

Supplementary figure 1: Averaged FTIR spectra of tissue-engineered skin with variable thicknesses (2-25 $\boldsymbol{\mu m}$ ). 10-um thick tissue section (green) is shown to be the optimal thickness to avoid nonlinear detector response or saturation that may be associated with higher absorbance intensities ( $>20-\mu \mathrm{m}$ ) seen in thicker tissue sections. Thinner tissue sections ( $<5-\mu \mathrm{m}$ ), given lower absorbance intensities, were also excluded to optimize the signal to noise ratio.


Supplementary Figure 2: Absorbance intensities FTIR spectra variability recorded from the generated tissue-engineered skins.
A) Overlay FTIR spectra from different tissue-engineered skins. B) Second derivative FTIR spectra calculated from the upper panel (A).


## Supplementary Figure 3: Increased cytoplasmic aggregated TDP-43 with antiparallel $\boldsymbol{\beta}$-sheet structures in ALS-derived TES quantified by ELISA.

For each sample, the amount of TDP-43 was normalised over the total protein content of the fraction and the ratio of the nuclear fraction over the cytoplasm fraction was calculated. A smaller nuclear to cytoplasm ratio indicates TDP-43 delocalization from the nucleus to the cytoplasm, a well-known pathological signature of ALS. Data is reported as mean $\pm$ SEM. Statistically significant smaller nuclear to cytoplasm ration can be observed in ALS-derived TES as expected (one tailed Mann-Whitney, $\mathrm{p}=0,0333$ ).

Supplementary Table 1: Parameters of the different absorbance filters used for spectra filtering and their purpose

| Region <br> $\mathrm{cm}^{-1}$ | Minimum <br> abs. <br> Au. | Maximum <br> abs. <br> Au | Purpose |
| :---: | :---: | :---: | :--- |
| $1700-1600$ | 0,2 | 0,9 | To remove the spectra from regions within the <br> TES that are too thin $(<0.1 \mathrm{Au})$ or too thick <br> $(>0.9 \mathrm{Au})$ |
| $1780-1730$ | 0,0 | 0,1 | To remove spectra associated with the presence <br> of OCT. |

