# EVBO Publication highlight – May 2021

**Control of endothelial quiescence by FOXO-regulated metabolites.**

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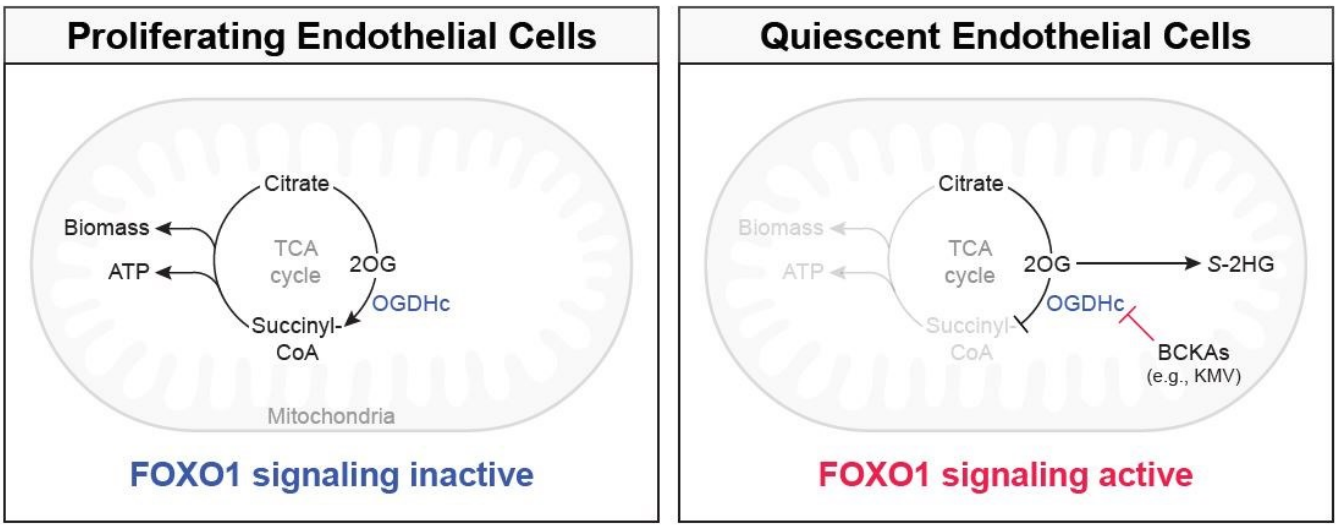


**Key findings:**

1. Activation of the quiescence-promoting transcription factor FOXO1 induces the levels of the 2-oxoglutarate (2OG)-derived metabolite S-2-hydroxyglutarate (S-2HG) in endothelial cells (ECs).
2. S-2HG arrests the endothelial cell cycle and promotes a quiescent state.
3. FOXO1 elicits S-2HG production by inhibiting the mitochondrial 2-oxoglutarate dehydrogenase complex (OGDHc), a central enzyme of the TCA cycle that converts 2OG to succinyl-CoA.
4. OGDHc activity is inhibited by branched-chain ketoacids (BCKAs) such as 3-methyl-2-oxovalerate (KMV), which accumulate in ECs with activated FOXO1 signaling.
5. Together, these findings identify a metabolic regulatory system in ECs that instructs the cell's decision to cycle or become quiescent and in which the signaling metabolite S-2HG plays a critical role.