Supplementary Figure 2. Quantitative tube formation analysis with S.CORE software (S.CO LifeScience GmbH). Sample image shows ATP-treated VVEC.

Object oriented image analysis approach is based on the first-class Cognition Network Technology, S.CORE tube formation quantification analysis includes three aspects:

1. **Single tube quality:** tubes are thin, long and linear
2. **Confluent areas:** the more confluent areas with the less tube formation potential
3. **Tube network:** the more complex the tube network with the more tube formation potential

All three aspects are integrated in the definition of the S.CORE Tube Formation Index.

S.CORE Tube Formation Index: $(\text{Mean Tube Index})^2 \times (1 - \text{Confluent area}) \times (\text{No. branching points} / \text{Total length skeleton})$

On images, cellular parts are divided into 3 categories:
• Confluent Areas (white)
• Nodal structures (blue)
• Tubes (yellow, orange, red)

Total length of well-developed tubes (yellow, calculated in pixels [px]) is defined as total length of tubes with a high tube index

Total length of satisfactory-developed tubes (orange, calculated in pixels [px]) is defined as total length of tubes with a medium tube index

Total length of poorly-developed tubes (red, calculated in pixelsin pixels [px]): is defined as total length of tubes with a low tube index