supplementary Figure 3: Predicted secondary structure of representative transcripts. NUPACK [1] secondary structure analysis was used to predict the structural conformations of RNA sequences included in this study. Equilibrium folding analysis at 37 ºC using default NUPACK parameters used sequences beginning at the transcription start site (beginning of the U6 leader sequence) through the end of the terminator module (through the Poly-U tract). Shown here are transcripts possessing a 4 nt poly-U tract. Colored positions (colorbar) indicate the probability that nucleotides

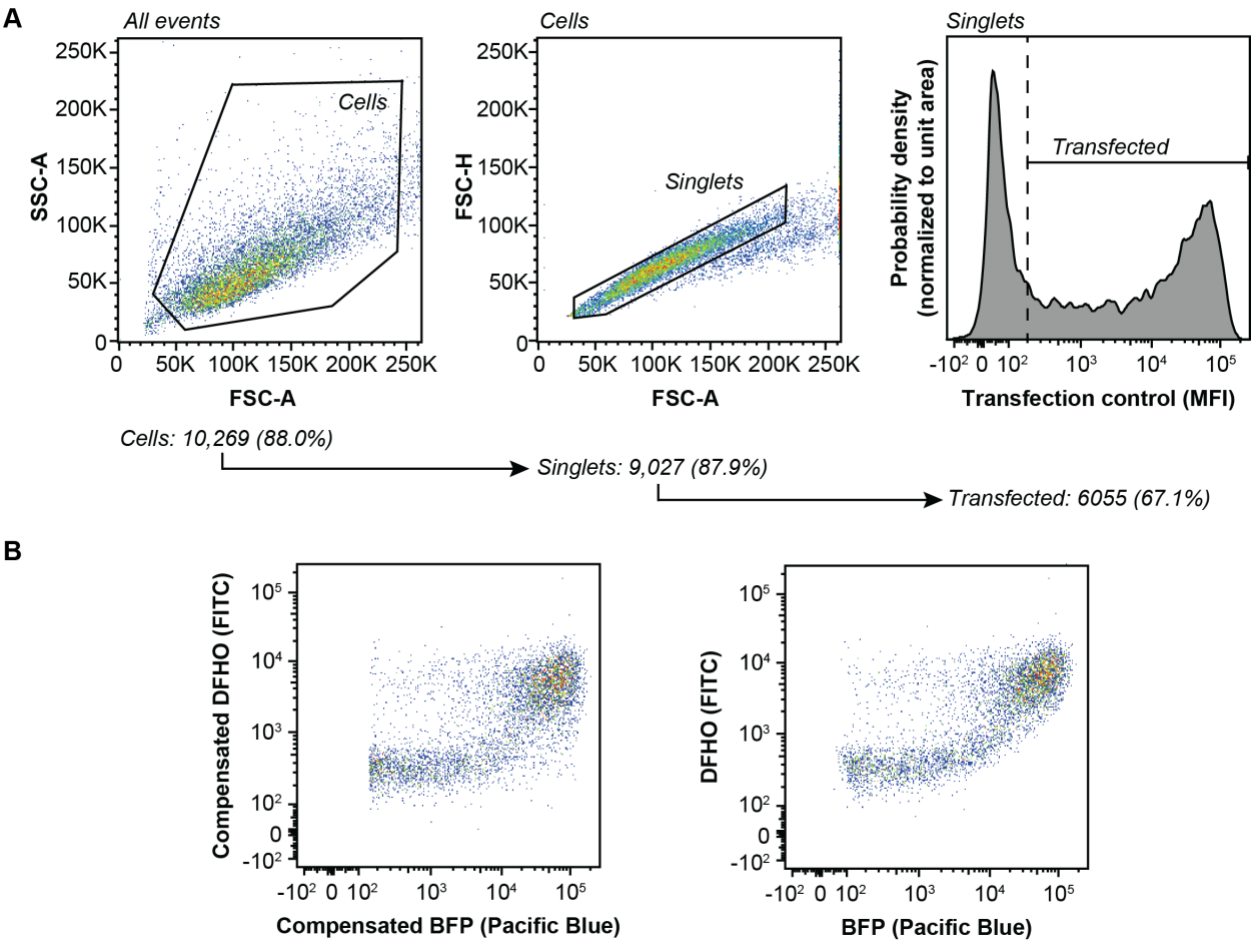
are in their indicated structural state (paired or unpaired) over the entire ensemble of possible structures. These examples illustrate sequences predicted to have a high probability of exhibiting the desired structure (e.g., single-stranded for linear regions, or correctly base-paired within the U6 leader and 5S ribosomal RNA hairpins).


A
No Hairpin
hU6
Terminator module
Reporter module
U6 leader
U-tract
Linear Region
U6 Leader
UUUU
Pol III
Linear Region
Hairpin distance = 10 nt
hU6
Terminator module
Reporter module
U6 leader
Linear Region
U-tract
Hairpin 10 nt upstream of U tract
5S rRNA Hairpin
Linear Region
UUUU
Pol III
U6 Leader
B
***
***
***
Linear-1
Poly-U=1
Poly-U=4
Fluorescence (MEFL x10⁴)
10
5
No Hairpin
Hairpin Distance = 10 nt
Tornado Corn
**
***
***
Linear-2
Poly-U=1
Poly-U=4
Fluorescence (MEFL x10⁴)
10
5
No Hairpin
Hairpin Distance = 10 nt
Tornado Corn

Supplementary Figure 4: RNA secondary structure 10 nt upstream of some poly-U tracts enhances termination. A) A schematic depicting the positioning of secondary structure upstream of the poly-U tract. This structure was either omitted (No Hairpin) or placed 10 nt upstream of the poly-U tract (Hairpin distance = 10 nt). The secondary structure utilized is a 23 nt portion of the 5S ribosomal RNA (rRNA) predicted to fold into a 9 bp hairpin following previous studies of Pol III termination *in vitro* [2]. **B)** The two different configurations were included upstream of poly-U tracts of length 1 and 4 nt for both the Linear-1 and Linear-2 sequence contexts. Colored bars represent the average of 3 biological replicates with individual points plotted as circles. Error bars represent the S.E.M. The dashed line represents the average of three replicates for the vector-only control (v) and the grey horizontal bar represents the S.E.M. of the vector-only control. Statistical significance of the indicated comparisons (brackets) was measured using a one-tailed heteroscedastic Welch's t-test followed by the Benjamini-Hochberg procedure with a false discovery rate cutoff of 0.05 (**Supplementary Table 2**). * = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$.

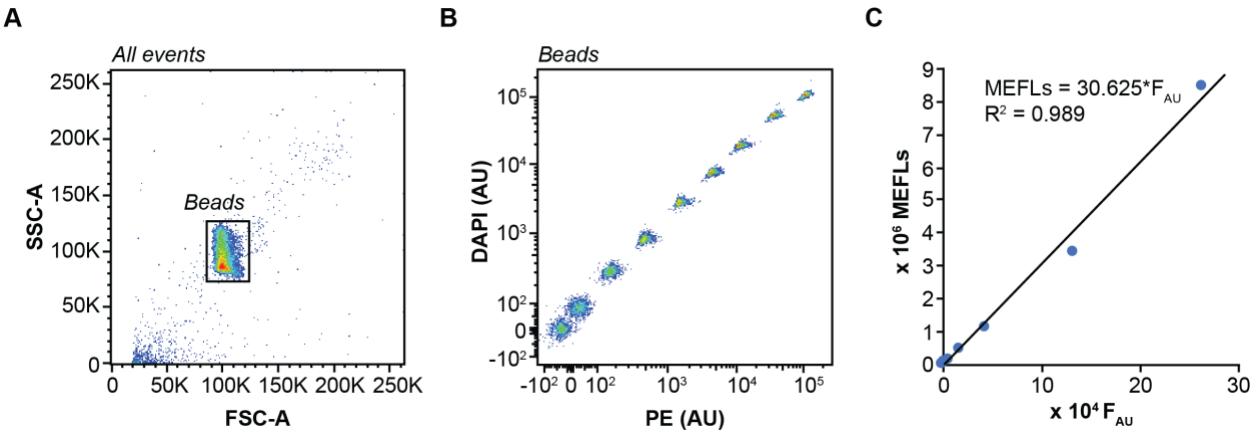


Supplementary Figure 5: Influence of Tornado construct DNA dose on output magnitude. A) Schematic of the tornado reporter module system from Fig. 1A. **B)** This construct was transfected into HEK293FT cells at various concentrations. For all samples, total DNA dose was held constant at 800 ng/well by adding in the required amount of empty vector DNA. The resulting signal was compared against the background fluorescence of the system measured by assaying cells transfected only with empty vector DNA (v). Colored bars represent the average of 3 biological replicates with individual points plotted as circles. Error bars represent the S.E.M. The dashed line represents the average of three replicates for the vector-only control (v), and the grey horizontal bar represents the S.E.M. of the vector-only control.

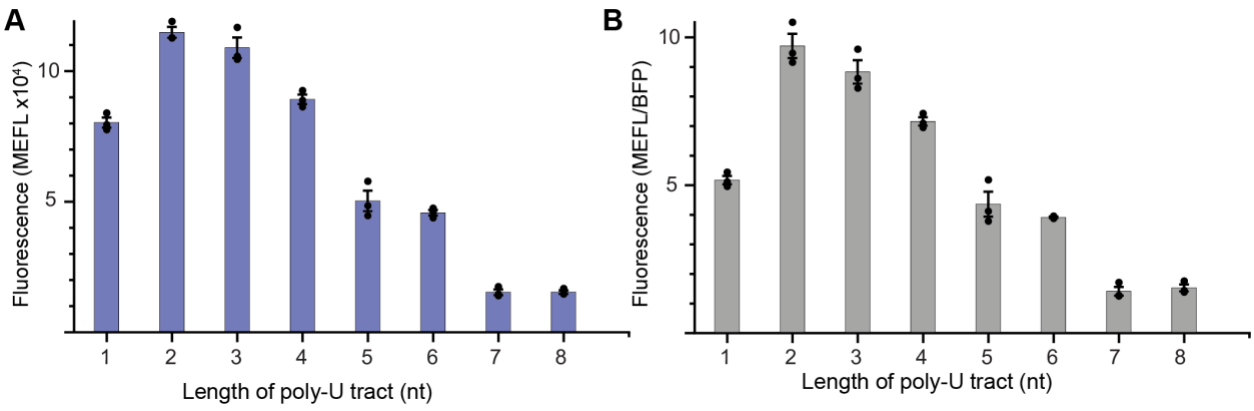


Supplementary Figure 6: Flow cytometry gating workflow. A) The plot shows cells transfected with empty vector only (pcDNA) that did not contain TORNADO expression cassettes and were treated with DFHO dye to illustrate the flow cytometry gating strategy used to identify single transfected cells. HEK293FT cells were identified by the FSC-A vs SSC-A profile (left). From this population, single cells were identified by the FSC-A vs. FSC-H profile (middle). Mean fluorescence intensity (MFI) of each cell was then collected and plotted as a distribution (right). The transfected population was defined as all single cells with a transfection control signal greater than the sample of single cells transfected with empty vector only, encompassing no more than 1% of the empty vector only transfected population. B) This figure illustrates the application of

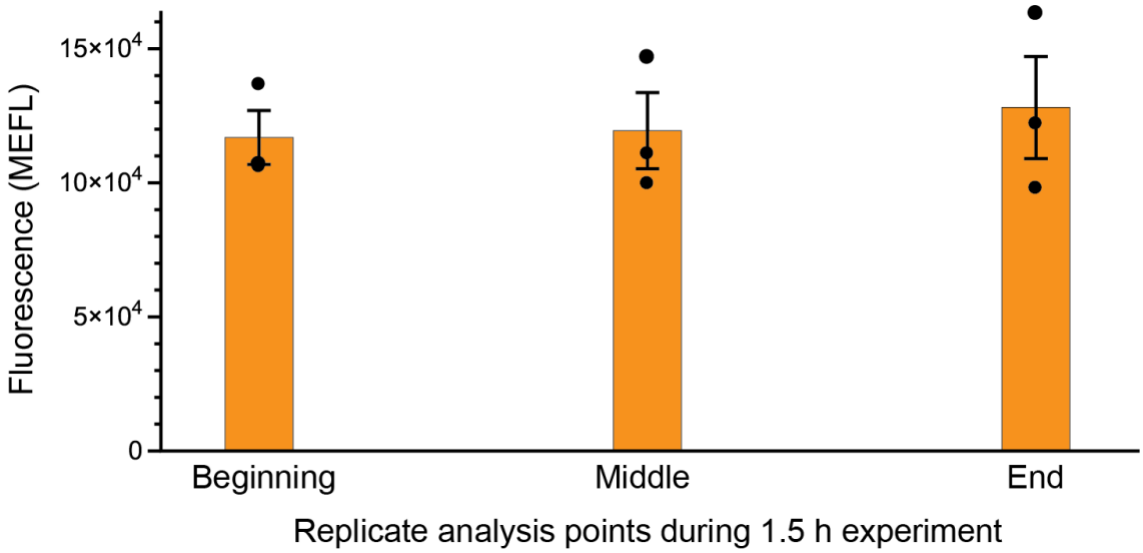
compensation to minimize spectral overlap between FITC and BFP signals. In this sample (only BFP+ cells are shown), all cells were transfected with constructs transcribing the Corn aptamer without an upstream Terminator module, and cells were treated with DFHO; cells receiving small amounts of these transfected plasmids (low BFP transfection control signal) are also low in FITC signal, as expected. Application of compensation (left) enables one to isolate the FITC and BFP signals, which in this experiment causes better separation of the various subpopulations compared to the uncompensated (right) version of these data.



Supplementary Figure 7: Flow cytometry fluorescence intensity calibration to absolute units with UltraRainbow beads. A) The bead population was identified based on the FSC-A vs. SSC-A profile. **B)** Two fluorescent channels, other than the channels of interest for the experiment, were used to identify the 9 beads population. **C)** The mean fluorescence intensity (MFI) of each population in the FITC channel (used for DFHO dye signal) in arbitrary unites (F_{AU}) was recorded and plotted against manufacturer provided values for molecules of equivalent fluorescein (MEFL) per bead peak for each population. A linear regression with y-intercept set to zero was used to create a calibration curve. This curve was used to convert exported MFI values to absolute units using the multiplier obtained from the regression for each characterized cell population that was gated for transfection as in **Supplementary Figure 6**.



Supplementary Figure 8: Analysis of data with and without normalization to the transfection control. A) Data from Figure 2C are reproduced here (evaluating the impact of the length of poly-U tracts on Pol III transcription termination). DFHO signals within this study are reported in MEFLs. **B)** To investigate whether observed patterns many be influenced by variations in transfection efficiency, we re-analyzed the data from part A by normalizing average MEFLs by average BFP transfection control signal for each sample. Since the pattern is unchanged, we opted not to normalize data in this fashion (in order to avoid potential artifacts and to minimize data manipulation). However, we did ensure that transfection efficiency did not vary substantially within any experiment (see **Methods**).



Supplementary Figure 9: Evaluation of signal variation of the positive control Tornado construct within an experiment. To identify potential sources of error and avoid misinterpretation, we evaluated whether reporter signal varies across the course of a single analytical flow cytometry data collection experiment. Within a 1.5 h long experiment, three samples (three biological replicate each) of cells transfected to express the Tornado construct (**Fig. 1A**) were assayed, at the beginning, middle, and end of the experiment, respectively. No statistical difference was observed between these points using a 2-tailed heteroscedastic Welch's t-test with no Benjamini-Hochberg correction (**Supplementary Table 2**). Colored bars represent the average of 3 biological replicates with individual points plotted as circles. Error bars represent the S.E.M.

Supplementary Table 1: Sequences of DNA parts and constructs.

Part/Construct	Sequence
U6 Promoter	gagggcctatttcccatgattccttcatatttgcatatacgatacaaggctgttagagagataatt agaattaatttgactgtaaacacaaagatattagtacaaaatacgtgacgtagaaagtaata atttcttgggtagtttgcagttttaaaattatgttttaaaatggactatcatatgcttaccgtaacttga aagtatttcgatttcttggctttatatatcttgtggaaaggac
GLN tRNA	gtctctcgtcggttccatggtgtaatggttagcactctggactctgaatccagcgatccgagttca aatctcggtggaacct
GLY tRNA	gtctctcgtcgcattggtggttcagtggtagaattctcgcctgccacgcgggaggcccgggttc gattcccggccaatgca
27 bp Leader	gtgctcgcttcggcagcacatatactag
27 bp Leader del(1-19)	atatactag
Linear-1	ttggc
Linear-2	tgattgatg
Linear-3	cagccaactccaa
5S rRNA Hairpin	ggttgcggctttctgctgcaatc
Corn/tRNA scaffold	caggcccggatagctcagtcggtagagcagcggccgcgcgattcgaggaaggaggtctg aggaggtcactgaatcgcgcggccgcgggtccagggttcaagtccctgttcgggcctgccat cagtc
5' Twister ribozyme	ggccatcagtcgccggtcccaagcccggataaaatgggaggggcgggaaaccgcctaa ccatgccgactgatgg
3' Twister ribozyme	ggcgtggactgtagaacactgccaatgccggtcccaagcccggataaaagtggagggtac agtccacgc
SV40 Terminator	aacttgtttattgcagcttataatggttacaaataaagcaatagcatcacaaatttcacaaataa agcatttttttcactgcattctagttgtggtttgtccaaactcatcaatgtatctta
Construct: Linear-1 with a poly-U tract of 4 and immediately 5' secondary structure (Supplementary Fig. 2B).	gagggcctatttcccatgattccttcatatttgcatatacgatacaaggctgttagagagataatt agaattaatttgactgtaaacacaaagatattagtacaaaatacgtgacgtagaaagtaata atttcttgggtagtttgcagttttaaaattatgttttaaaatggactatcatatgcttaccgtaacttga aagtatttcgatttcttggctttatatatcttgtggaaaggacgaaacaccgtgctcgcttcggca gcacatatactagttggcggttgcggctttctgctgcaatctttcgacggccatcagtcgccggt cccaagcccggataaaatgggaggggcgggaaaccgcctaaccatgccgactgatggc aggcccggatagctcagtcggtagagcagcggccgcgcgattcgaggaaggaggtctga ggaggtcactgaatcgcgcggccgcgggtccagggttcaagtccctgttcgggcctgccatc agtcggcgtggactgtagaacactgccaatgccggtcccaagcccggataaaagtggagg gtacagtccacgctctagagcggacttcggtccgcttttactaggacctgcaggcatgcaag cttgacgtcggttaccgatatccatatggcggccgcatcgatctcgagccgcggactagtaac ttgtttattgcagcttataatggttacaaataaagcaatagcatcacaaatttcacaaataaagc atttttttcactgcattctagttgtggtttgtccaaactcatcaatgtatctta

Supplementary Table 2: Statistical comparisons using the Benjamini-Hochberg procedure. Multiple statistical comparisons utilizing a 1-sided heteroscedastic Welch's t-test were corrected following the Benjamini-Hochberg procedure in order to control the false discover rate (FDR) [3]. For each figure where this is used, rank order t-tests are given along with the comparisons where the null hypothesis (that the comparisons are equal) is rejected (TRUE) or not rejected (FALSE) for three different FDR cutoffs.

Figure	Ranked Comparison	Ranked t-test	Null hypothesis rejected		
Fig. 1B	vs Tornado Corn		FDR=0.05	FDR=0.01	FDR=0.001
	Vector-only Control (v)	7.52E-04	TRUE	TRUE	TRUE
	Corn	1.09E-03	TRUE	TRUE	FALSE
Fig. 2C	vs Vector-only Control (v)				
	Linear-1, PolyU(6)	1.94E-03	TRUE	FALSE	FALSE
	Linear-1, PolyU(4)	2.14E-03	TRUE	TRUE	FALSE
	Linear-1, PolyU(3)	4.25E-03	TRUE	FALSE	FALSE
	Linear-1, PolyU(2)	5.14E-03	TRUE	FALSE	FALSE
	Linear-1, PolyU(7)	5.58E-03	TRUE	TRUE	FALSE
	Linear-1, PolyU(1)	7.51E-03	TRUE	FALSE	FALSE
	Linear-1, PolyU(5)	2.68E-02	TRUE	FALSE	FALSE
	Linear-1, PolyU(8)	3.67E-02	TRUE	FALSE	FALSE
	Linear-2, PolyU(2)	1.63E-04	TRUE	TRUE	FALSE
	Linear-2, PolyU(4)	2.06E-04	TRUE	TRUE	TRUE
	Linear-2, PolyU(6)	2.44E-04	TRUE	TRUE	TRUE
	Linear-2, PolyU(1)	3.01E-04	TRUE	TRUE	TRUE
	Linear-2, PolyU(3)	7.72E-04	TRUE	TRUE	FALSE
	Linear-2, PolyU(5)	5.09E-03	TRUE	TRUE	FALSE
	Linear-2, PolyU(8)	1.76E-02	TRUE	FALSE	FALSE
	Linear-2, PolyU(7)	5.35E-02	FALSE	FALSE	FALSE
Fig. 3C	vs Linear-1, PolyU(4), Hairpin Distance = 0nt				
	Linear-1, PolyU(4), No Hairpin	3.98E-05	TRUE	TRUE	TRUE
	Linear-1, PolyU(1), Hairpin Distance 0nt	7.44E-04	TRUE	TRUE	TRUE
Fig. 3C	vs Linear-2, PolyU(4), Hairpin Distance = 0nt				

	Linear-2, PolyU(4), No Hairpin	2.95E-04	TRUE	TRUE	TRUE
	Linear-2, PolyU(1), Hairpin Distance 0nt	1.78E-03	TRUE	TRUE	FALSE
Fig. 4B	vs Linear-3, PolyU(4), Hairpin Distance 0nt				
	Linear-3, PolyU(1), Hairpin Distance 0nt	7.73E-04	TRUE	TRUE	FALSE
	Linear-3, PolyU(4), No Hairpin	4.11E-03	TRUE	TRUE	FALSE
Fig. 4B	vs Linear-3, PolyU(4), Hairpin Distance 10nt				
	Linear-3, PolyU(1), Hairpin Distance 10nt	3.06E-05	TRUE	TRUE	TRUE
	Linear-3, PolyU(4), No Hairpin	1.29E-03	TRUE	TRUE	FALSE
Fig. S1	vs Vector-only control (v)				
	Corn [200ng]	1.34E-01	FALSE	FALSE	FALSE
	Corn [400ng]	2.43E-01	FALSE	FALSE	FALSE
	Corn [800ng]	2.64E-01	FALSE	FALSE	FALSE
Fig. S4	Linear-1, PolyU(4) , Hairpin Distance 10nt				
	Linear-1, PolyU(4), No Hairpin	3.09E-04	TRUE	TRUE	TRUE
	Linear-1, PolyU(1), Hairpin Distance 10nt	4.16E-04	TRUE	TRUE	TRUE
Fig. S4	Linear-2, PolyU(4), Hairpin Distance 10nt				
	Linear-2, PolyU(1), Hairpin Distance 10nt	3.12E-04	TRUE	TRUE	TRUE
	Linear-2, PolyU(4), No Hairpin	5.25E-04	TRUE	TRUE	TRUE

Pol III type 3 promoter transcript	Poly-U tract length	Reference	Location
U6	4	NCBI: NR_004394.1	Chr 15: 67840045
7SK	4	NCBI: NR_001445.2	Chr 6: 52995951
H1	5	NCBI:NR_002312.1	Chr 14: 4460
RNA Y	4	NCBI: NR_004391.1	Chr 7: 148987248

Supplementary Table 3: Poly-U tract lengths of transcripts from representative Pol III type 3 promoters. Genome sequence references are given for each type 3 promoter transcript along with their chromosomal and nucleotide position.

Supplementary Table 4: All statistical comparisons not utilizing multiple hypothesis correction procedures. Each figure utilizing a Welch's t-test without a Benjamini-Hochberg procedure is tabulated to demonstrate the statistical significance between tested points.

Figure	Comparison	# sided t-test	p-value
Fig. 3B	Linear-1, PolyU=0 vs Linear-1, PolyU=0, Hairpin Distance= 0nt	1	3.84E-01
Fig. 3B	Linear-2, PolyU=0 vs Linear-2, PolyU=0, Hairpin Distance 0nt	1	2.61E-03
Fig. 4C	Linear-3, PolyU=4, Hairpin Distance =10nt vs Linear-3, PolyU=4, Hairpin Distance =14nt	1	1.01E-04
Fig. 5B	tRNA(GLN), Linear-3, PolyU=1 vs Linear-1, PolyU=1, Hairpin Distance= 10nt	1	2.93E-02
Fig. 5B	tRNA(GLN), Linear-3, PolyU=4 vs tRNA(GLN), Linear-3, PolyU=4, Hairpin Distance= 10nt	1	9.45E-02
Fig. 5B	tRNA(GLY), Linear-3, PolyU=1 vs tRNA(GLY), Linear-3, Hairpin Distance= 10nt	1	1.25E-01
Fig. 5B	tRNA(GLY), Linear-3, PolyU=4 vs tRNA(GLY), Linear-3, PolyU=4, Hairpin Distance= 10nt	1	4.17E-02
Supp. Fig. 4B	Linear-1, PolyU=1 vs Linear-1, PolyU=1, Hairpin Distance =10nt	1	1.79E-05
Supp. Fig. 4B	Linear-2, PolyU=1 vs Linear-2, PolyU=1, Hairpin Distance =10nt	1	1.27E-03
Supp. Fig 9	Beginning vs (Middle & End)	2	6.58E-01
Supp. Fig 9	Middle vs (Beginning & End)	2	7.37E-01
Supp. Fig 9	End vs (Beginning & End)	2	6.67E-01

Supplementary Table 5: Addgene ID # for plasmids generated for this study. The following constructs are available on Addgene.org.

Addgene ID #	Construct Name
106233	pAV-U6+27-tCORN
159479	pAV-U6+27-Linear-1_PolyU(1)
159480	pAV-U6+27-Linear-1_PolyU(2)
159481	pAV-U6+27-Linear-1_PolyU(3)
159482	pAV-U6+27-Linear-1_PolyU(4)_Tornado-Corn
159483	pAV-U6+27-Linear-1_PolyU(5)_Tornado-Corn
159484	pAV-U6+27-Linear-1_PolyU(6)_Tornado-Corn
159485	pAV-U6+27-Linear-1_PolyU(7)_Tornado-Corn
159486	pAV-U6+27-Linear-1_PolyU(8)_Tornado-Corn
159487	pAV-U6+27-Linear-2_PolyU(1)_Tornado-Corn
159488	pAV-U6+27-Linear-2_PolyU(2)_Tornado-Corn
159489	pAV-U6+27-Linear-2_PolyU(3)_Tornado-Corn
159490	pAV-U6+27-Linear-2_PolyU(4)_Tornado-Corn
159491	pAV-U6+27-Linear-2_PolyU(5)_Tornado-Corn
159492	pAV-U6+27-Linear-2_PolyU(6)_Tornado-Corn
159493	pAV-U6+27-Linear-2_PolyU(7)_Tornado-Corn
159494	pAV-U6+27-Linear-2_PolyU(8)_Tornado-Corn
159495	pAV-U6+27-Linear-1_PolyU(1)_HairpinDistance(0)nts_Tornado-Corn
159496	pAV-U6+27-Linear-1_PolyU(4)_HairpinDistance(0)_Tornado-Corn
159497	pAV-U6+27-Linear-1_PolyU(1)_HairpinDistance(10)_Tornado-Corn
159498	pAV-U6+27-Linear-1_PolyU(4)_HairpinDistance(10)nts_Tornado-Corn
159499	pAV-U6+27-Linear-2_PolyU(1)_HairpinDistance(0)nts_Tornado-Corn
159500	pAV-U6+27-Linear-2_PolyU(4)_HairpinDistance(0)nts_Tornado-Corn
159501	pAV-U6+27-Linear-2_PolyU(1)_HairpinDistance(10)nts_Tornado-Corn
159502	pAV-U6+27-Linear-2_PolyU(4)_HairpinDistance(10)nts_Tornado-Corn

159503	pAV-U6+27-Linear-3_PolyU(1)_Tornado-Corn
159504	pAV-U6+27-Linear-3_PolyU(1)_HairpinDistance(10)nts_Tornado-Corn
159505	pAV-U6+27-Linear-3_PolyU(4)_Tornado-Corn
159506	pAV-U6+27-Linear-3_PolyU(4)_HairpinDistance(10)nts_Tornado-Corn
159507	pAV-U6+27-Linear-3_PolyU(1)_HairpinDistance(0)nts_Tornado-Corn
159508	pAV-U6+27-Linear-3_PolyU(4)_HairpinDistance(0)nts_Tornado-Corn
159509	pAV-U6+27-Linear-3_PolyU(4)_HairpinDistance(14)_Tornado-Corn
159510	pAV-U6+27-Linear-3_PolyU(4)_HairpinDistance(15)nts_Tornado-Corn
159511	pAV-U6+27-Linear-3_PolyU(4)_HairpinDistance(16)nts_Tornado-Corn
159512	pAV-U6+27-Linear-3_PolyU(4)_HairpinDistance(17)nts_Tornado-Corn
159513	pAV-U6+27-Linear-3_PolyU(4)_HairpinDistance(18)nts_Tornado-Corn
159514	pAV-U6+27-Linear-3_PolyU(4)_HairpinDistance(19)nts_Tornado-Corn
159515	pAV-U6+27-Linear-3_PolyU(4)_HairpinDistance(20)nts_Tornado-Corn
159516	pAV-U6+27-Linear-1_PolyU(3)_HairpinDistance(10)nts_Tornado-Corn
159517	pAV-U6+27-Linear-2_PolyU(3)_HairpinDistance(10)nts_Tornado-Corn
159518	pAV-U6+27-Linear-2_PolyU(5)_HairpinDistance(10)nts_Tornado-Corn
159519	pAV-U6+27-Linear-1_PolyU(5)HairpinDistance(10)nts_Tornado-Corn
166984	GLN, Linear-3, PolyU(1)
166985	GLN, Linear-3, PolyU(4)
166986	GLN, Linear-3, PolyU(1), Hairpin Distance = 0nt
166987	GLN, Linear-3, PolyU(4), Hairpin Distance = 0nt
166988	GLY, Linear-3, PolyU(1)
166989	GLY, Linear-3, PolyU(4)
166990	GLY, Linear-3, PolyU(1), Hairpin Distance = 0nt
166991	GLY, Linear-3, PolyU(4), Hairpin Distance = 0nt
166992	pAV-U6+27-Linear-1, PolyU(0)

166993	pAV-U6+27Linear-1, PolyU(0), Hairpin Distance = 0nt
166994	pAV-U6+27Linear-2, PolyU(0)
166995	pAV-U6+27Linear-2, PolyU(0), Hairpin Distance = 0nt

References cited in Supplementary Information

[1] Zadeh JN, Steenberg CD, Bois JS, Wolfe BR, Pierce MB, Khan AR, et al. NUPACK: analysis and design of nucleic acid systems. J Comput Chem. 2011;32:170-3.

[2] Nielsen S, Yuzenkova, Y., & Zenkin, N. Mechanism of Eukaryotic RNA polymerase III transcription termination. Science. 2013;340:1577-80

[3] Benjamini Y, Hochberg Y. Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. Journal of the Royal Statistical Society. 1995;57:289-300.