



Friedrich-Schiller-University Jena

*Institute of Molecular Cell Biology
Center for Molecular Biomedicine*



Molecular Signatures of Adaptive Stress Responses; Studying Molecular Mechanisms Of Adaptation

Ignacio Rubio

Dose-response meeting, Amherst 2011



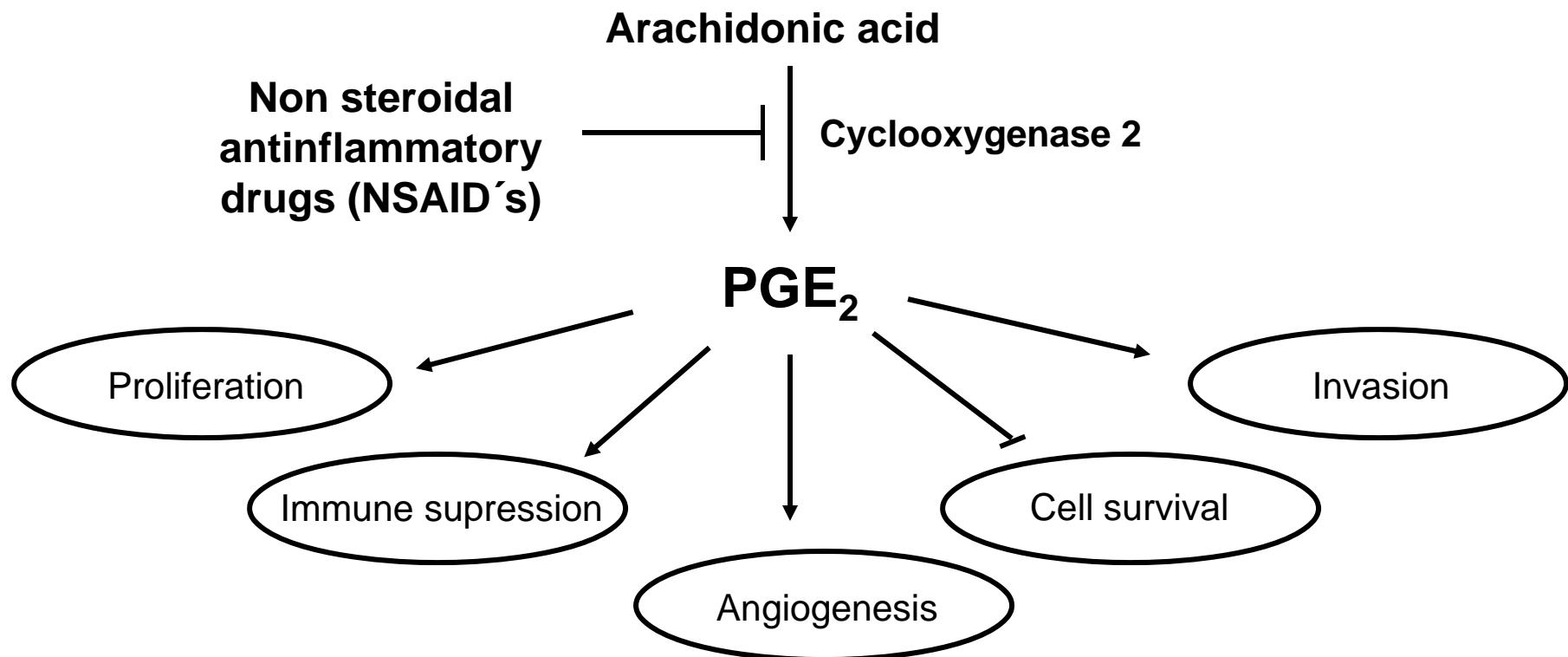
Molecular Signatures of Adaptive Stress Responses



Research Training Group Initiative
Friedrich-Schiller-Universität Jena



Role of PGE₂ in colorectal cancer cell growth

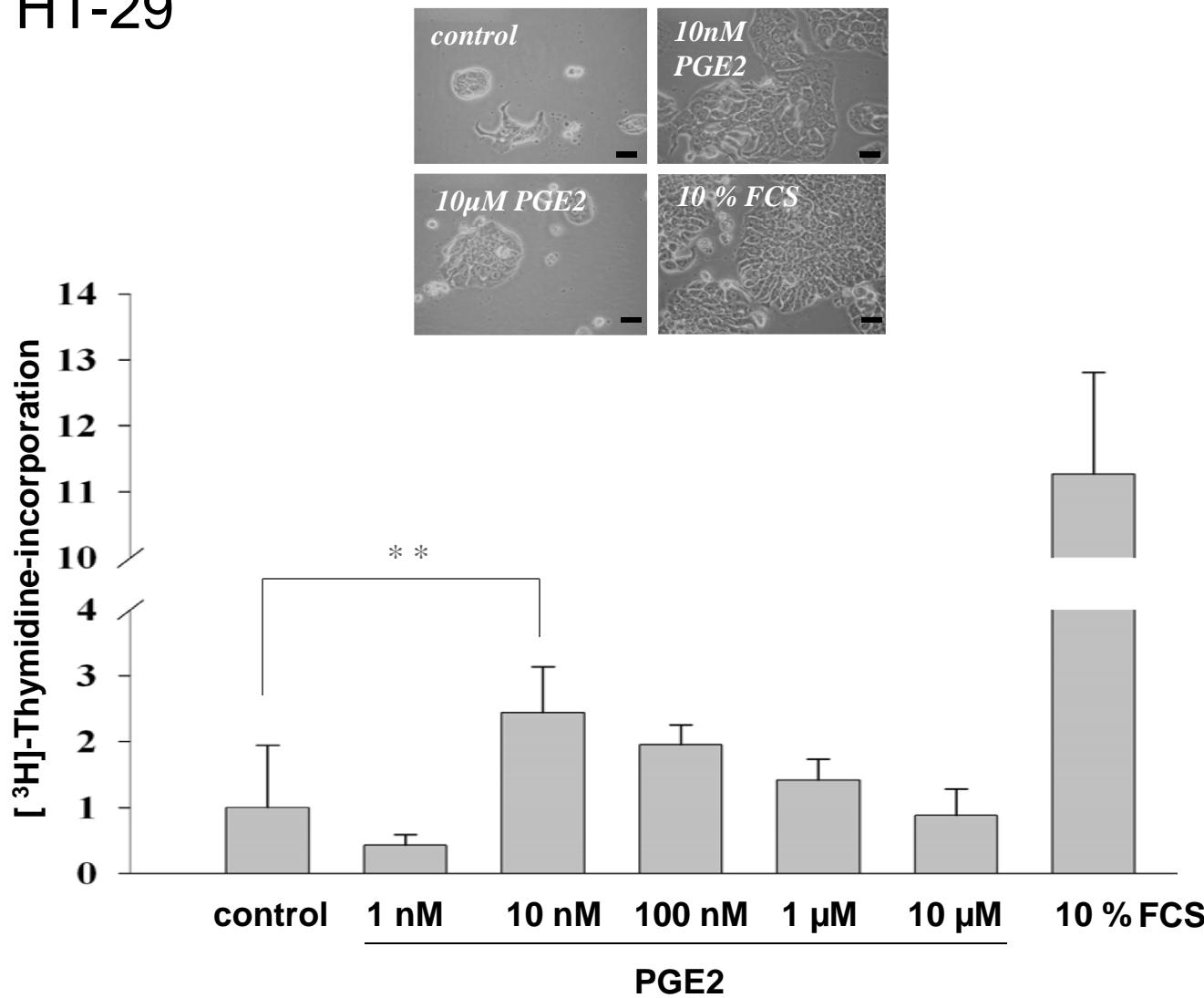


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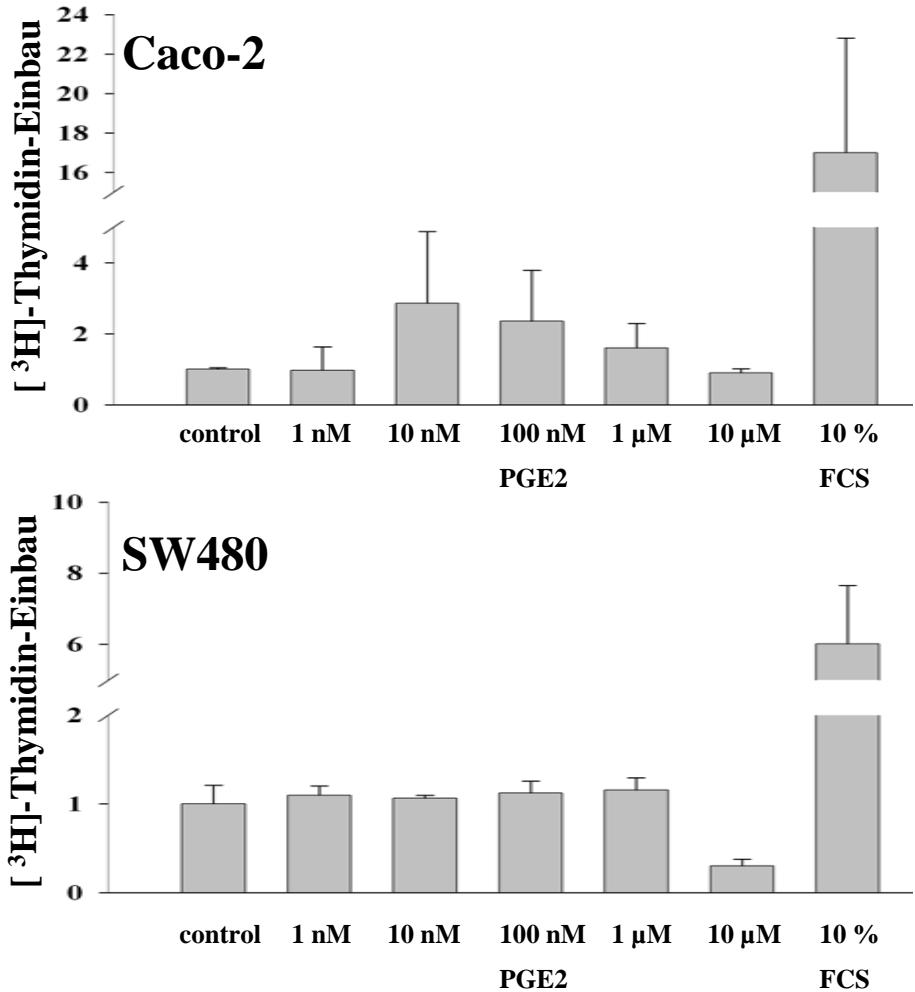
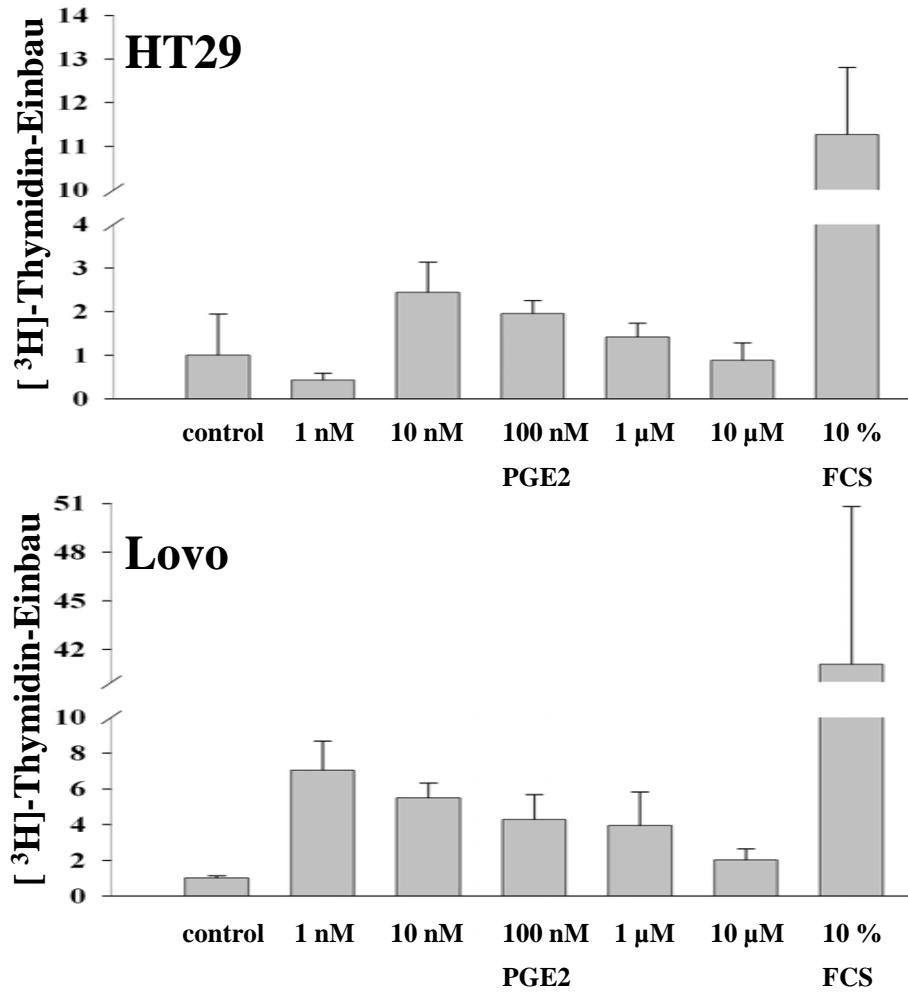
	Caco-2	HT29	Lovo	SW480
K-Ras	-	-	G13D	G12V
B-Raf	-	V599E	-	-
P53	E204Stop	R273H	-	R273H
APC	1, LOH	2, no LOH	2, no LOH	1, LOH

Role of PGE₂ in colorectal cancer cell growth

HT-29

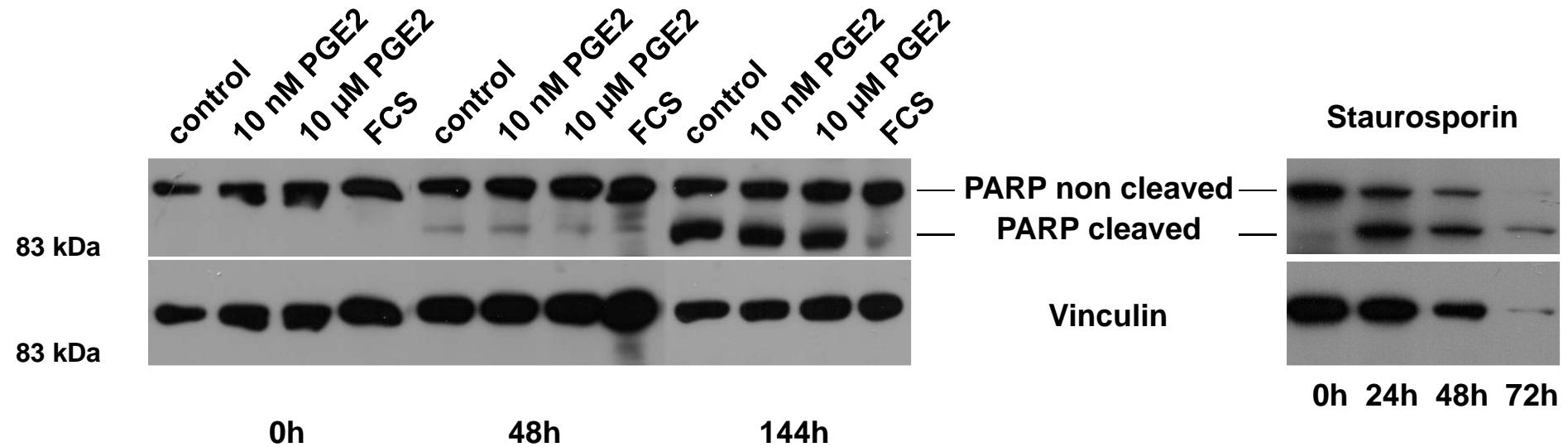


Nonlinear effect of PGE₂ in CRC cell proliferation

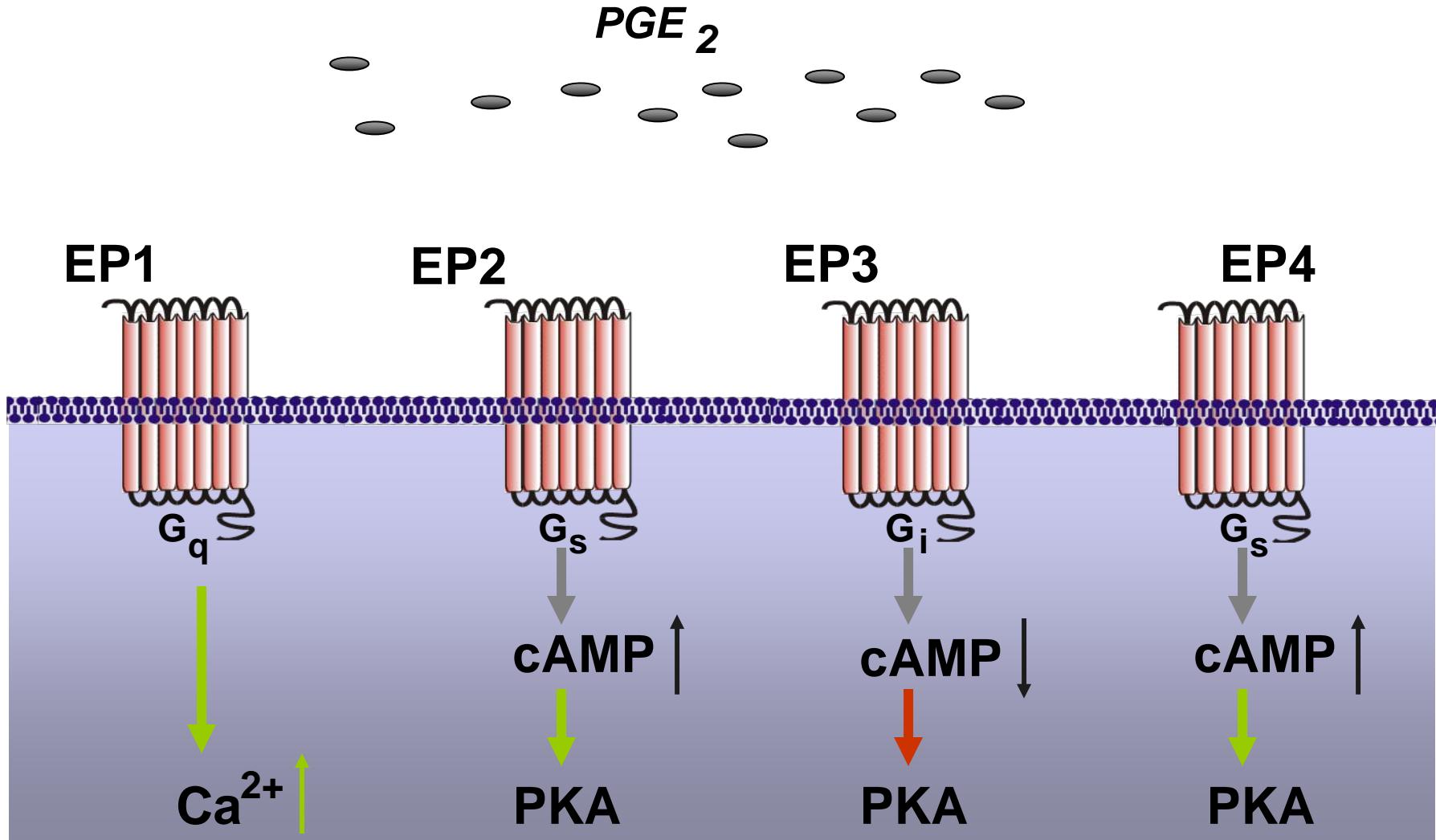


PGE₂ does not affect colorectal cancer cell survival

No major effect of PGE2 on apoptosis in serum-deprived cells



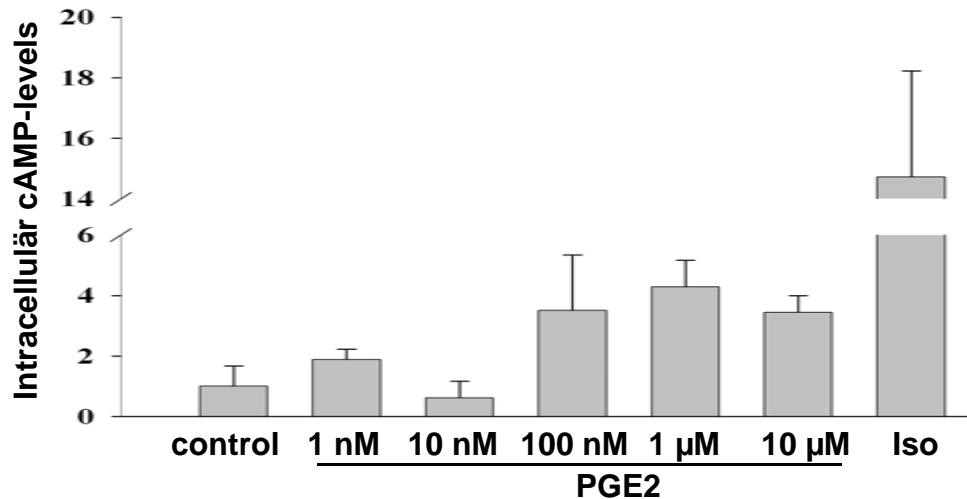
What is the mechanism underlying the hormetic dose-dependency in PGE₂ driven CRC proliferation



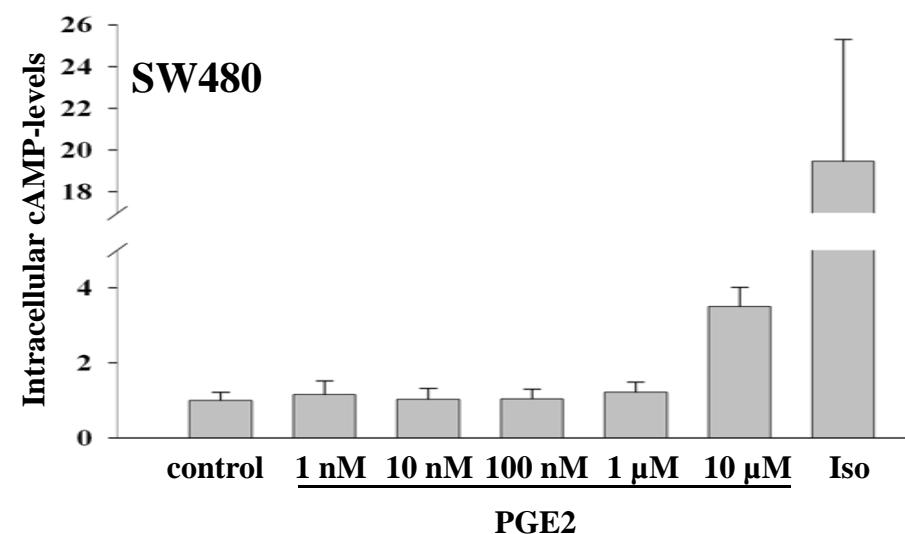
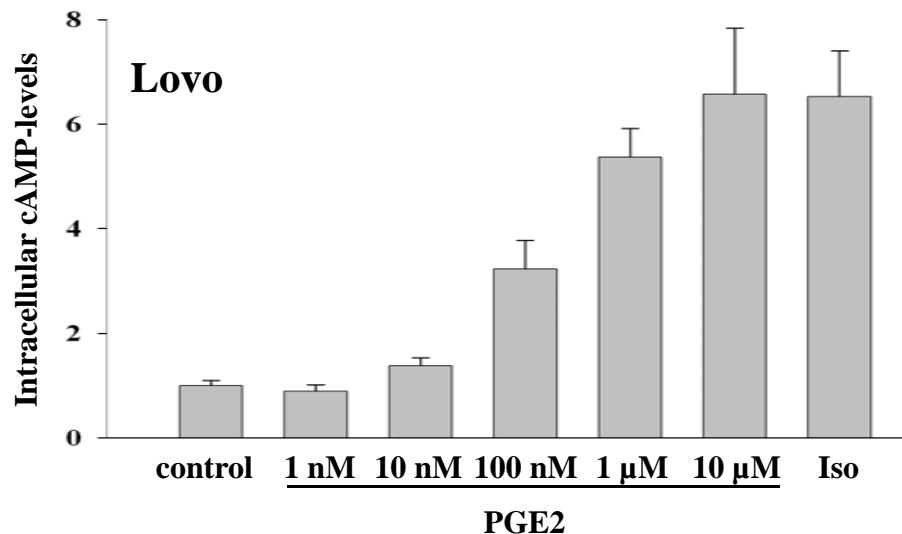
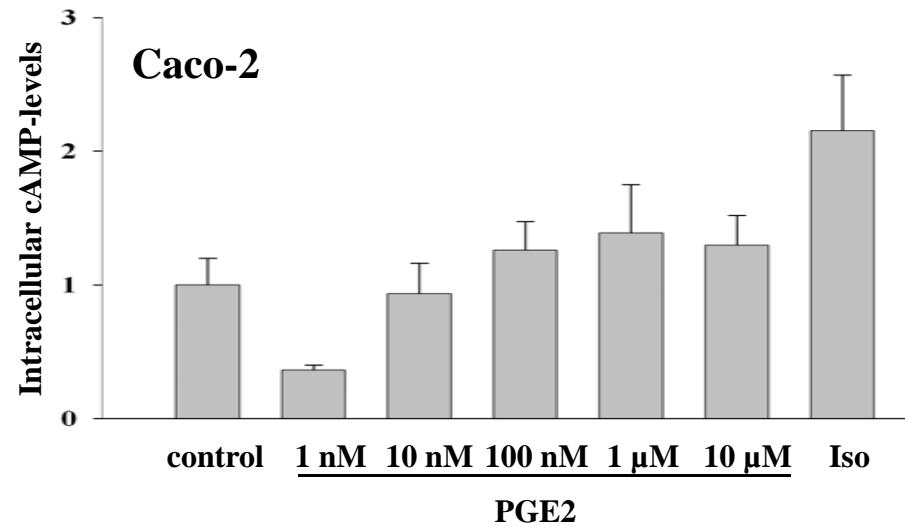
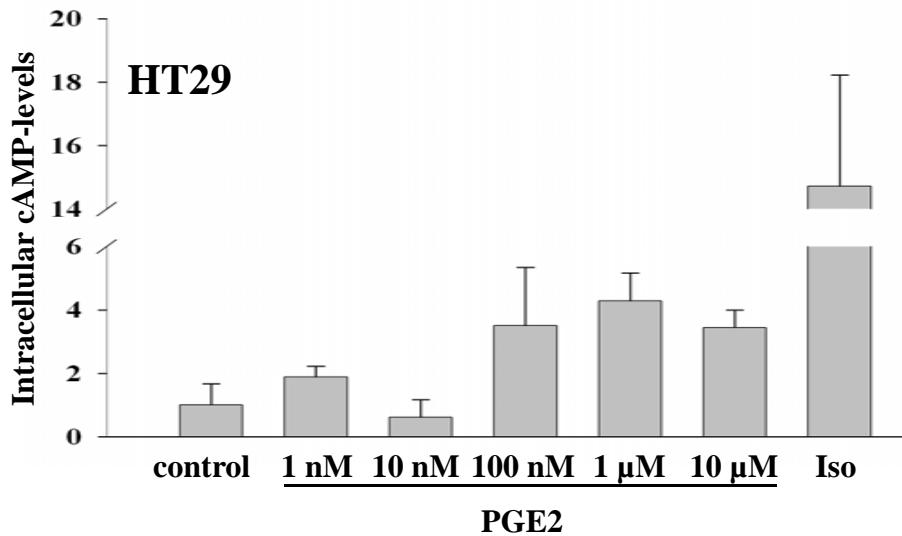
Downstream mediators of PGE₂ signaling in colorectal cancer cells

Dose-dependent, non-linear effect of PGE2 on cAMP production

HT29

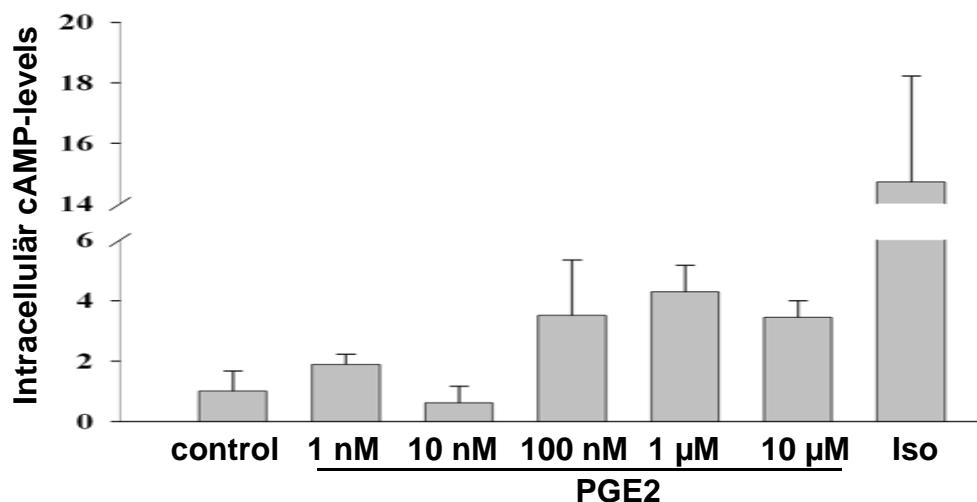
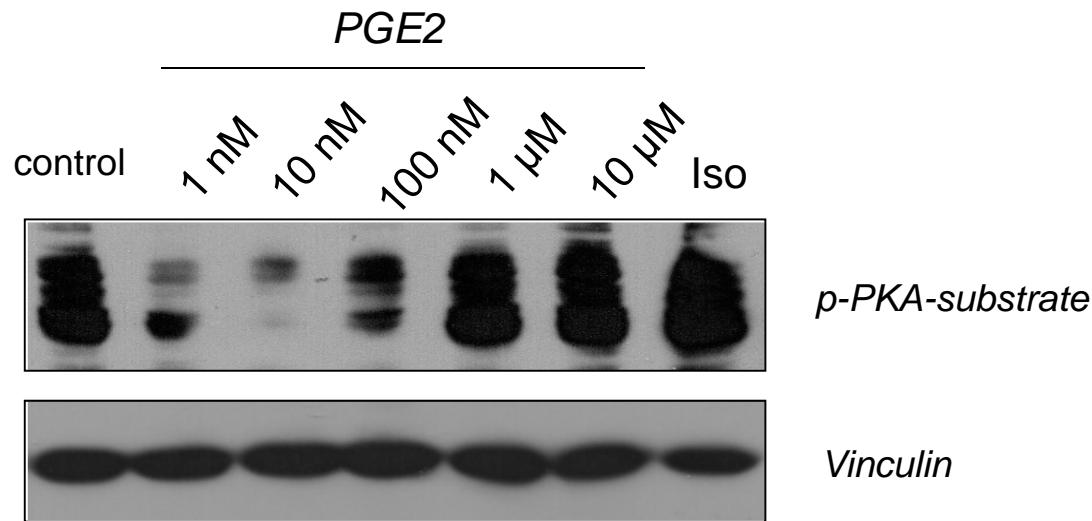


Nonlinear effect of PGE₂ on cAMP accumulation

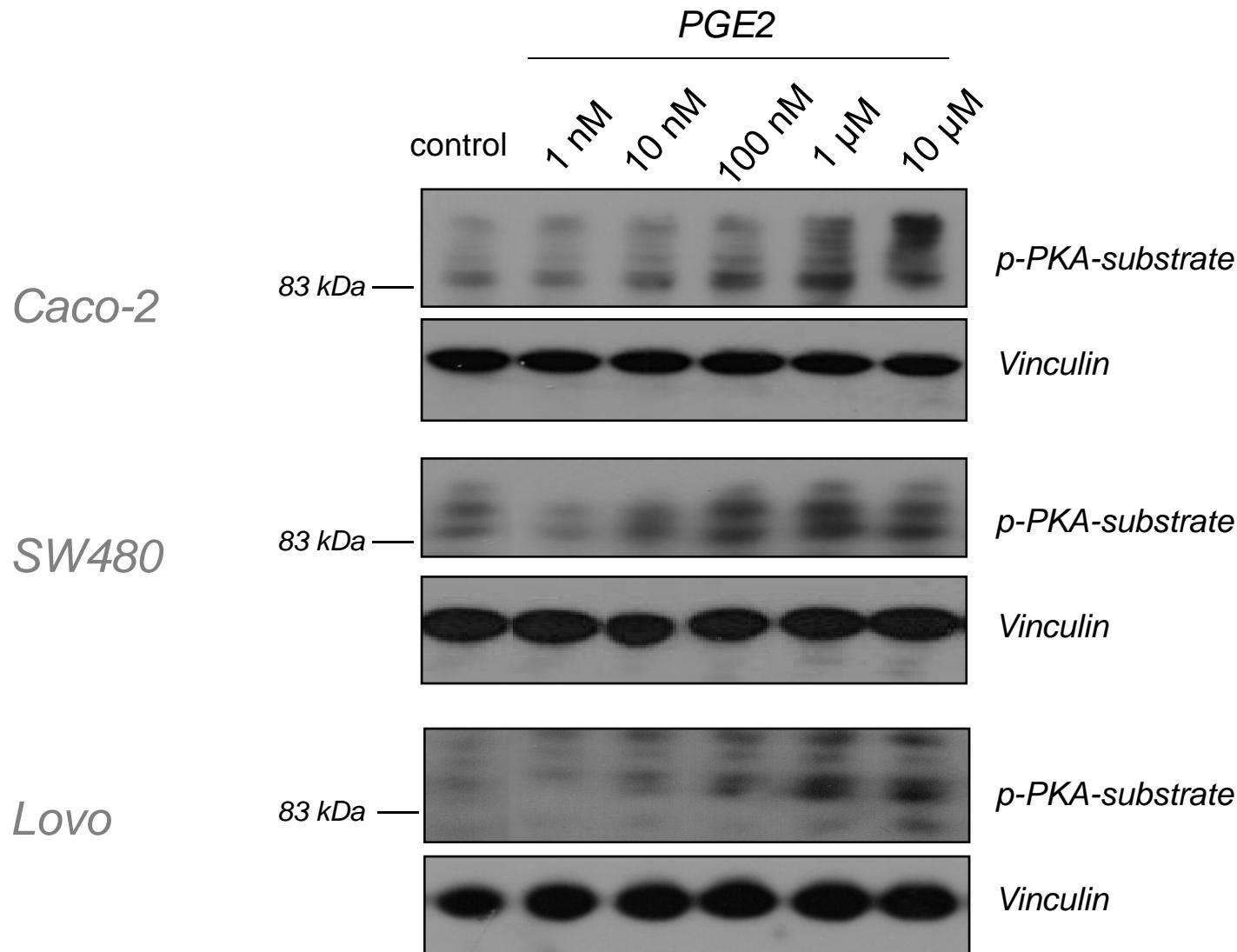


Role of PGE₂ in colorectal cancer cell growth

HT29

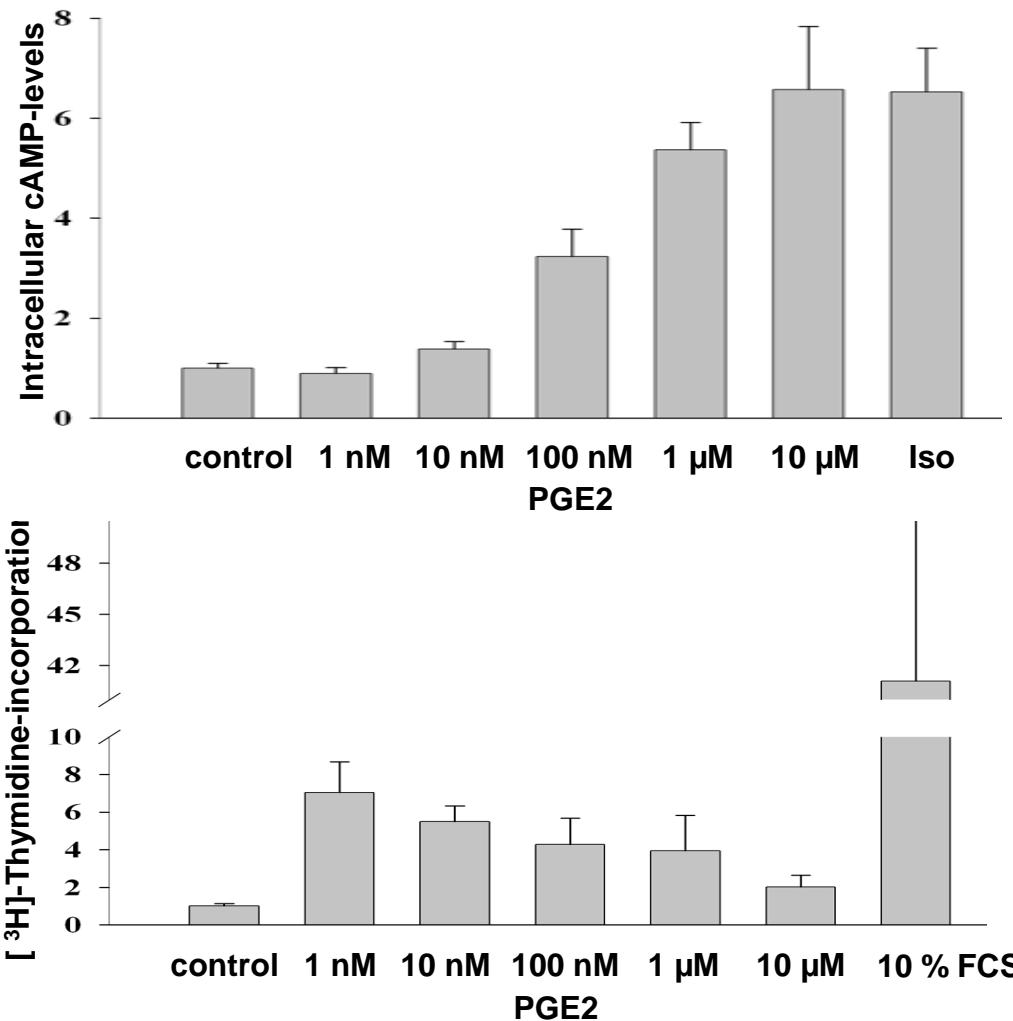


Role of PGE₂ in colorectal cancer cell growth

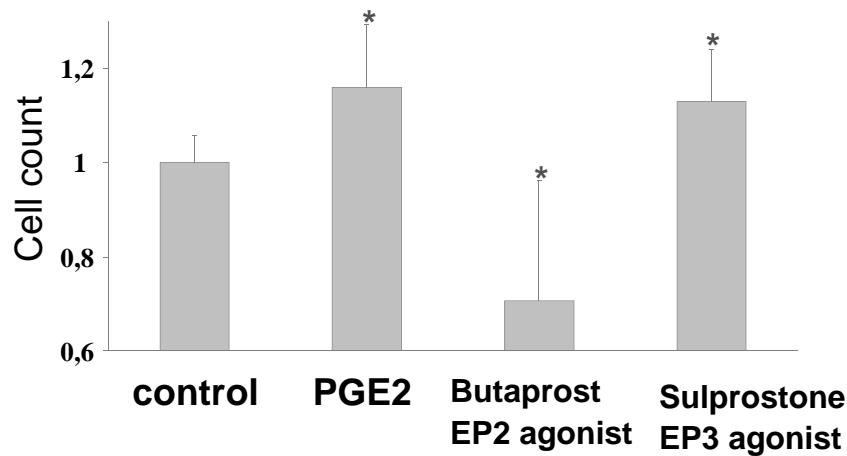
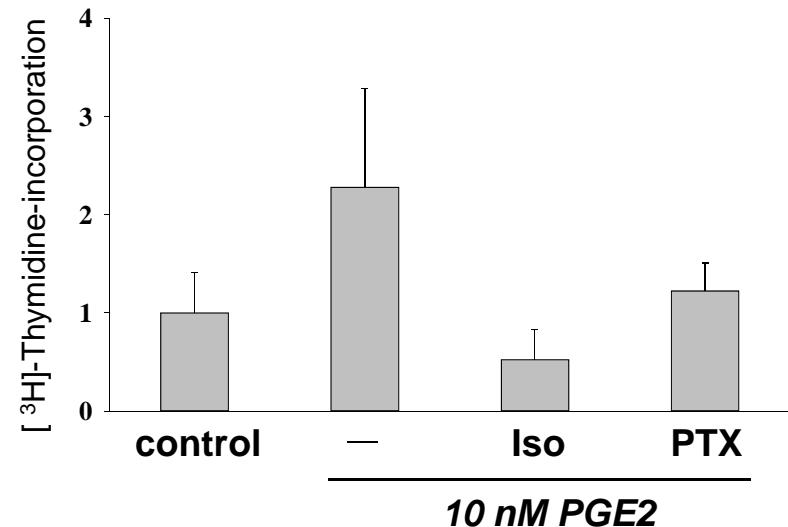
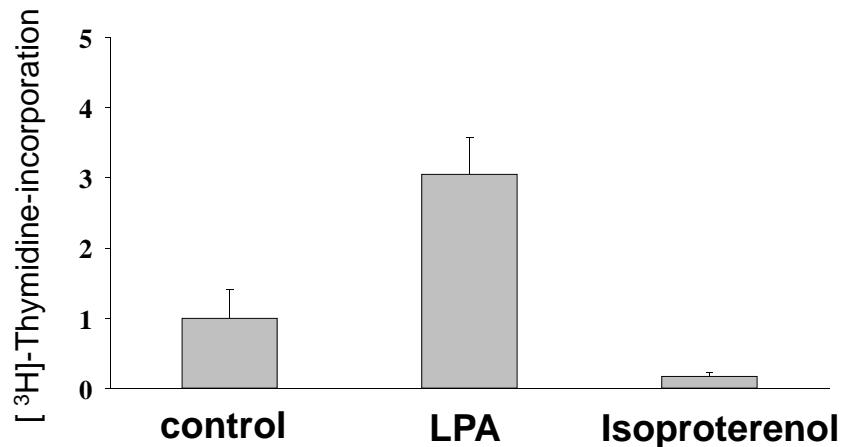


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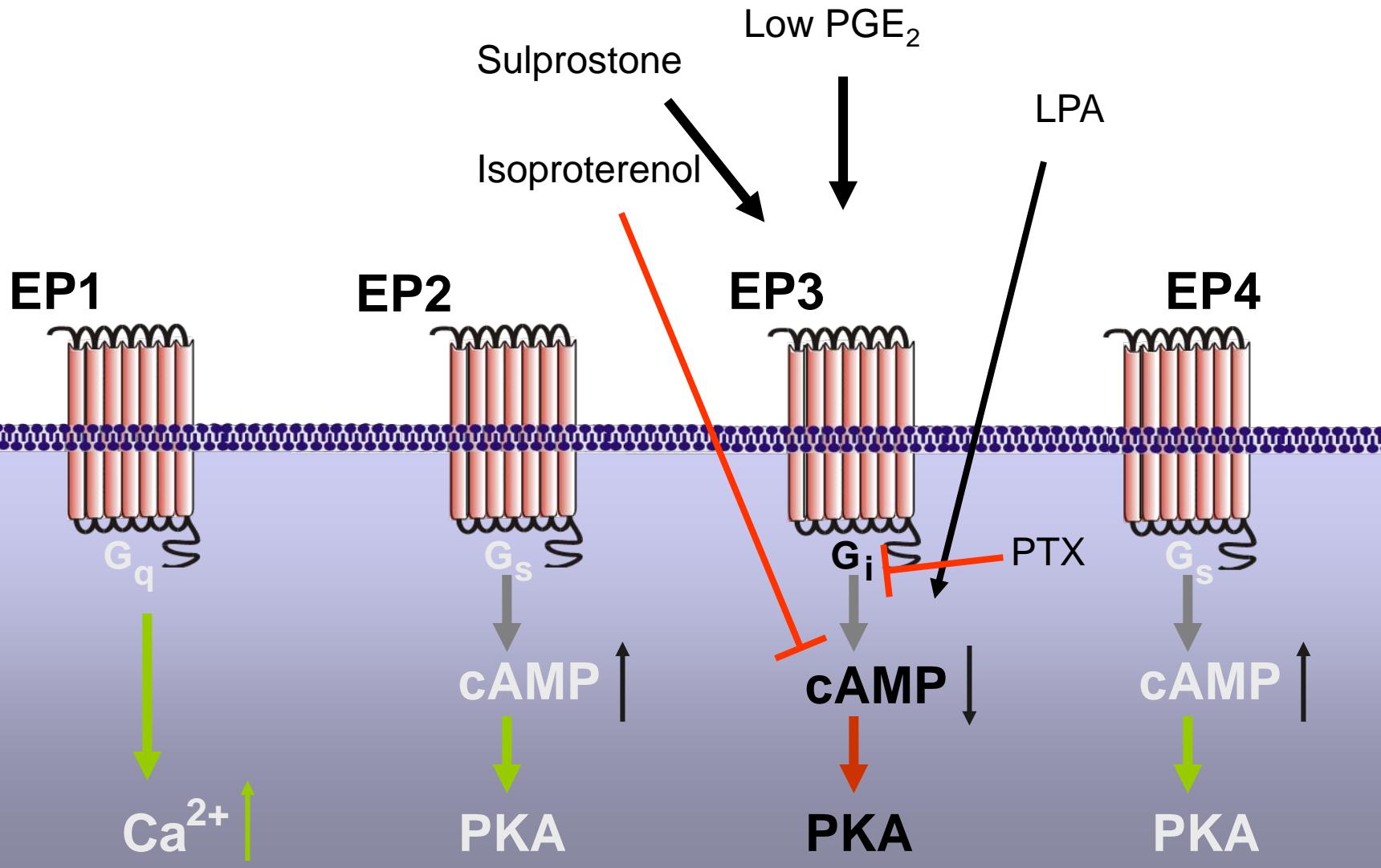
Inverse relation of PGE 2 effects on cAMP-levels and cell proliferation



Role of PGE₂ in colorectal cancer cell growth



Low PGE₂ doses promote CRC cell proliferation via a downregulation of cAMP levels



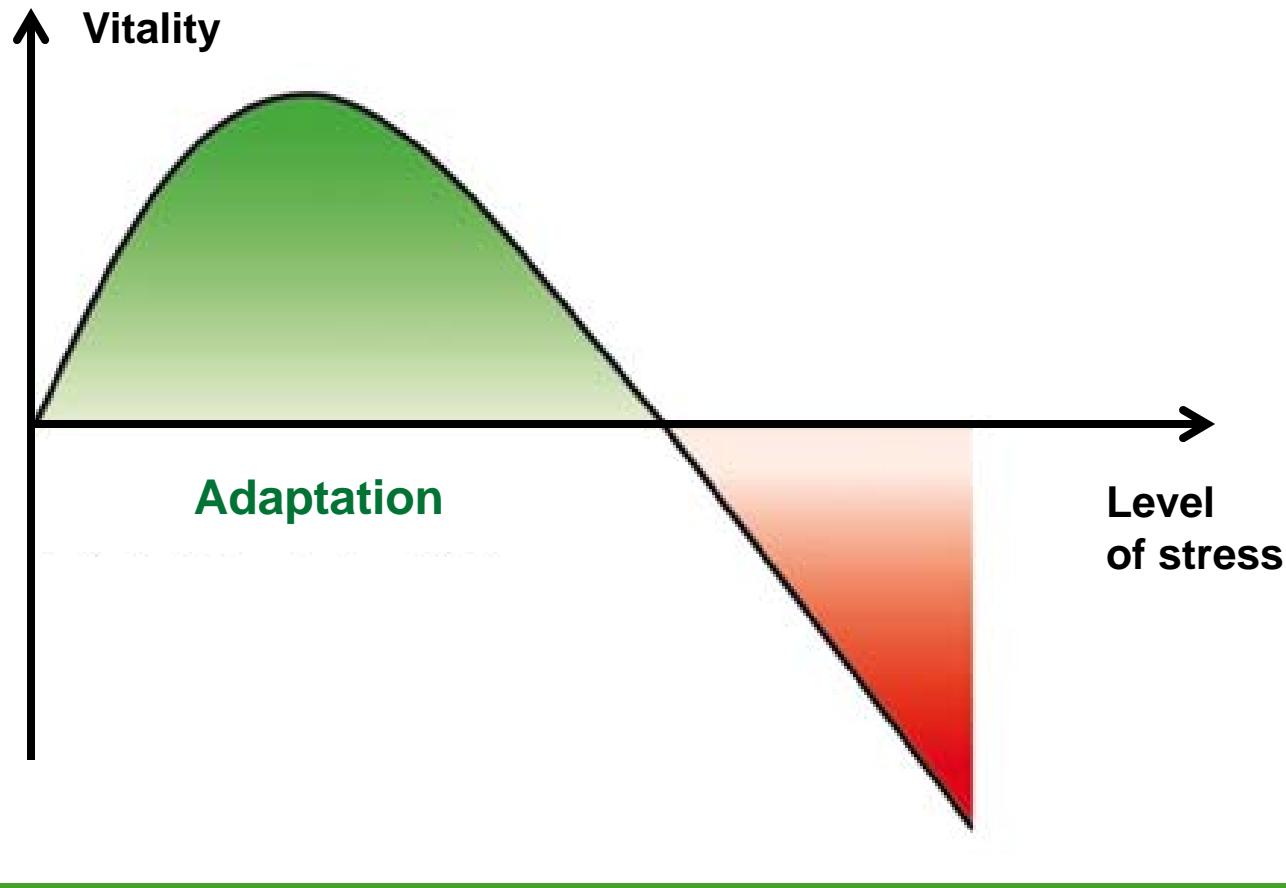
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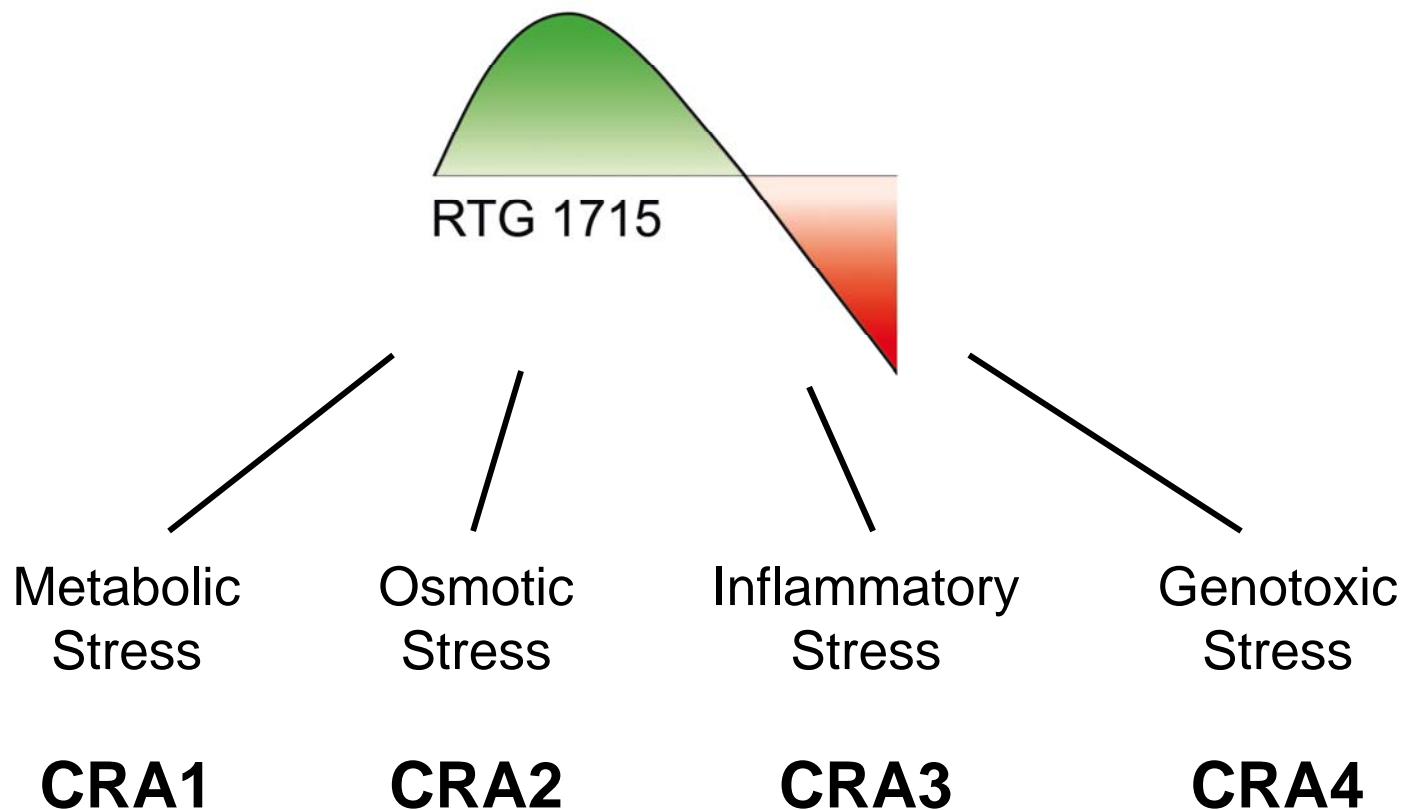


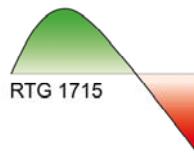
Biphasic stress response



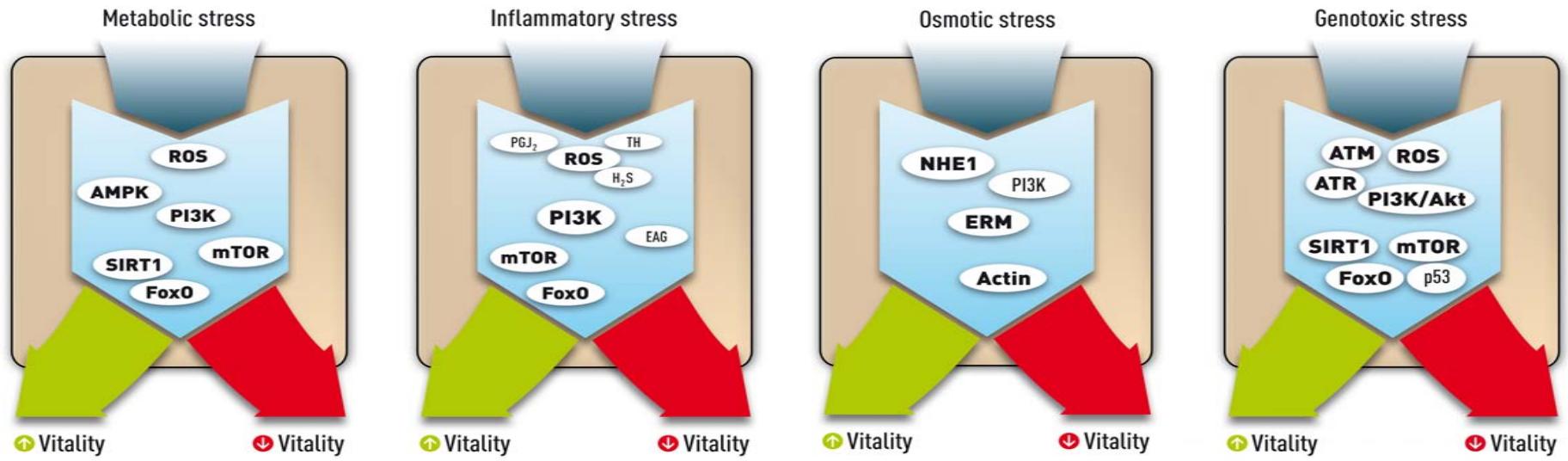
Central project idea

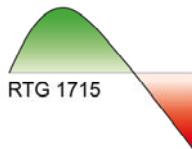
4 major core research areas





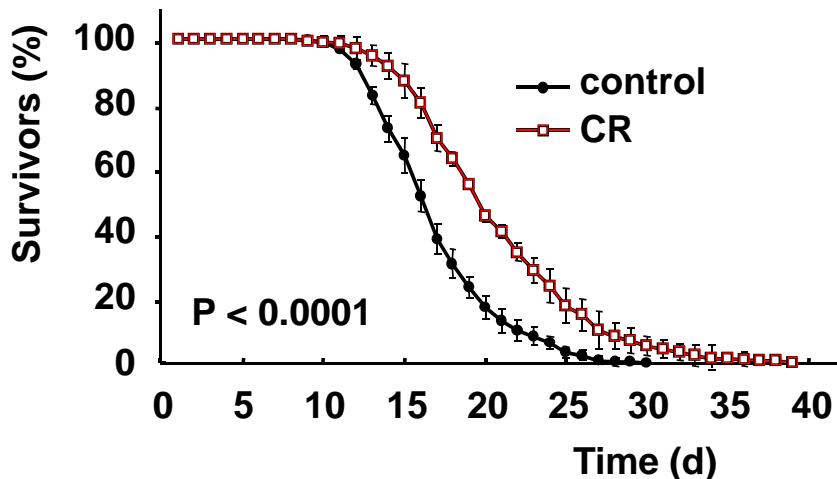
4 core research areas



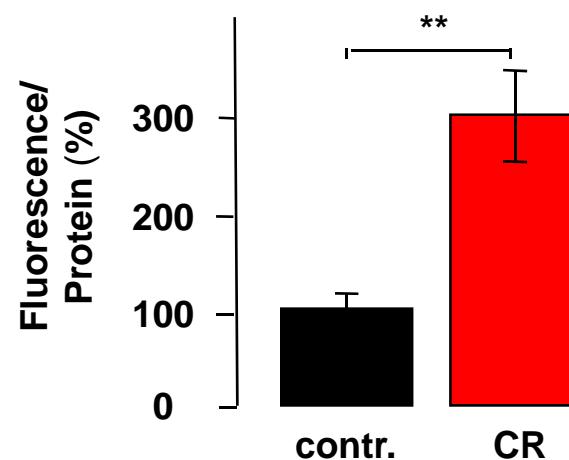


Adaptive response of *C. elegans* to calorie restriction

Calorie restriction (CR) extends lifespan

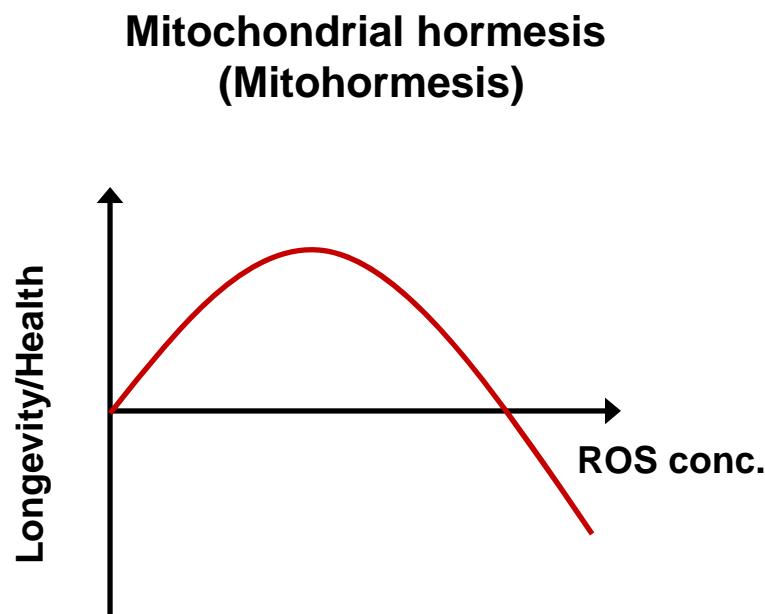
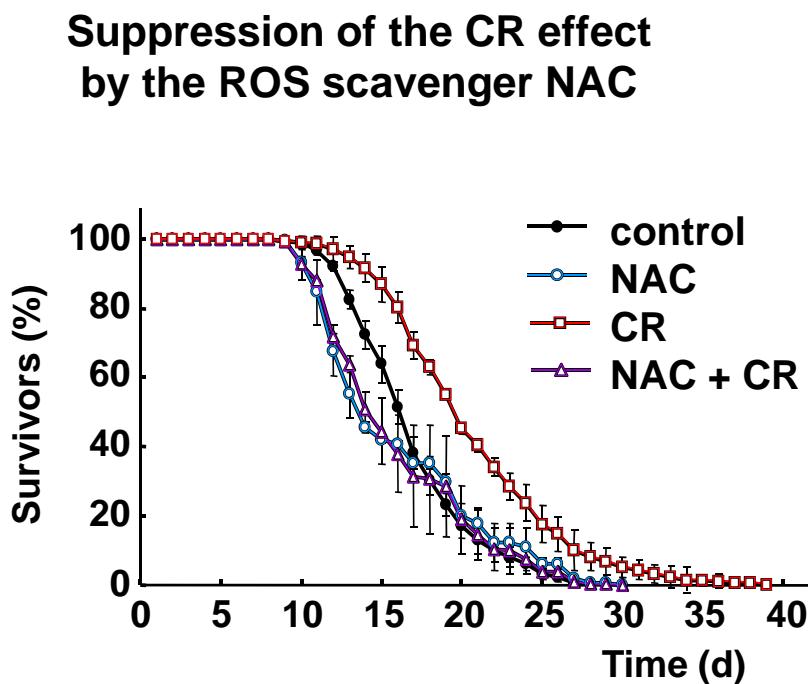


Calorie restriction promotes ROS production



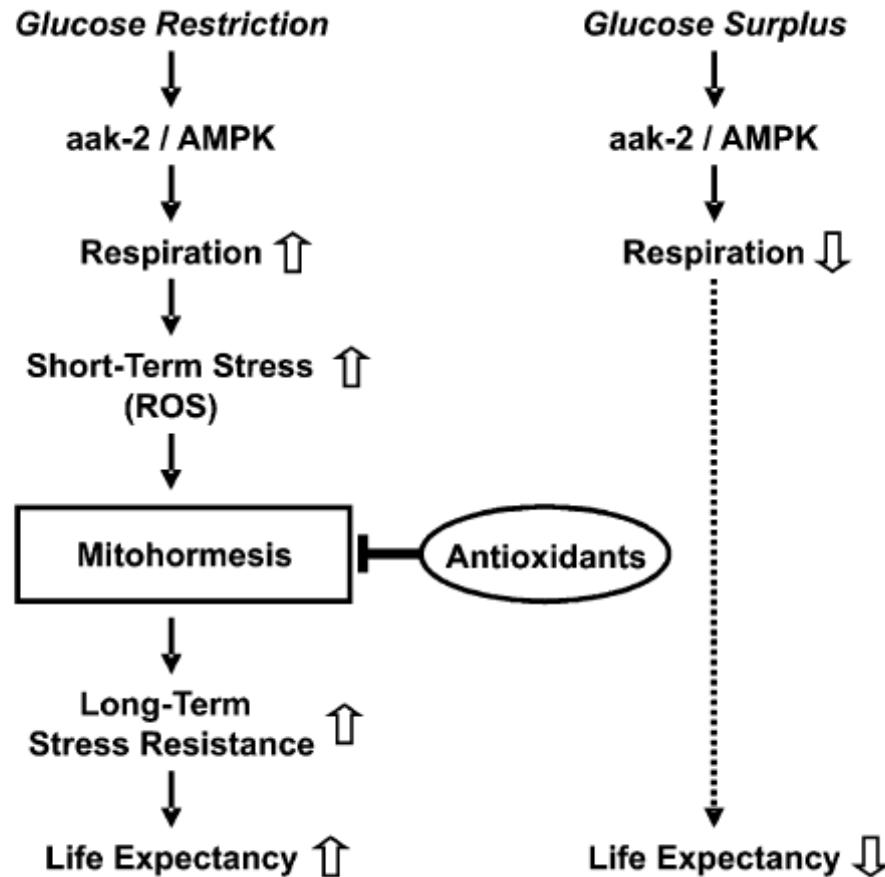
Schulz et al., *Cell Metab* (2007)

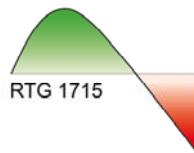
Adaptive response of *C. elegans* to calorie restriction



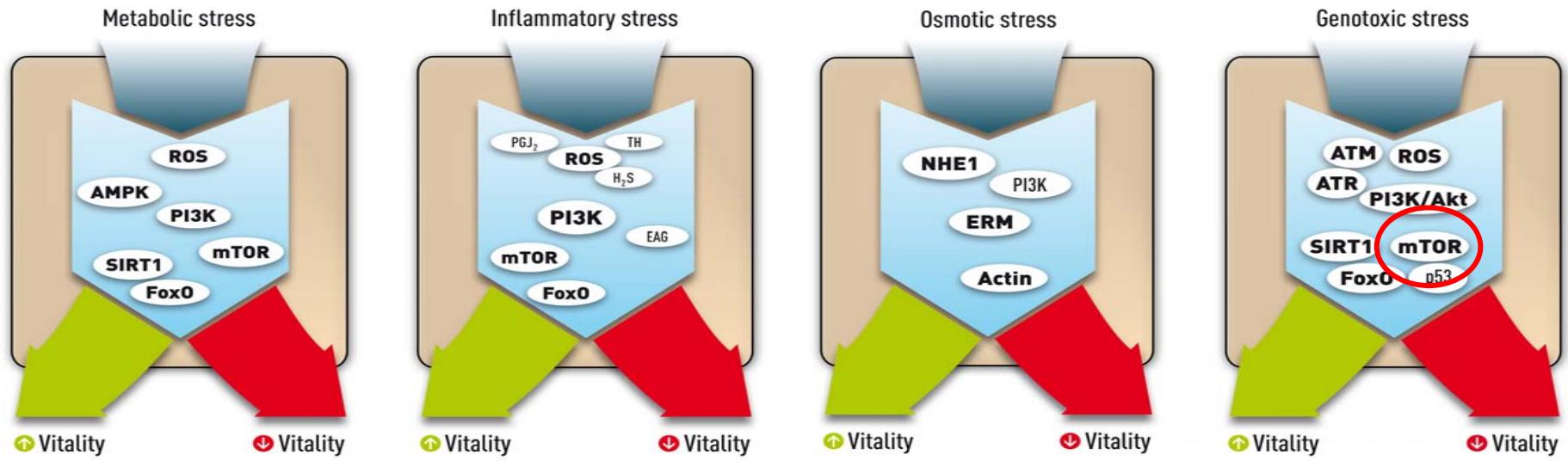
Schulz et al., *Cell Metab* (2007)

Mitohormesis: adaptation to metabolic stress

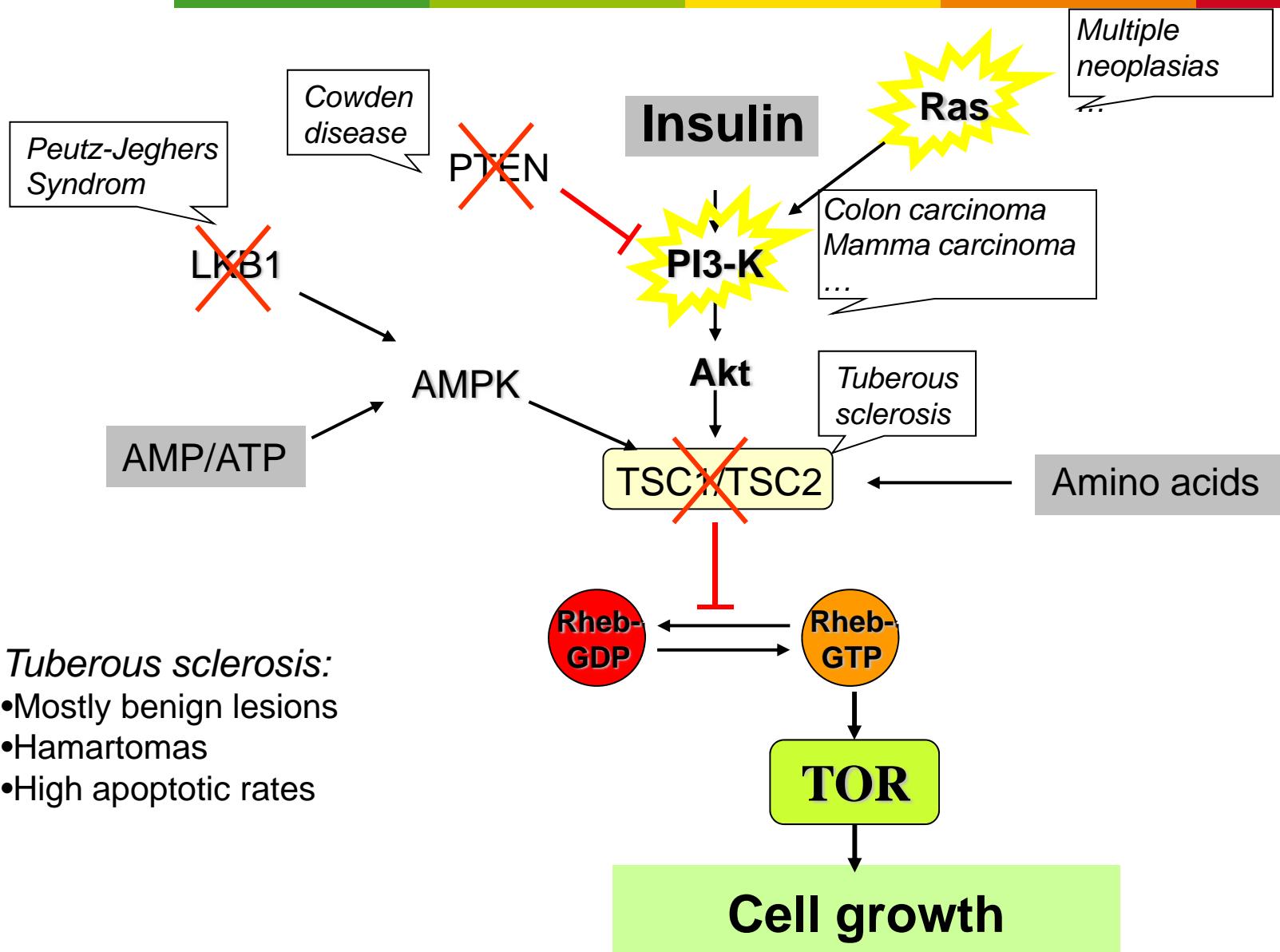




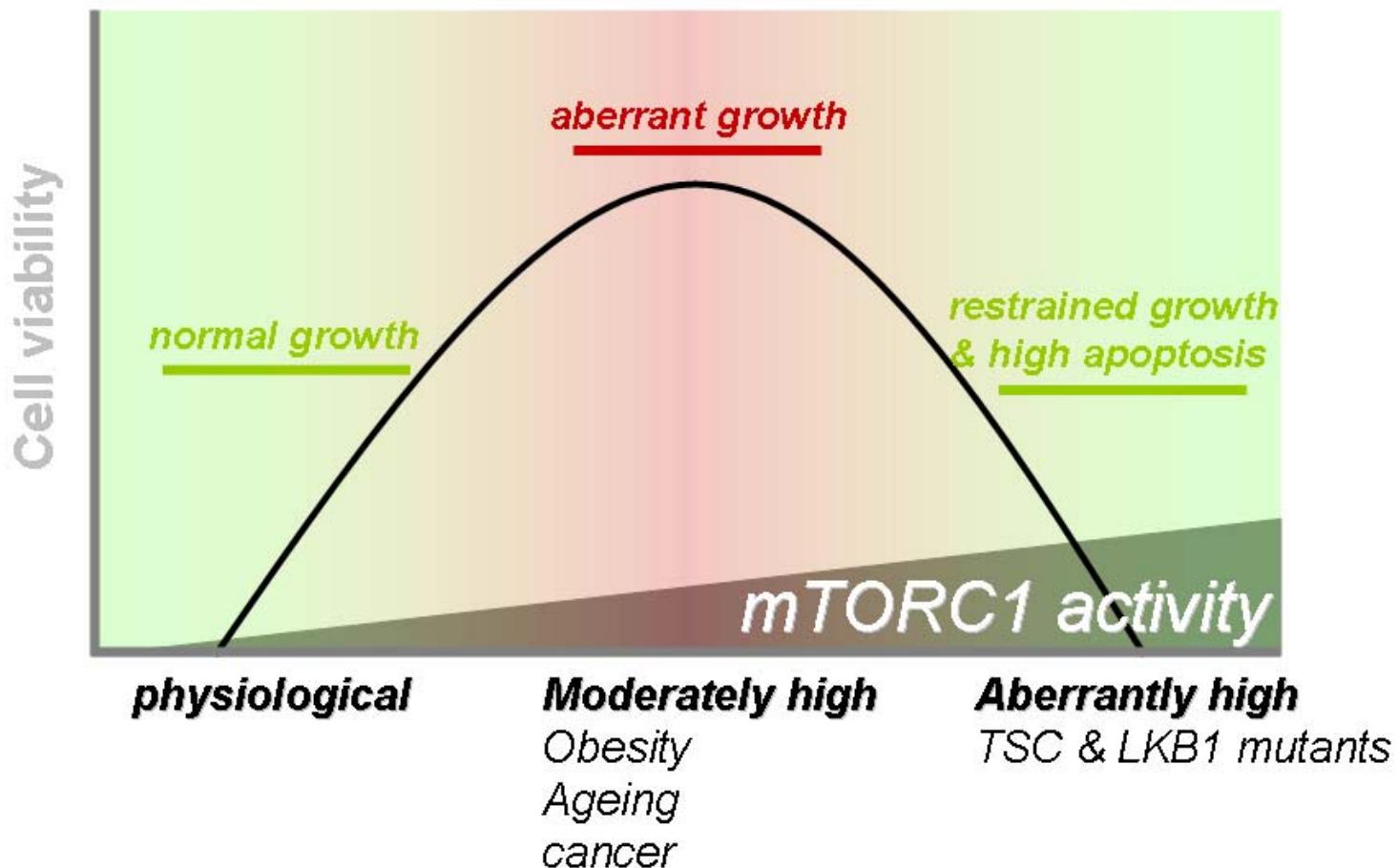
4 core research areas



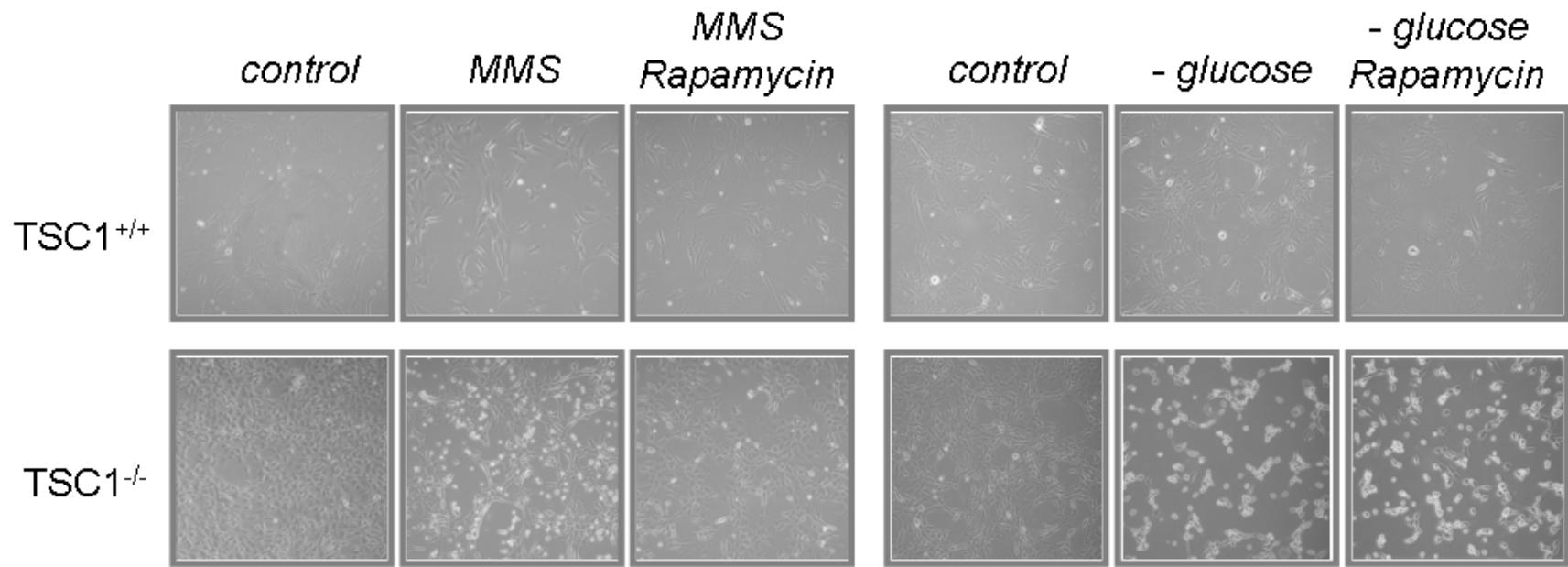
Dose-dependent role of mTOR as a sensitizer to genotoxic stress



Dose-dependent role of mTOR as a sensitizer to genotoxic stress



Dose-dependent role of mTOR as a sensitizer to genotoxic (and metabolic) stress





CENTER FOR MOLECULAR BIOMEDICINE

Friedrich-Schiller-University Jena

Institute of Molecular Cell Biology

PGE2 project

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Frank Böhmer
Ute Wittig

Mitohormesis project

Michael Ristow
Tim Schulz



Cooperations

Christoph Biskup, Jena

Stefanie Kliche, Magdeburg

Reagents

TSC MEFs

David Kwiatkowski, Boston, USA

PGE2-receptor agonists

Merck Frosst, Kirkland, Canada