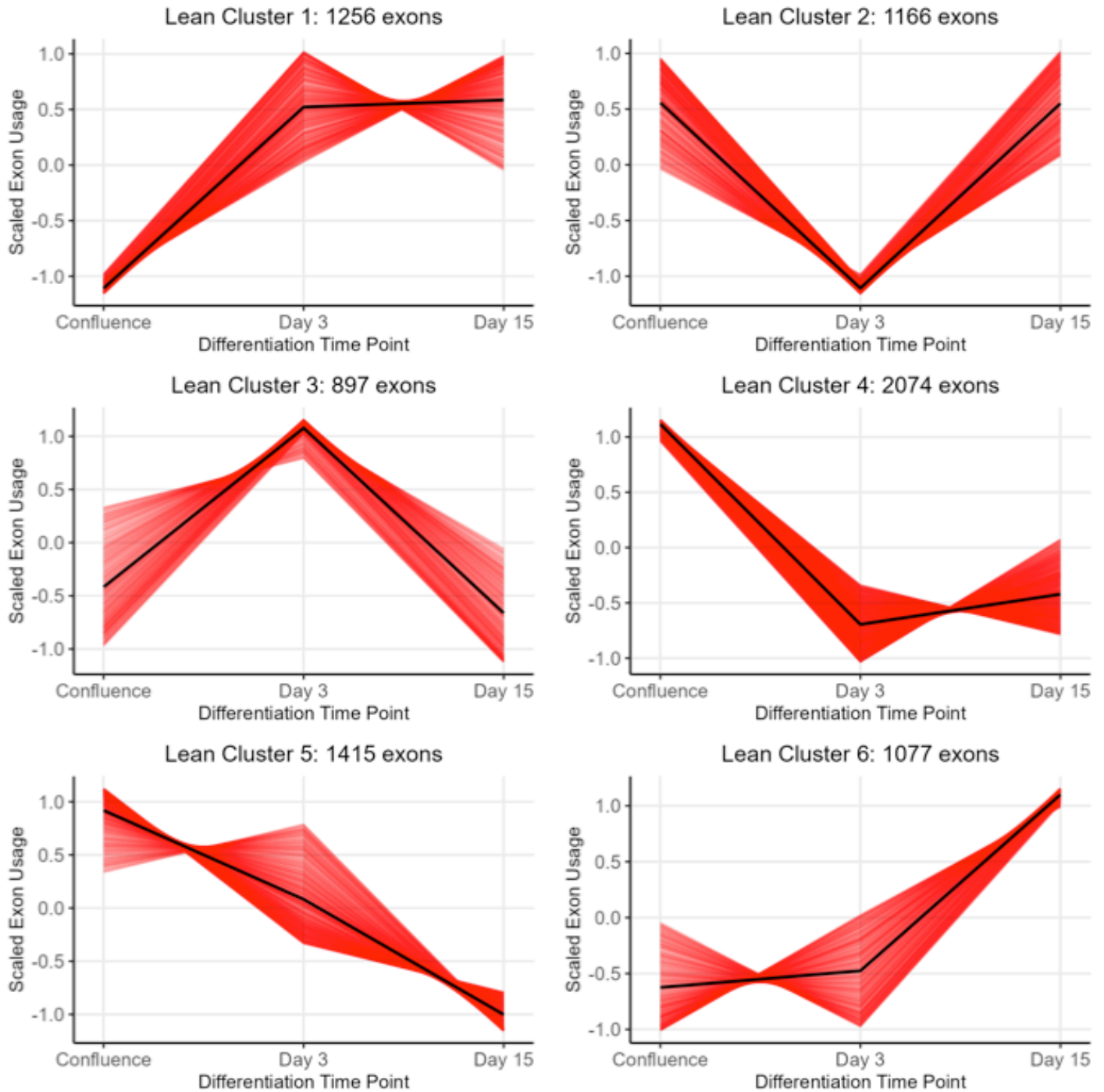
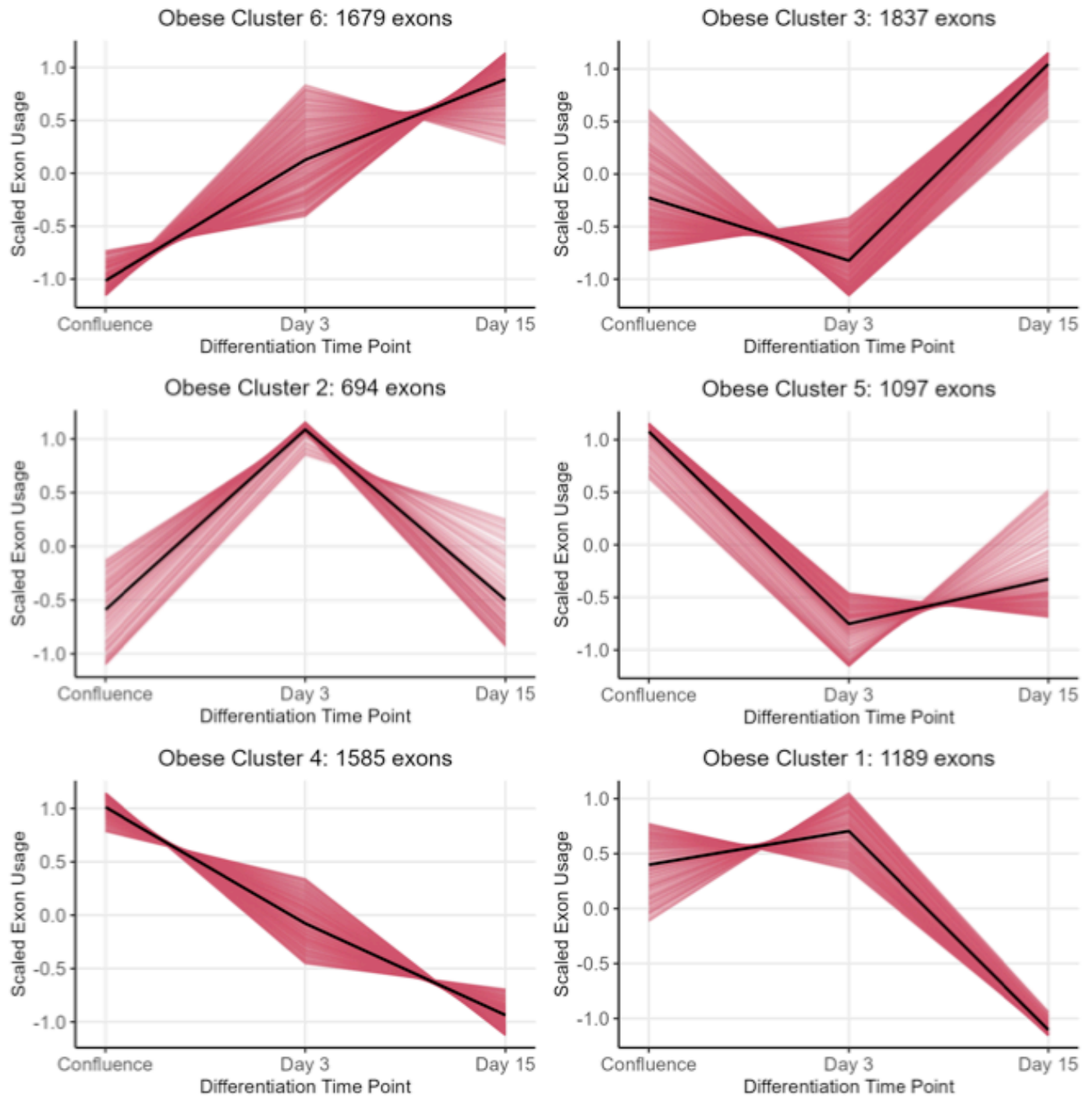


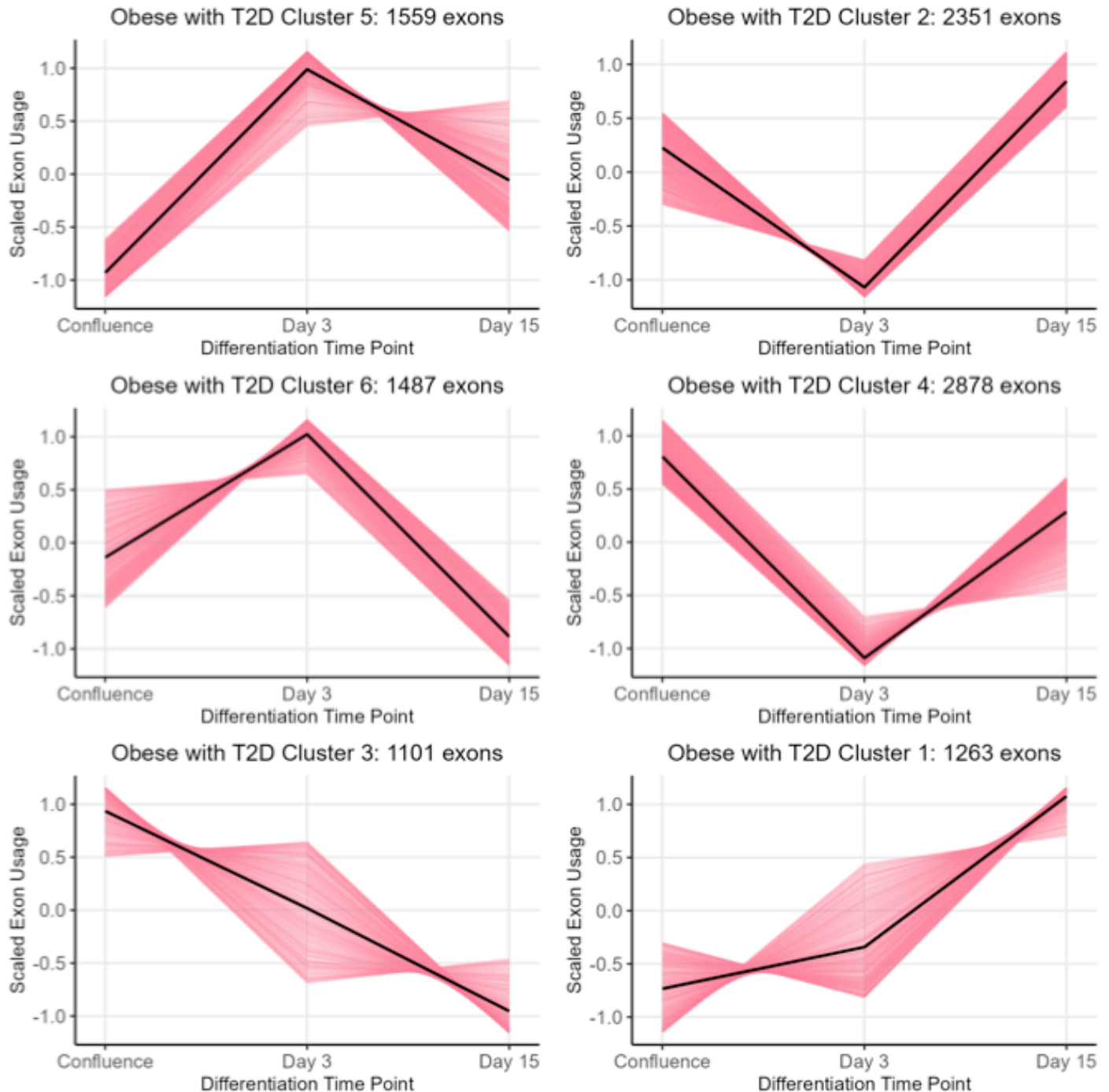
Supplementary Figure 1. **Lean splicing clusters.** Plots showing the centered and scaled exon usage for each exon assigned to one of six clusters. For each plot, the black line connects the cluster centroids of the cluster. Clusters were generated by using fuzzy c-means clustering to cluster all differentially spliced exons from the lean cohort with  $k = 6$ .



Supplementary Figure 2. **Obese splicing clusters.** Plots showing the centered and scaled exon usage for each exon assigned to one of six clusters. For each plot, the black line connects the cluster centroids of the cluster. Clusters were generated by using fuzzy c-means clustering to cluster all differentially spliced exons from the obese cohort with  $k = 6$ .



Supplementary Figure 3. **Obese with T2D splicing clusters.** Plots showing the centered and scaled exon usage for each exon assigned to one of six clusters. For each plot, the black line connects the cluster centroids of the cluster. Clusters were generated by using fuzzy c-means clustering to cluster all differentially spliced exons from the obese with T2D cohort with  $k = 6$ .



Supplementary Table 1. **Clinical parameters of study subjects.** Data are mean  $\pm$  SD

	<b>Lean</b>	<b>Obese</b>	<b>Obese type 2 diabetic</b>
<b>N (male)</b>	5	4	5
<b>Age [years]</b>	43.8 $\pm$ 10.7	37.8 $\pm$ 4.5	47.6 $\pm$ 2.2
<b>Weight [kg]</b>	79.0 $\pm$ 10.2	150.5 $\pm$ 23.8	150.3 $\pm$ 26.2
<b>Height [cm]</b>	179.8 $\pm$ 4.4	184.0 $\pm$ 10.6	182.2 $\pm$ 4.6
<b>BMI [kg/m<sup>2</sup>]</b>	24.4 $\pm$ 2.1	44.3 $\pm$ 3.5	45.3 $\pm$ 7.5
<b>Waist [cm]</b>	93.4 $\pm$ 4.1	151.0 $\pm$ 14.7	163.3 $\pm$ 35.9
<b>Hip [cm]</b>	101.4 $\pm$ 4.0	139.7 $\pm$ 13.3	132.5 $\pm$ 9.3
<b>Waist/Hip [cm]</b>	0.9 $\pm$ 0.0	1.1 $\pm$ 0.0	1.2 $\pm$ 0.2
<b>SBP [mmHg]</b>	120.0 $\pm$ 11.0	132.8 $\pm$ 8.2	127.3 $\pm$ 10.5
<b>DBP [mmHg]</b>	76.8 $\pm$ 8.3	91.5 $\pm$ 8.0	78.3 $\pm$ 12.1
<b>C-Reactive Protein [mg/l]</b>	0.7 $\pm$ 0.4	9.8 $\pm$ 3.0	10.5 $\pm$ 10.1
<b>HbA1c [mmol/mol]</b>	35.0 $\pm$ 3.7	37.3 $\pm$ 1.7	46.8 $\pm$ 4.1
<b>gHbA1c [%]</b>	5.9 $\pm$ 0.5	6.3 $\pm$ 0.3	7.7 $\pm$ 0.6
<b>C-peptide [pmol/l]</b>	584.0 $\pm$ 111.6	1458.5 $\pm$ 288.0	1789.8 $\pm$ 493.7
<b>Cholesterol [mmol/l]</b>	4.5 $\pm$ 0.4	5.3 $\pm$ 0.5	3.7 $\pm$ 1.2
<b>HDL [mmol/l]</b>	1.4 $\pm$ 0.4	1.0 $\pm$ 0.3	1.0 $\pm$ 0.2
<b>LDL [mmol/l]</b>	2.6 $\pm$ 0.4	3.7 $\pm$ 0.4	2.2 $\pm$ 1.1
<b>VLDL [mmol/l]</b>	0.5 $\pm$ 0.3	0.6 $\pm$ 0.2	0.6 $\pm$ 0.2
<b>Triglyceride [mmol/l]</b>	1.1 $\pm$ 0.7	1.4 $\pm$ 0.5	1.4 $\pm$ 0.5
<b>Leukocytes [x 10<sup>9</sup>/l]</b>	5.8 $\pm$ 1.1	7.6 $\pm$ 1.5	6.8 $\pm$ 1.2
<b>Insulin [pmol/l]</b>	34 $\pm$ 0	183.3 $\pm$ 101.2	143.5 $\pm$ 73.9
<b>Alcohol/week [units]</b>	6 $\pm$ 7.2	0 $\pm$ 0	0.3 $\pm$ 0.5
<b>Smoking/day [units]</b>	0.6 $\pm$ 1.3	0 $\pm$ 0	0 $\pm$ 0

Supplementary Table 2. **RNA-seq study design.**

<b>Individual</b>	<b>Confluence</b>	<b>Day 3</b>	<b>Day 15</b>
Lean 1	x	x	x
Lean 2		x	x
Lean 3	x		x
Lean 4	x		
Lean 5		x	
Obese 1	x		x
Obese 2		x	x
Obese 3	x	x	x
Obese 4	x	x	
Obese T2D 1	x	x	x
Obese T2D 2	x		x
Obese T2D 3		x	
Obese T2D 4		x	x
Obese T2D 5	x		