

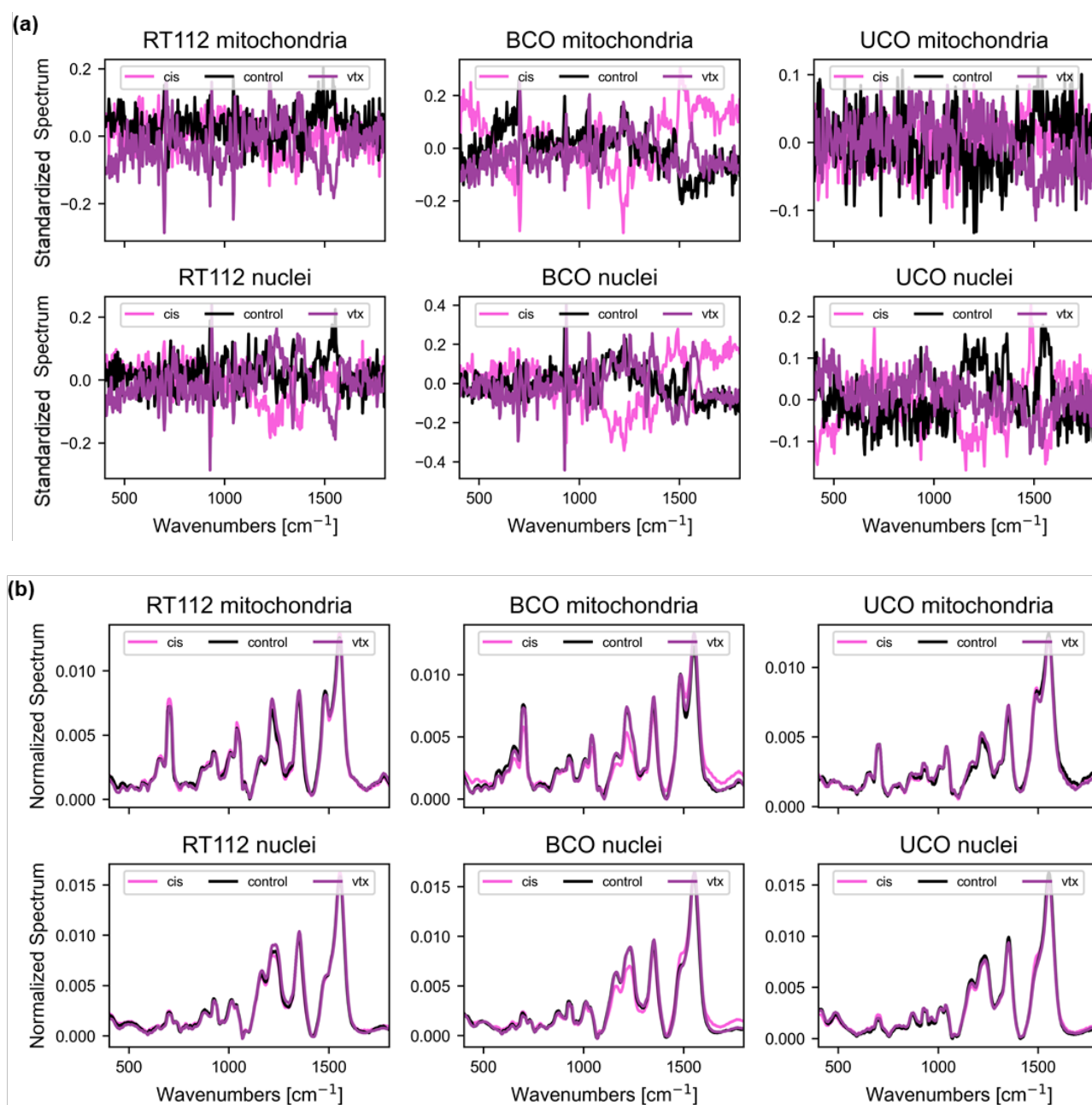
## Supplementary Materials

**Table S1.** Most relevant features identified in PCA loadings.

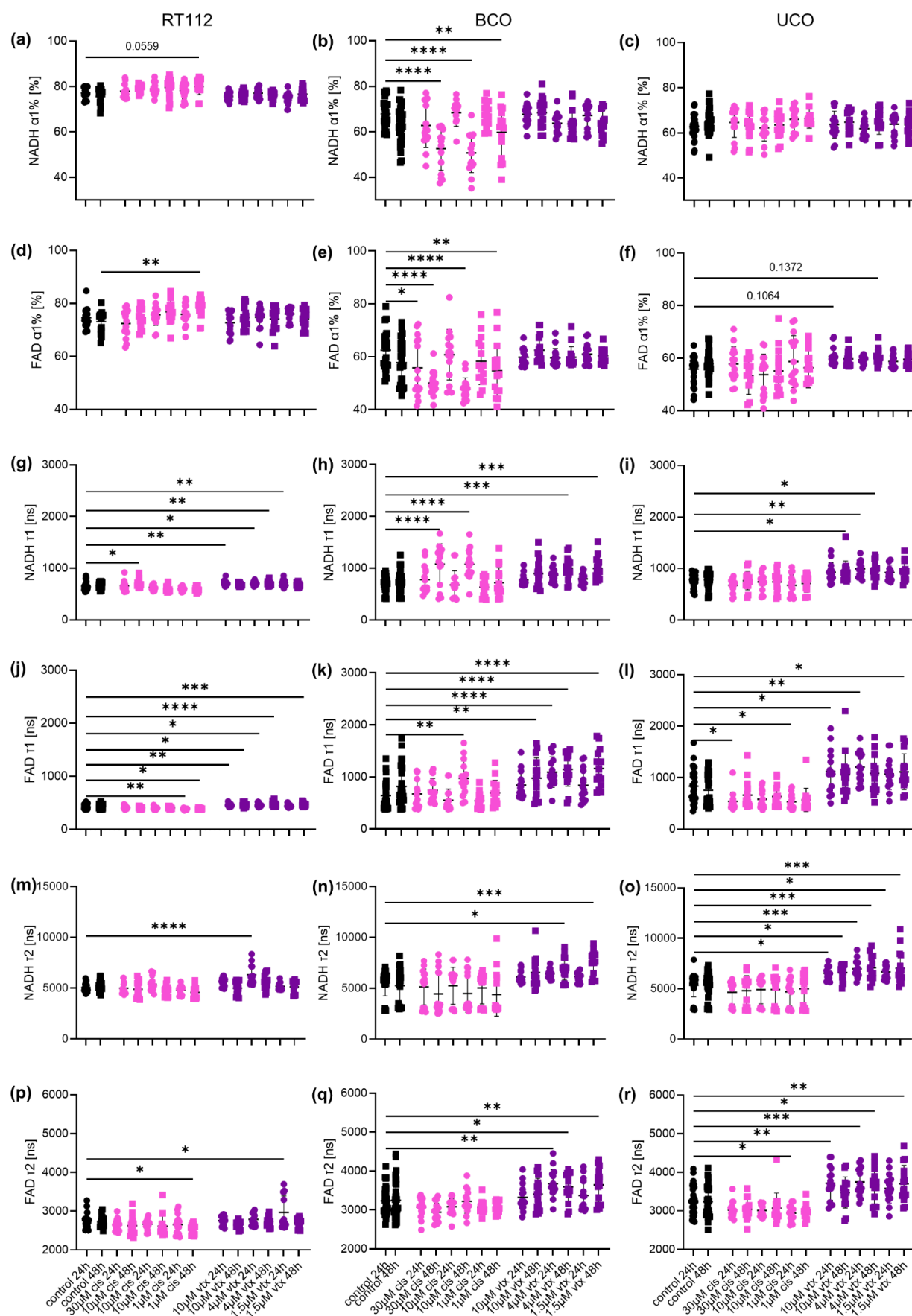
<b>Dataset</b>	<b><math>\nu_1</math> [cm<sup>-1</sup>]</b>	<b><math>\nu_2</math> [cm<sup>-1</sup>]</b>	<b><math>\nu_3</math> [cm<sup>-1</sup>]</b>	<b><math>\nu_4</math> [cm<sup>-1</sup>]</b>	<b><math>\nu_5</math> [cm<sup>-1</sup>]</b>
<i>Nuclei</i>					
RT112	744	1315	1450	1585	1660
BCO	751	1308	1447	1591	1660
UCO	680	1406	1499	1591	1666
<i>Mitochondria</i>					
RT112	1092	1251	1321	1635	1700
BCO	1255	1325	1460	1600	1730
UCO	1138	1242	1317	1451	1658

**Table S2.** Relative improvement [%] of the FeaSel-Net biomarker retrieval compared to the PCA loadings method (accuracy ACC, sensitivity SEN, and specificity SPE).

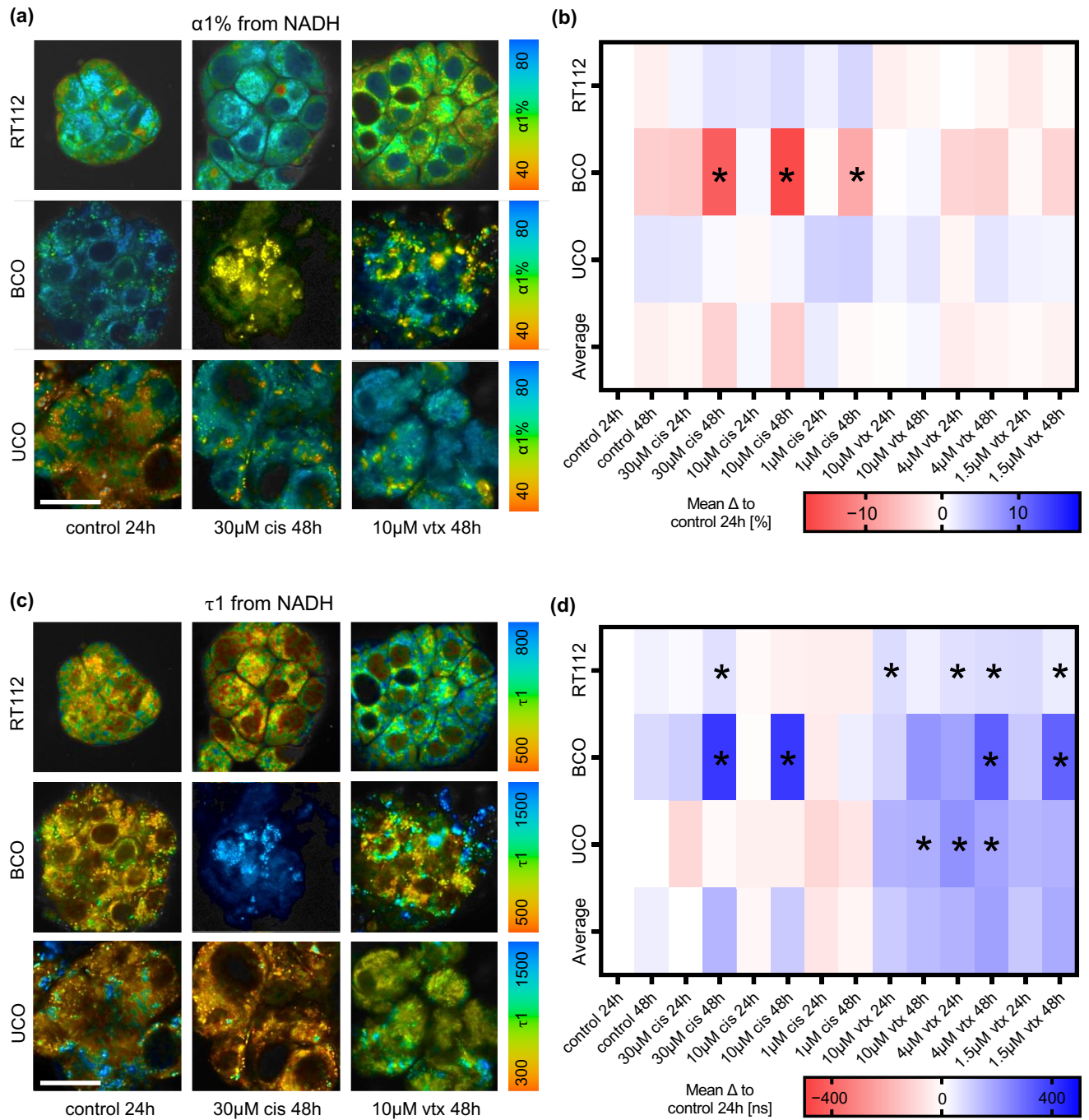
<b>Dataset</b>	<b>ACC</b>	<b>SEN</b>	<b>SPE</b>
<i>Nuclei (average)</i>	10.1	18.0	7.1
RT112	13.6	23.9	9.5
BCO	7.2	12.6	5.1
UCO	9.6	17.6	6.6
<i>Mitochondria (average)</i>	5.3	9.1	3.6
RT112	8.3	14.6	5.7
BCO	1.9	3.2	1.4
UCO	5.5	10.1	3.8
<i>All Data</i>	7.3	12.8	5.1



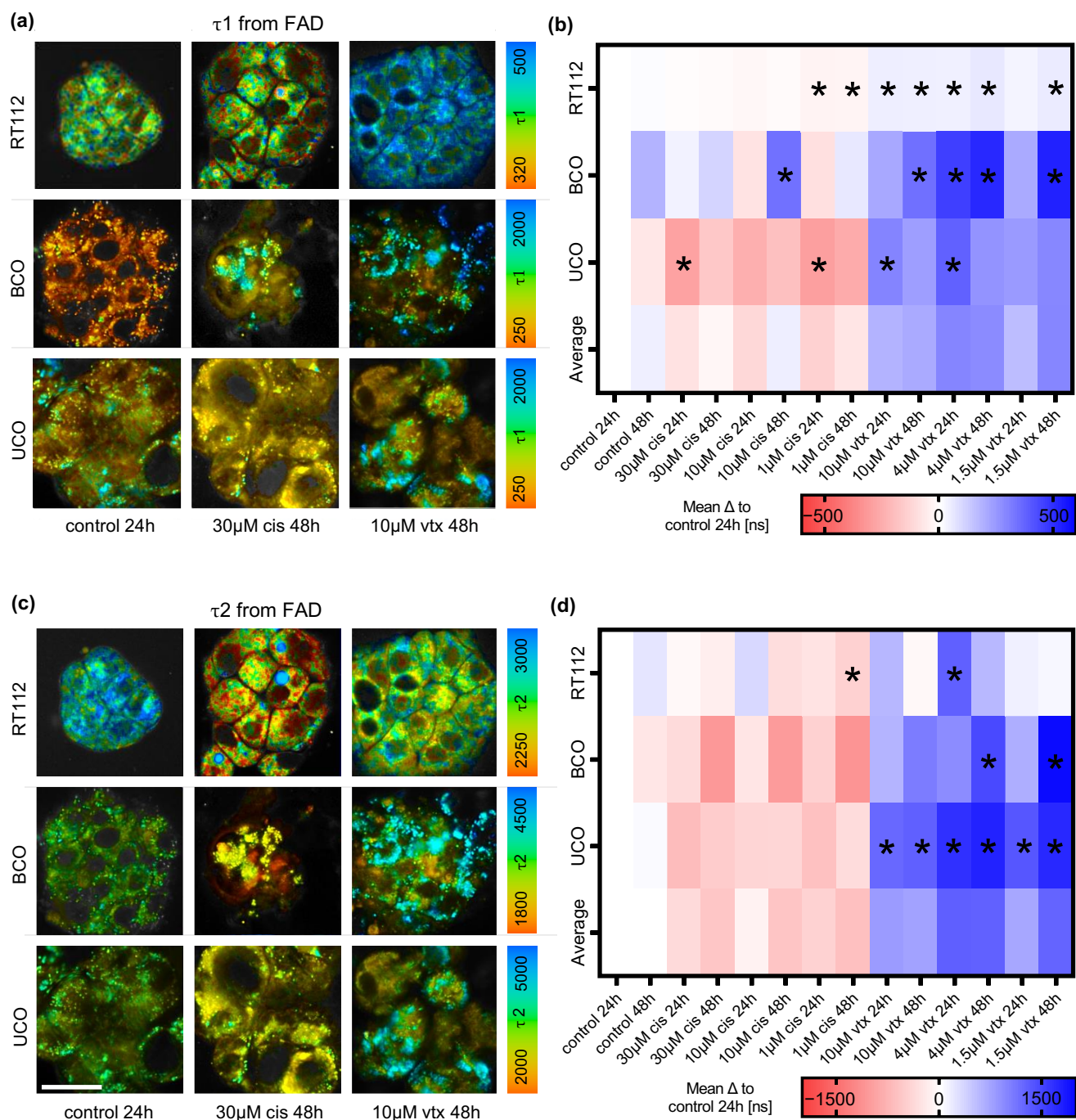
**Figure S1. Raman spectra averaged over each class. (a)** shows the mean spectra for the standardized spectra along the feature axis whereas **(b)** shows the normalized spectrum along the sample axis.



**Figure S2. FLIM results for organoids derived from the cell line RT112, BCO and UCO. (a-c) α1% from NADH. (d-f) α1% from FAD. (g-i) τ1 from NADH. (j-l) τ1 from FAD. (m-o) τ2 from NADH. (p-r) τ2 from FAD. Data represent average FLIM parameters per organoid, n=15, One-way ANOVA, p<0.05.**



**Figure S3. NADH FLIM of bladder cancer organoids.** (a)  $\alpha 1\%$  and (c)  $\tau 1$  of RT112, BCO and UCO. Displayed are untreated organoids after 24 hours, 30  $\mu$ M *cis* treated organoids after 48 hours and 10  $\mu$ M *vtx* treated organoids after 48 hours. Scale bar: 25  $\mu$ m. (b) Heatmap of mean differences of NADH  $\alpha 1\%$  to the control after 24 hours. (d) Heatmap of mean differences of NADH  $\tau 2$  to the control after 24 hours. One-way ANOVA,  $n=15$ ,  $p<0.05$ .



**Figure S4. FAD FLIM of bladder cancer organoids.** (a)  $\tau_1$  from FAD and  $\tau_2$  from FAD (c) of RT112, BCO and UCO. Displayed are untreated organoids after 24 hours, 30 $\mu$ M *cis* treated organoids after 48 hours and 10 $\mu$ M *vtx* treated organoids after 48 hours. Scale bar: 25 $\mu$ m. (b) Heatmap of mean differences of  $\tau_1$  from FAD to the control after 24 hours. (d) Heatmap of mean differences of  $\tau_2$  from FAD to the control after 24 hours. Statistical analysis: One-way ANOVA,  $n=15$ ,  $p<0.05$ .

**Table S3.** Information on tumor samples.

<b>Patient</b>	<b>UCO</b>	<b>BCO</b>
Age (years)	85	64
Gender	male	male
Localization	bladder	bladder
Tumor Stage (pT)	pT1	pT2
Tumor Grade (G)	G2	G3
Specimen retrieval	Rinsing urine	Radical cystectomy

**Table S4.** Parameters for the FeaSel-Net Callback.

<b>Parameter</b>	<b>Symbol</b>	<b>Value</b>
Number of features	$n_f$	3
Evaluation type	-	accuracy
Threshold value	$\tau_{acc}$	0.98
Threshold decay	$\sigma_{acc}$	0.0
Minimum number of epochs	$d_{min}$	20
Maximum number of epochs	$d_{max}$	150
Pruning rate	$\pi$	0.2
Pruning type	-	exponential
Number of samples per class (eval.)	$n_s$	10
Normalization of eval. loss	-	min-max norm
Decision metric	-	average