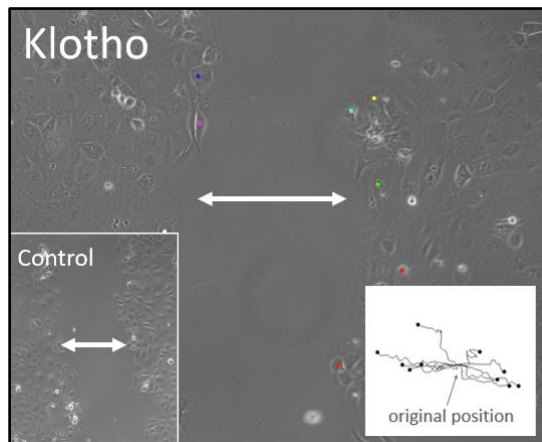
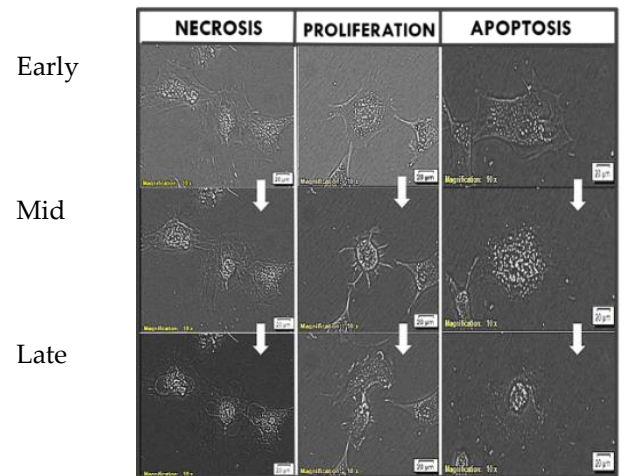


**(A)**



**(B)**



**Supplemental Figure S1.** Live cell image of phenotypic changes in VSMC in the presence and absence of Klotho (A) Live cell time-lapse imaging following scratch assay closure with improved migration of klotho treated monolayers over 24 hrs (n=3),(Image-J cell track module). (B) Representative images tracking the different live cell phenotypes over time (white arrows show progression from top to bottom images) for necrosis, mitosis and apoptosis.

**Supplemental Table S1.** List of drugs screened for changes in cell energetics.

Compound	Doses	Stimulation (hr)	Mechanism	References
AICAR (in H <sub>2</sub> O)	0.1; 0.25; 0.5; 1; 2 mM	2 h	AMP mimetic	Goirand et al 2007, [21] Sun et al 2007,[22]
A-769662 (in DMSO)	5; 10; 20; 50; 100 $\mu$ M	2 h	Allosteric activation of AMPK (Acting on AMPK $\beta$ 1)	Treibak 2009, [23] Goransson, 2007[24]
Berberine (in DMSO)	10; 20; 50; 100; 200 $\mu$ M	24 h	Complex 1 inhibition	Wang et al, 2011[18] Lee et al 2006[25]
Etoposide (in DMSO)	5; 10; 20; 50; 100 $\mu$ M	24 h	ATM-dependent mitochondrial biogenesis and AMPK activation	Fu et al, 2008[26]
Klotho (in H <sub>2</sub> O) ( <sup>1</sup> membrane <sup>2</sup> soluble <sup>3</sup> intracellular)	1.0 to 0.0001ng/mL	2-24 h	<sup>1</sup> FGF23 co-receptor <sup>2</sup> Inhibitor of IGF/TGF- $\beta$ 1 <sup>3</sup> Cytokine suppressant & antioxidant	Wolf I 2008[11] Imura et al 2007 [12] Kurosu et al 2005[7]
Losartan (in H <sub>2</sub> O)	1; 2.5; 5; 20; 50 $\mu$ M	24 h	p21 and p53 expression	Kim et al 2010[17]
Metformin (in H <sub>2</sub> O)	0.1; 0.5; 1.0; 5; 10 mM	2 h	Complex 1 inhibition	Zho et al[27]
Resveratrol (in DMSO)	10; 20; 50; 70; 100 $\mu$ M	24 h	SIRT1-dependent mitochondrial biogenesis	Price et al, 2012[28]
Trimetazidine (in H <sub>2</sub> O)	0.1;1.0;10;100 $\mu$ M	2-24 h	Inhibitor of free fatty acid oxidation and increased glucose utilisation	Zheng, S. <i>et al</i> 2018[29] Chrusciel et al 2014[30] Marzilli et al 2019[31]
Troglitazone (in DMSO)	5; 10; 20; 50; 100 $\mu$ M	24h	Mitochondrial membrane depolarisation	Le Brasseur et al, 2006[32]
Salicylate (in H <sub>2</sub> O)	0.5; 1; 2; 5; 10 mM	24h	Allosteric activation of AMPK	Hawley et al, 2012[20]

**Supplemental Table S2.** Primary and secondary antibodies used in immunocytochemistry and immunohistochemistry. (All others as previously described Mercer *et al* 2005).

Pathway	Antibody	ICC 1 <sup>o</sup> Ab	IHC 1 <sup>o</sup> Ab	Company	Secondary antibody
<b>p-ACC 280kDa (Cyto and SR)</b>	Phospho-Acetyl-CoA Carboxylase (Ser 79) Antibody #11818 (inhibitory side phosphorylation)	1:100	1:200	Cell Signalling Technology ©	Anti-Rabbit Alexa543 1:500
<b>Total ACC 280kDa</b>	ACC Antibody #3676 Cyto and SR) (not shown)	1:250	1:400	Cell Signalling Technology ©	Anti-Rabbit Alexa543 1:500
<b><math>\alpha</math>-SM-Actin Cytoplasm)</b>	$\alpha$ -SM-Actin Antibody (Mouse)	1:100	1:200	Abcam ©	Anti-Mouse (alexa543) 1:500
<b>AMPK 62kDa (Cytoplasm)</b>	Phospho-AMPK $\alpha$ (Thr172) Antibody (Rb) #2535	1:100	1:200	Abcam ©	IgG Anti-Mouse 1:500
<b>Phospho-Pink1</b>	Ab117091 Ab237070	1:100	1:200	Abcam©	IgG Donkey Anti-rabbit Ab150073 and Ab175780 RP