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mTOR is an essential gate in adapting the functional response of ovine trophoblast cells under stress-inducing environments

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1 BACKGROUND

During early pregnancy (Day 16-23 in sheep), vascularization is insufficient for supporting embryo nourishment due to immature placentation. The placenta copes with suboptimal conditions, allowing trophoblast cells to adopt adaptive strategies. In this view, the autophagy process promotes cell survival in response to stress, through the mammalian target of rapamycin (mTOR), known as the placental nutrient sensor.

2 OPEN QUESTION

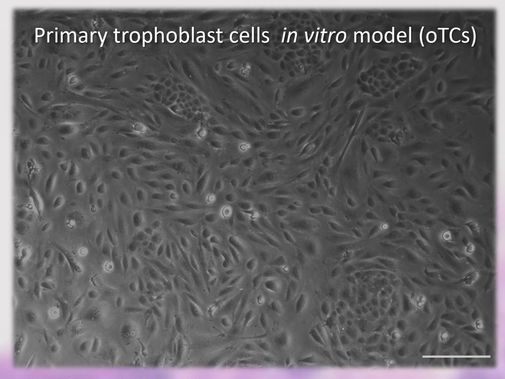
Is autophagy an effective strategy in case of nutrient deprivation?

3 GOAL

Shed light on how autophagy drives placenta adaptive response to low-nutrient environments.

4 METHODOLOGY

21-day-old sheep placenta



5x Magnification, Scalebar 100 µm

24h treatment

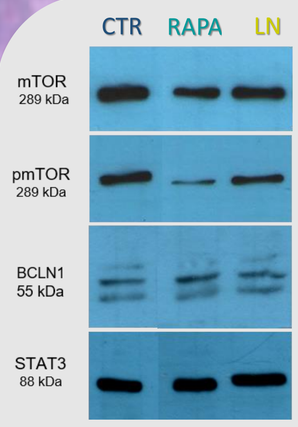
CTR (trophoblast growth medium: supplemented DMEM/F12)

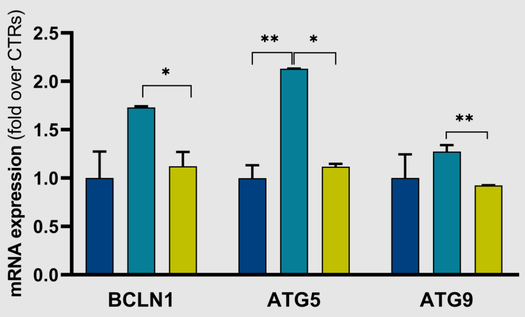
RAPA (chemical autophagy induction: CTR + 100nM rapamycin)

LOW NUTRIENT (MEM)

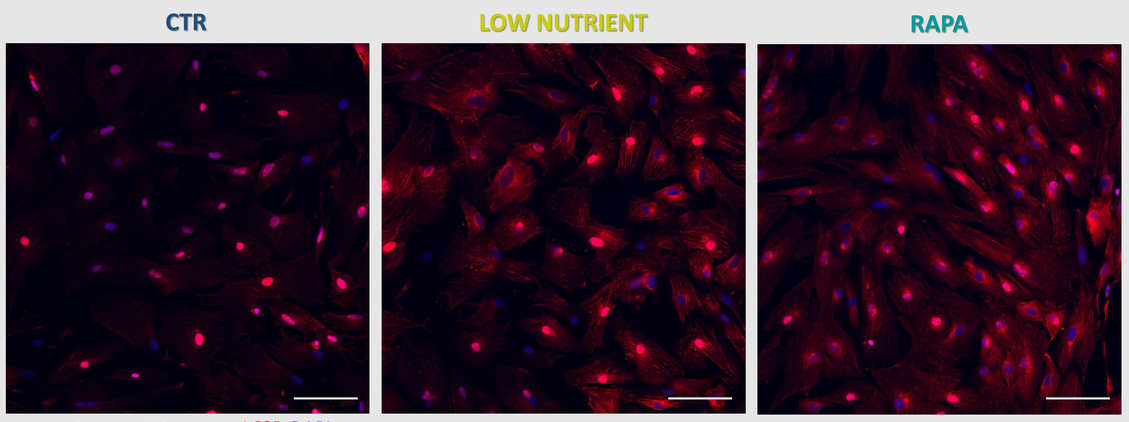
Autophagy process modulation	mTOR	WB
	ATGs	qPCR
	LC3B	IF, WB
Cell funcionality	Motility	Wound Healing
	SLCs	qPCR

5 RESULTS

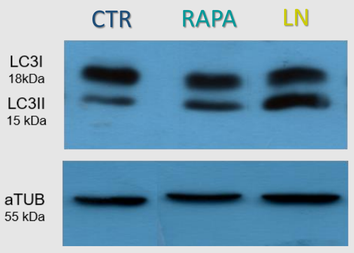




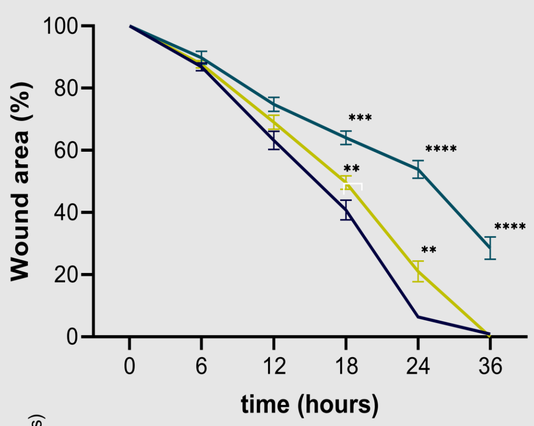
* p < 0.05; ** p < 0.01



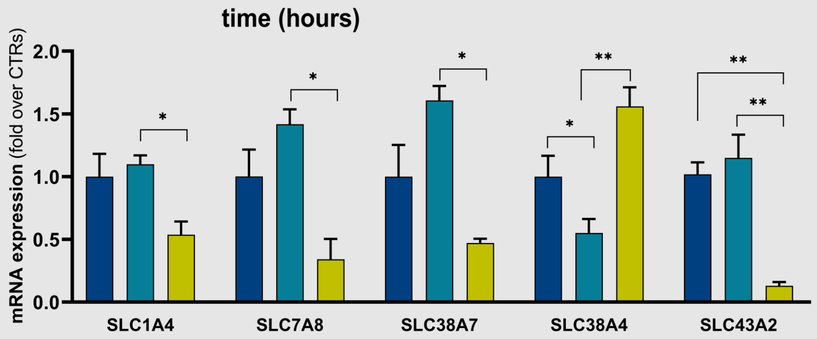
20x Magnification, Scalebar 100 µm LC3B DAPI



LC3BII higher expression confirmed autophagy activation in **rapa** & **low nutrient** environments.
However, mTOR activation was severely modified only following **rapa** whereas prolonged **starvation** allowed **mTOR** reactivation.



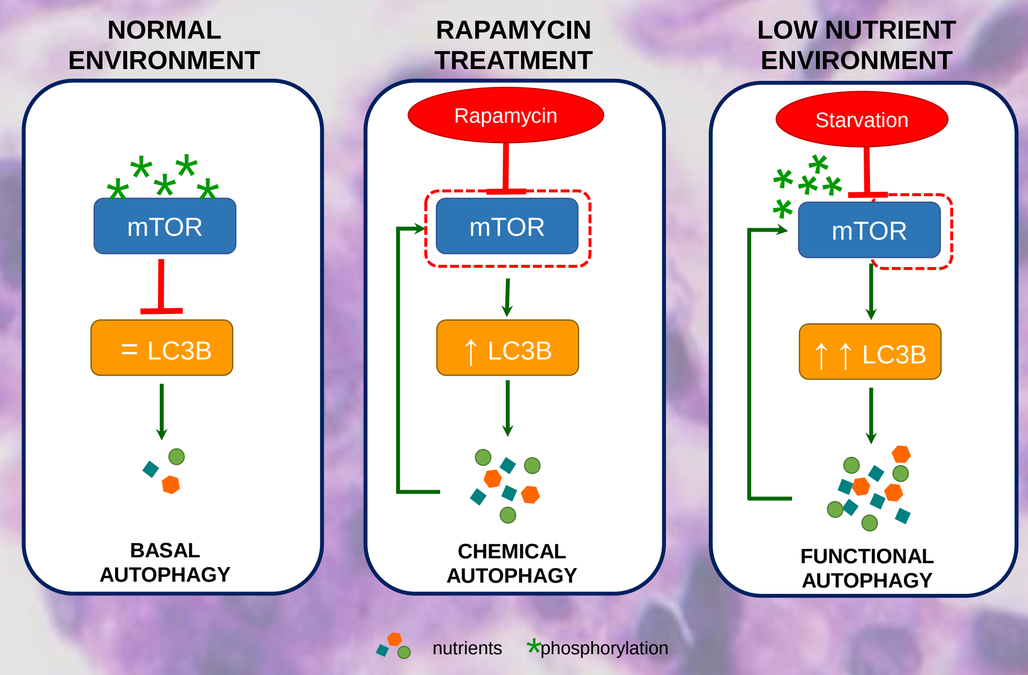
Nutrient-deprived oTCs increased migrative activity, while **rapa** drastically decreased trophoblast functionality.



SLCs expression was differentially influenced by **rapa** and **starvation** treatments.

* p < 0.05; ** p < 0.01; *** p < 0.001; **** p < 0.0001

6 FINAL HYPOTHESIS



7 CONCLUSION

Sheep trophoblast cells adapt to low nutrient conditions in the early stage of placentation by balancing, in an mTOR-dependent manner, nutrient recycling and transport with relevant effects for *in vitro* functional properties, potentially impacting conceptus development and survival.

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