Insulin and energy formation in muscle cells

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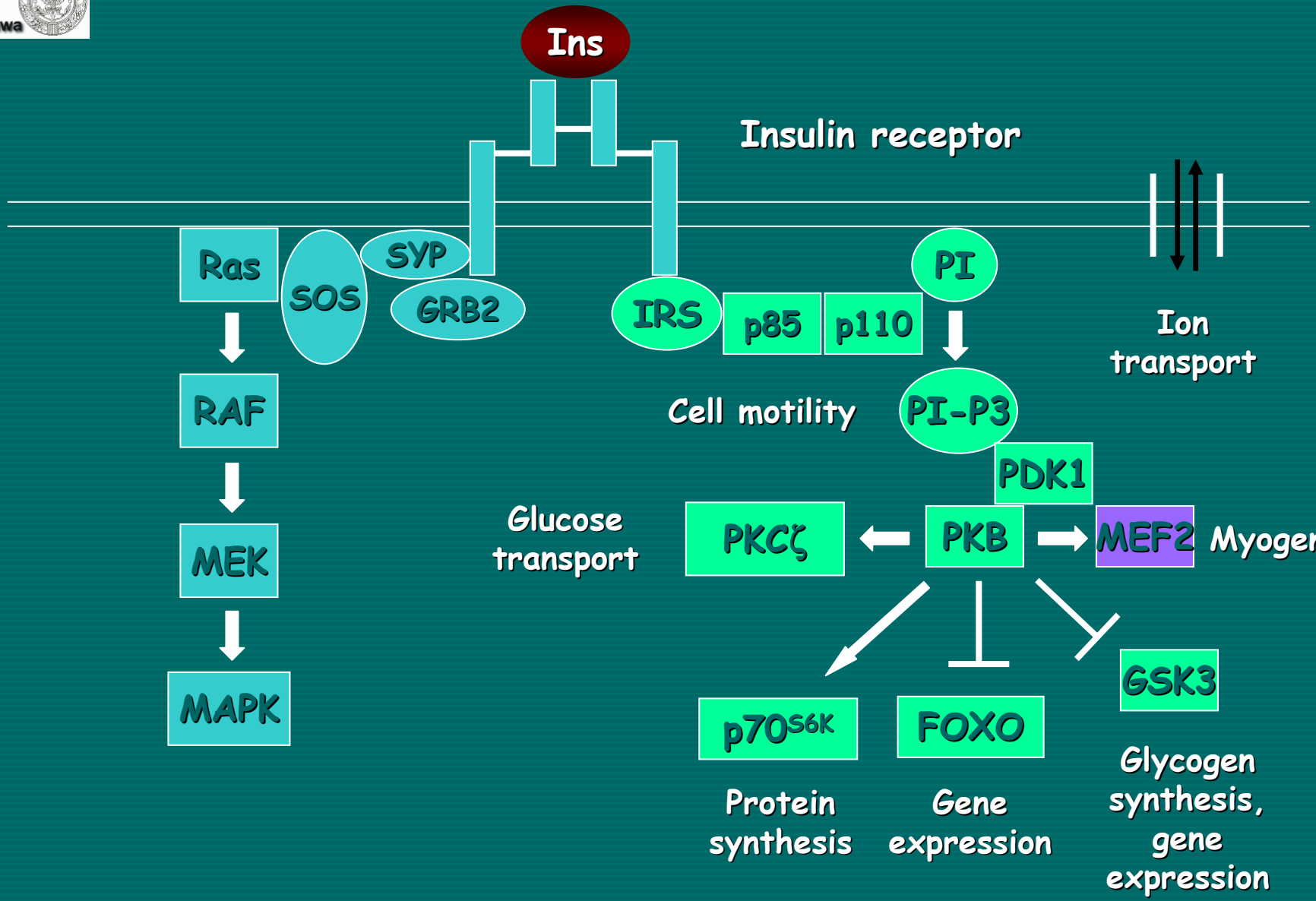
ISEP 2007, Vichy, France

Insulin pleiotropic effects

- Kinase cascade
- Cell motility
- Ion/Glucose transport
- Glycogen synthesis
- Protein synthesis/myogenesis
- Lipid synthesis
- Proliferation
- Viability/Antiapoptosis

Simplified outline of insulin signaling pathway



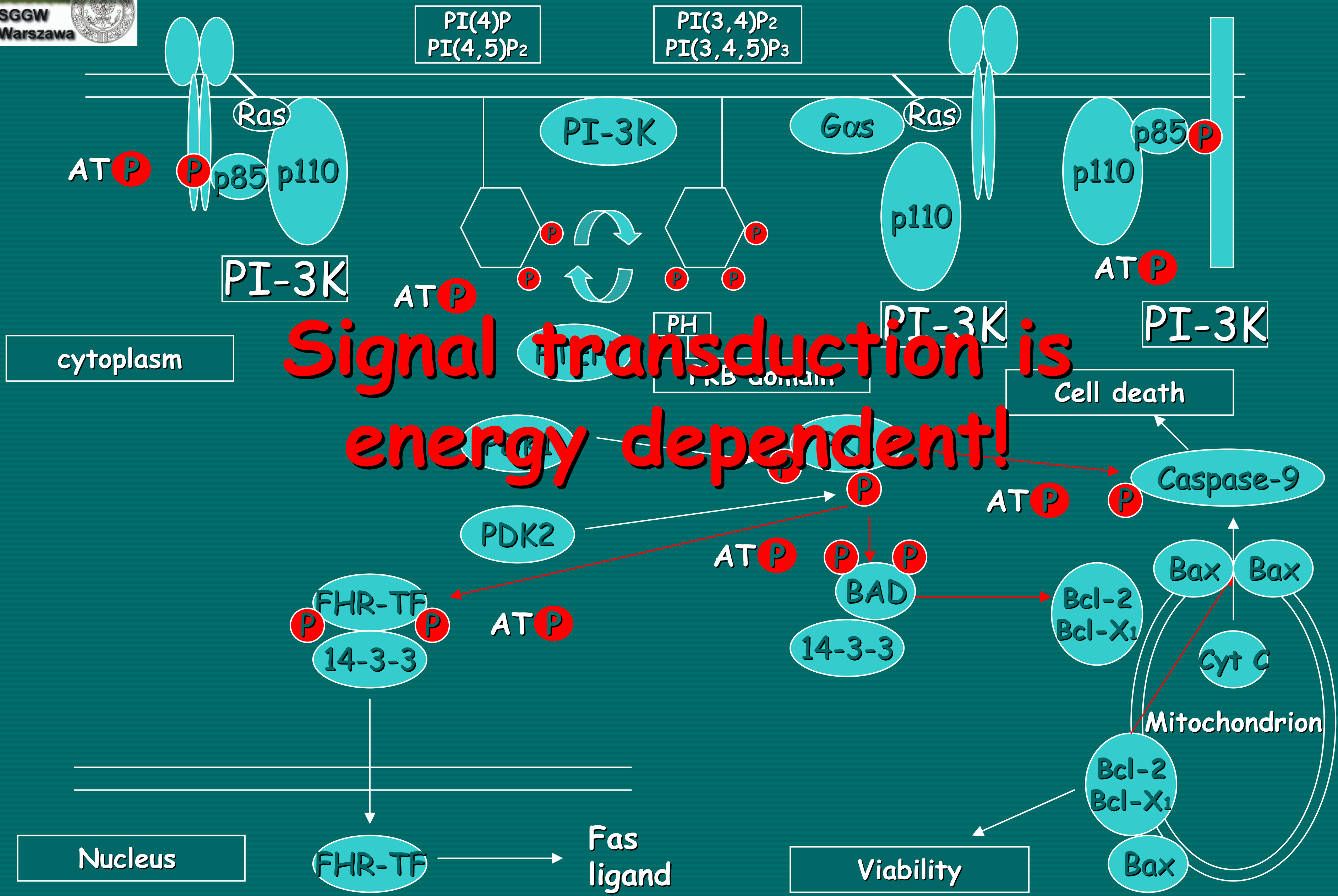
Insulin pleiotropic effects

Is energy the limit for insulin-mediated effects?

Insulin pleiotropic effects

- Kinase cascade

Simplified outline of insulin signaling pathway



Signal transduction is energy dependent!

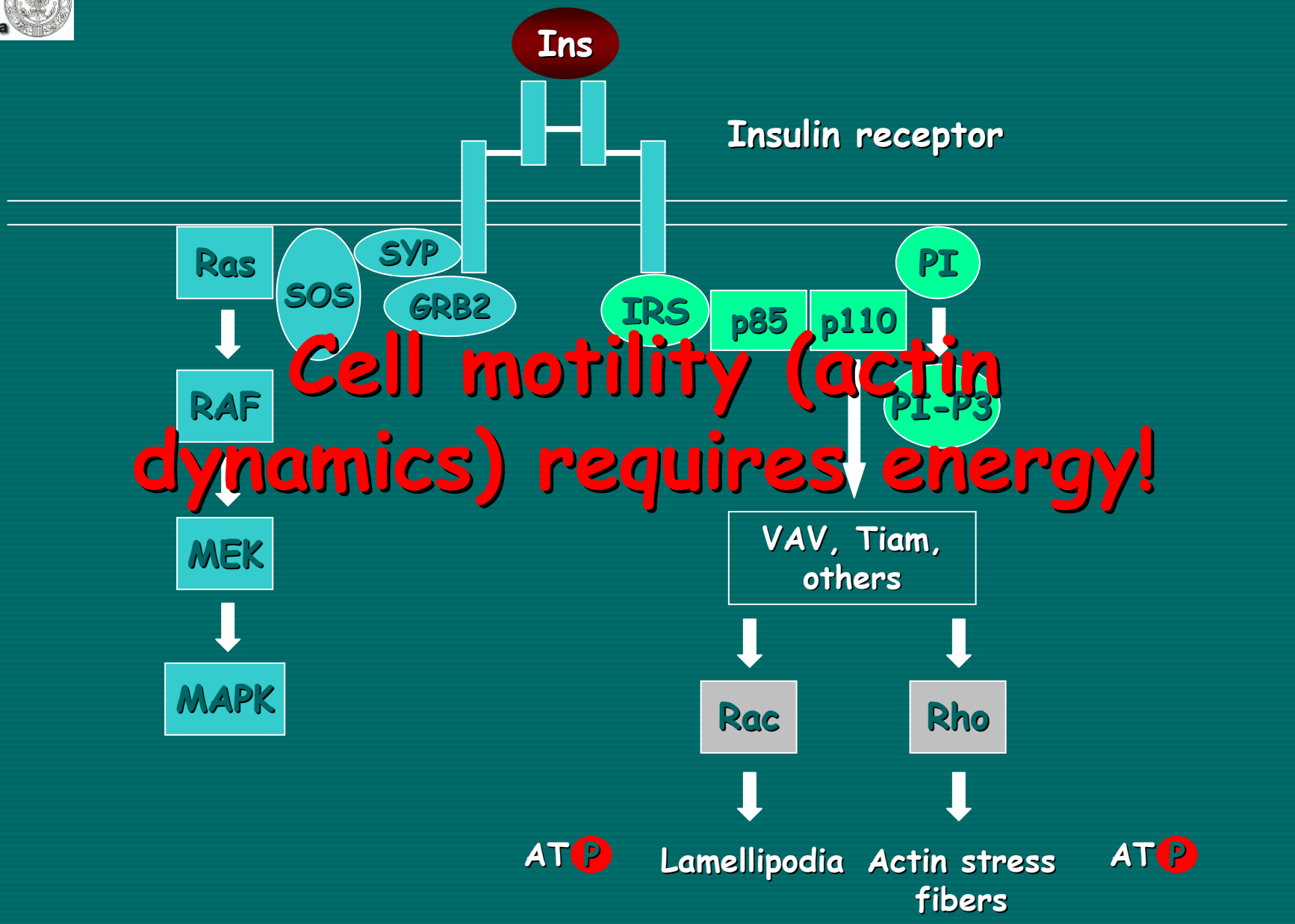
Evidence that supports affected cell signalling in catabolic states

- „Development of low grade inflammation during aging impaired post-prandial muscle protein synthesis in rat skeletal muscle" by Rieu et al.
- „The ubiquitin and caspase systems are sequentially regulated in the rat gastrocnemius muscle during casting immobilization and recovery" by Vazeille et al.
- „Relation between protein degradation and oxidative stress during aging in rat muscle" by Mosoni et al.
- „AMPK regulates the S6K1 pathway and synthesis in avian QM7 myoblasts" by Coustard et al.
- „Decreased nutritional responsiveness of S6K1 in the breast muscle of genetically fat chickens" by Duchene et al.

Insulin pleiotropic effects

- Cell motility

Simplified outline of insulin signaling pathway

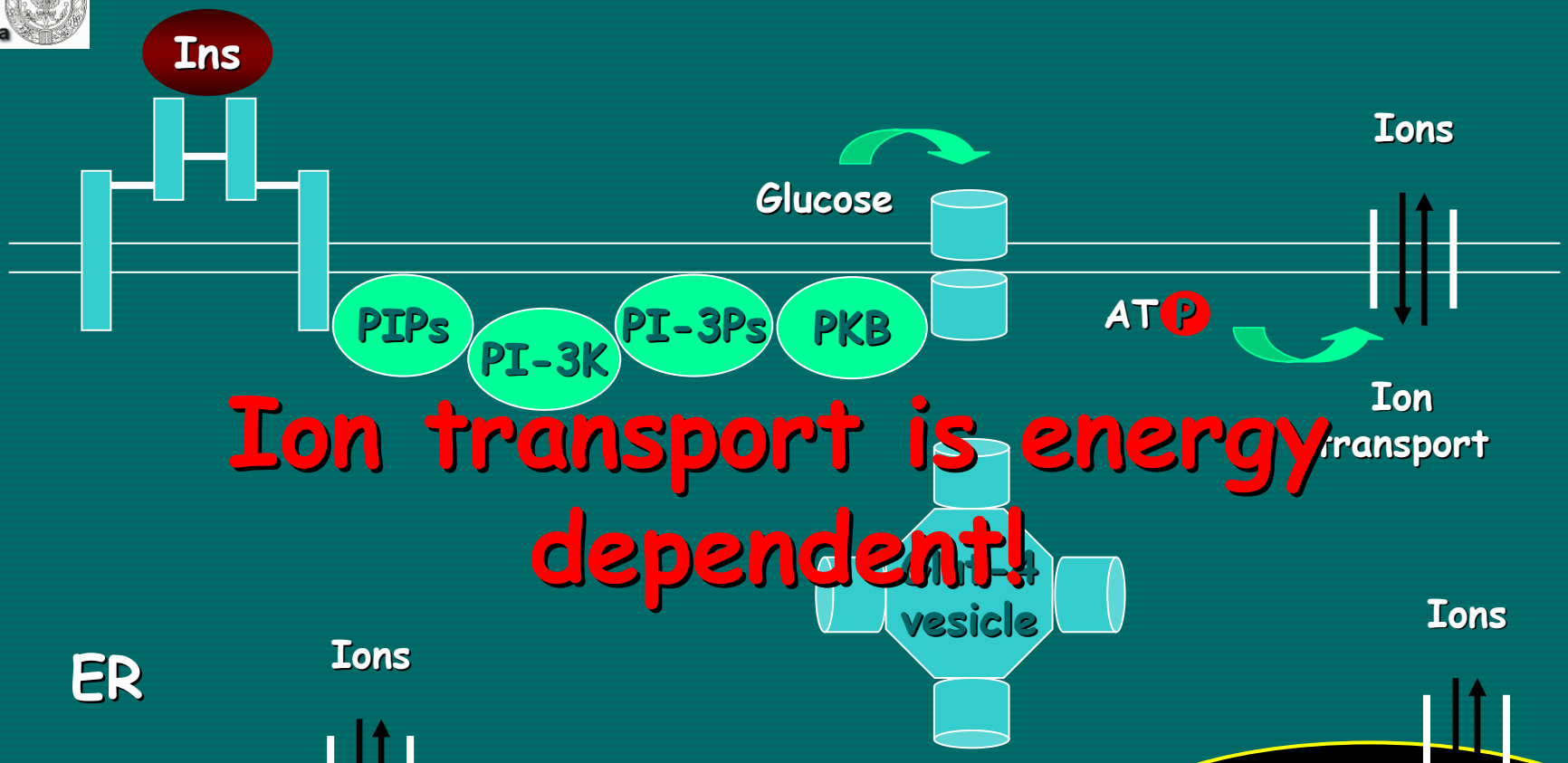


Cell motility (actin dynamics) requires energy!

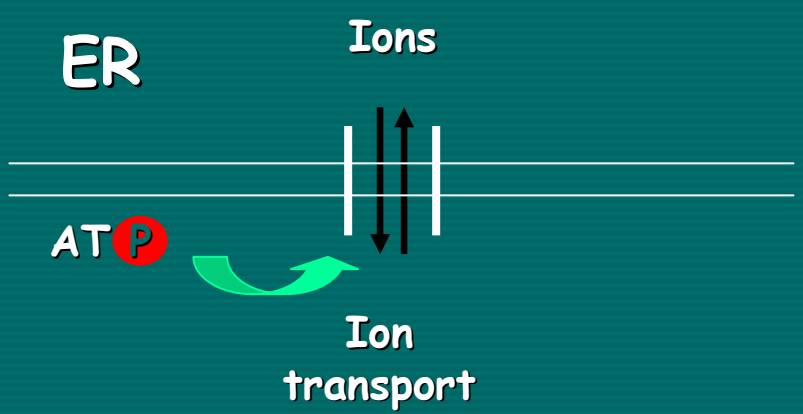
Insulin pleiotropic effects

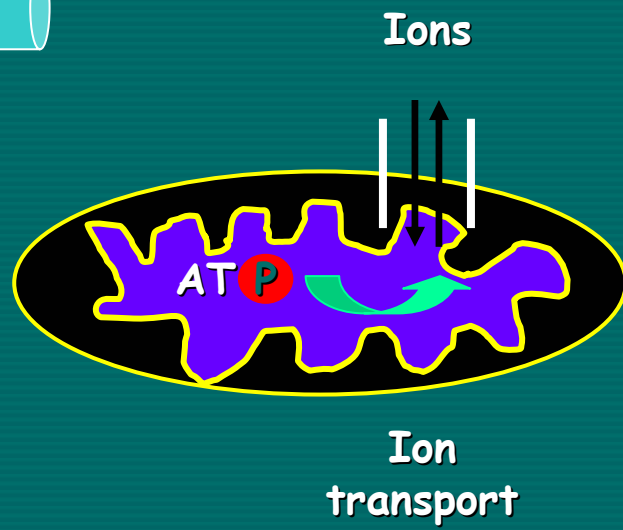
- Ion/Glucose transport

Insulin-mediated ion/glucose transport



Ion transport is energy dependent!

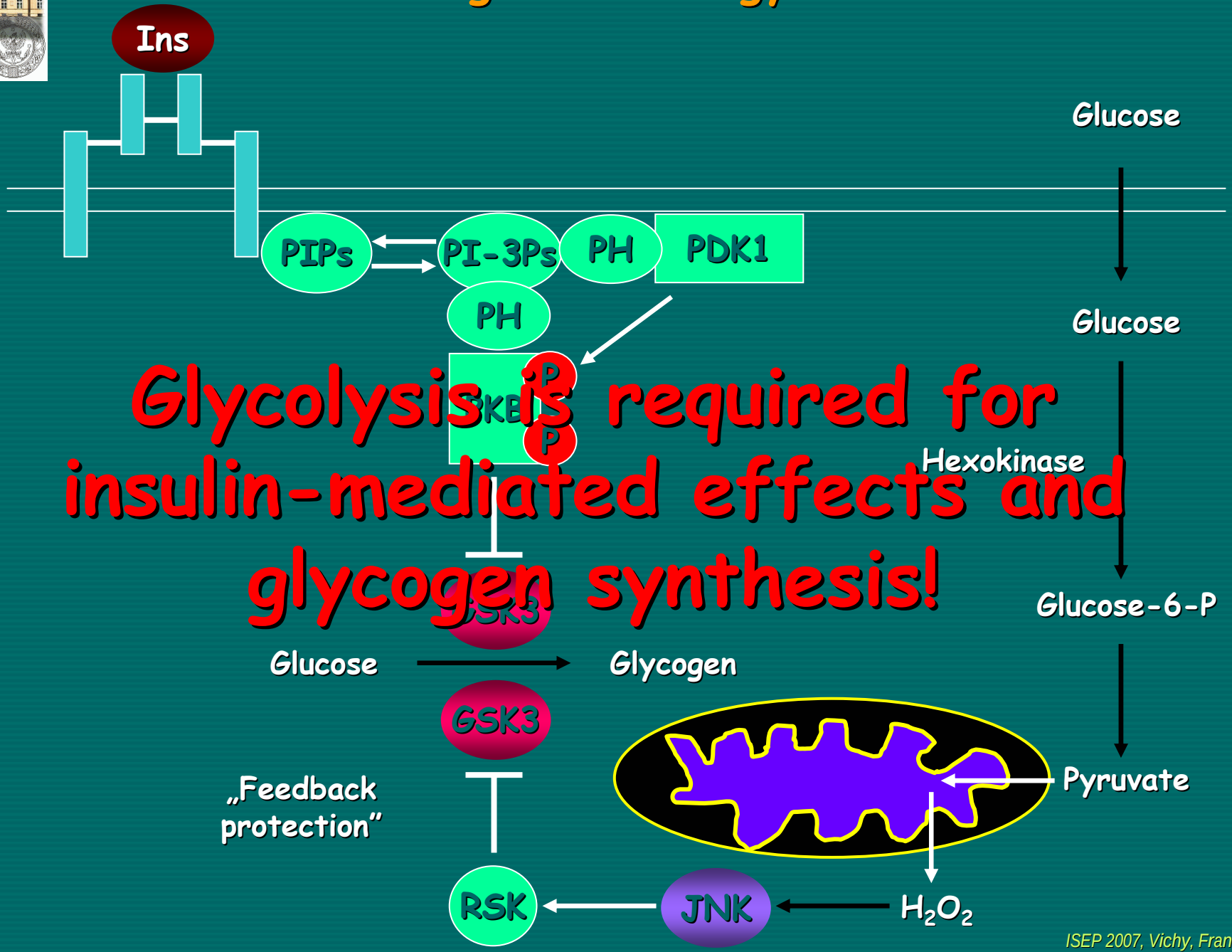




Insulin pleiotropic effects

- Glycogen synthesis

Insulin regulates energy metabolism



Glycolysis is required for insulin-mediated effects and glycogen synthesis!

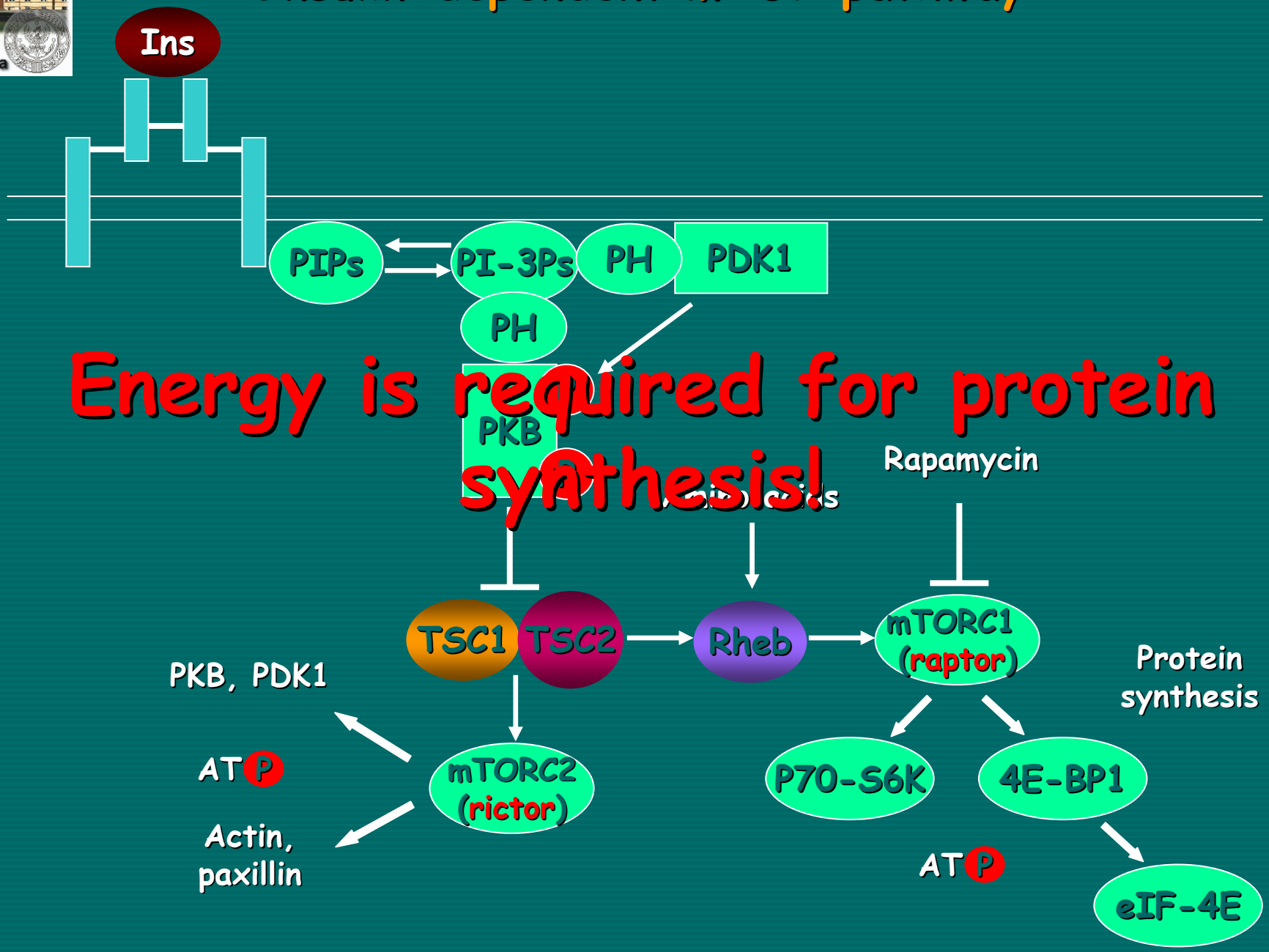
Evidence that supports affected carbohydrate/energy metabolism in catabolic states

- „Changes in the expression of selected proteins elucidate skeletal muscle type-specific resistance to glucocorticoid-induced muscle cachexia" by Pawlikowska et al.

Insulin pleiotropic effects

- Protein synthesis/myogenesis

Insulin-dependent mTOR pathway



Insulin-dependent mTOR pathway

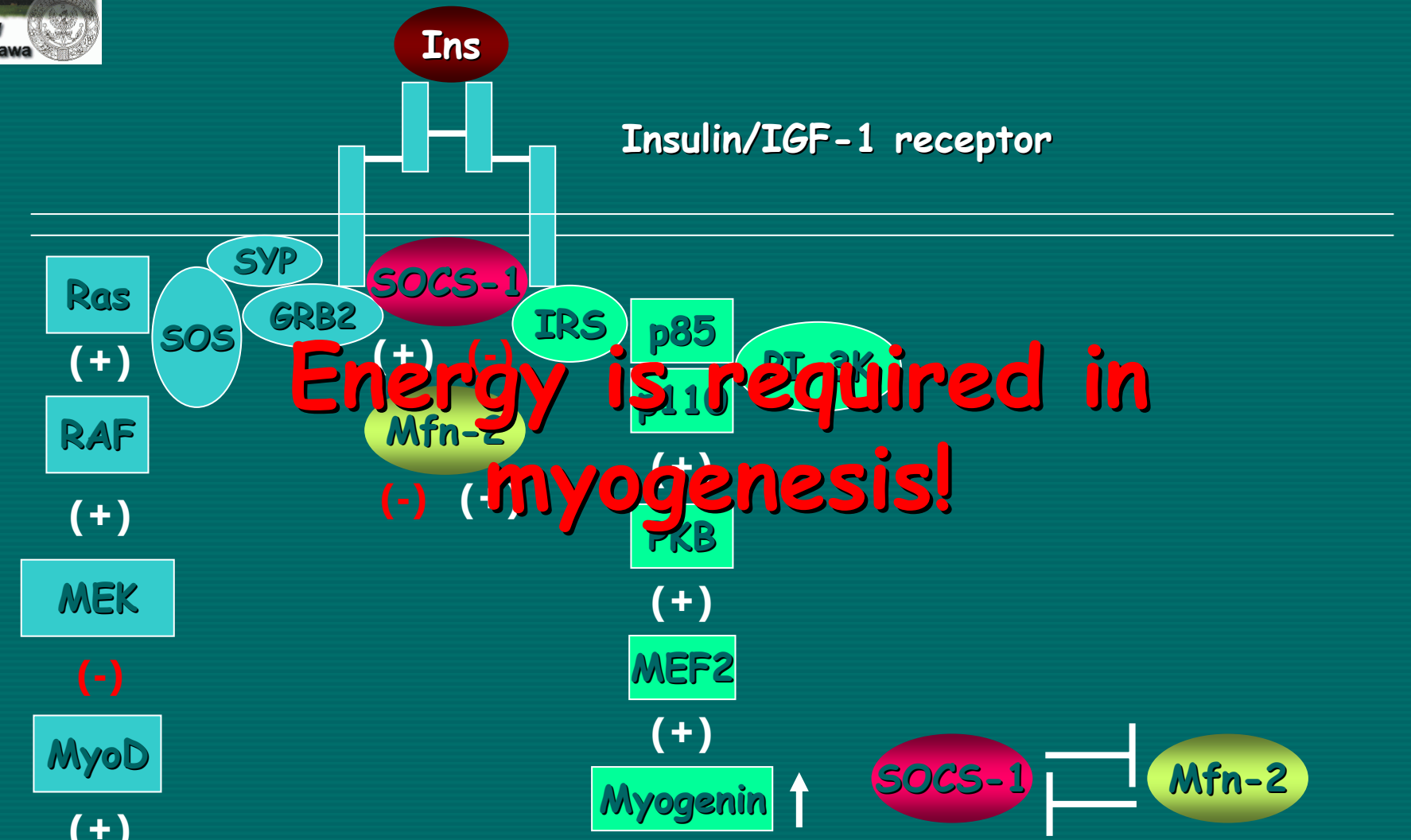
mTORC1 (raptor KO) → In muscle it reduces oxidative capacity and „slow-twitch" fiber type muscle, increases glycogen content and „fast-twitch" fiber type. In adipose tissue it prevents diet induced obesity and render more tolerant to glucose.

mTORC1 (rictor KO) → In muscle it induces oxidative capacity and „slow-twitch" fiber type muscle, decreases glycogen content and „fast-twitch" fiber type. In adipose tissue it promotes to diet induced obesity and render less tolerant to glucose.

mTORC1 (raptor KO) ⊣⊢ **mTORC1 (rictor KO)**

mTORC1 (raptor) and mTORC2 (rictor) have opposite roles in controlling animal metabolism and energy homeostatsis.
Mark Hill, FEBS lecture, Spetses, Greece, 2007

Insulin-dependent regulation of myogenesis



Energy is required in myogenesis!

SOCS1 and Mfn-2 have opposite roles in controlling myogenesis and energy metabolism in muscle

Evidence that supports affected protein deposition in catabolic states

- „Development of low grade inflammation during aging impaired post-prandial muscle protein synthesis in rat skeletal muscle" by Rieu et al.
- „The ubiquitin and caspase systems are sequentially regulated in the rat gastrocnemius muscle during casting immobilization and recovery" by Vazeille et al.
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- „AMPK regulates the S6K1 pathway and synthesis in avian QM7 myoblasts" by Coustard et al.

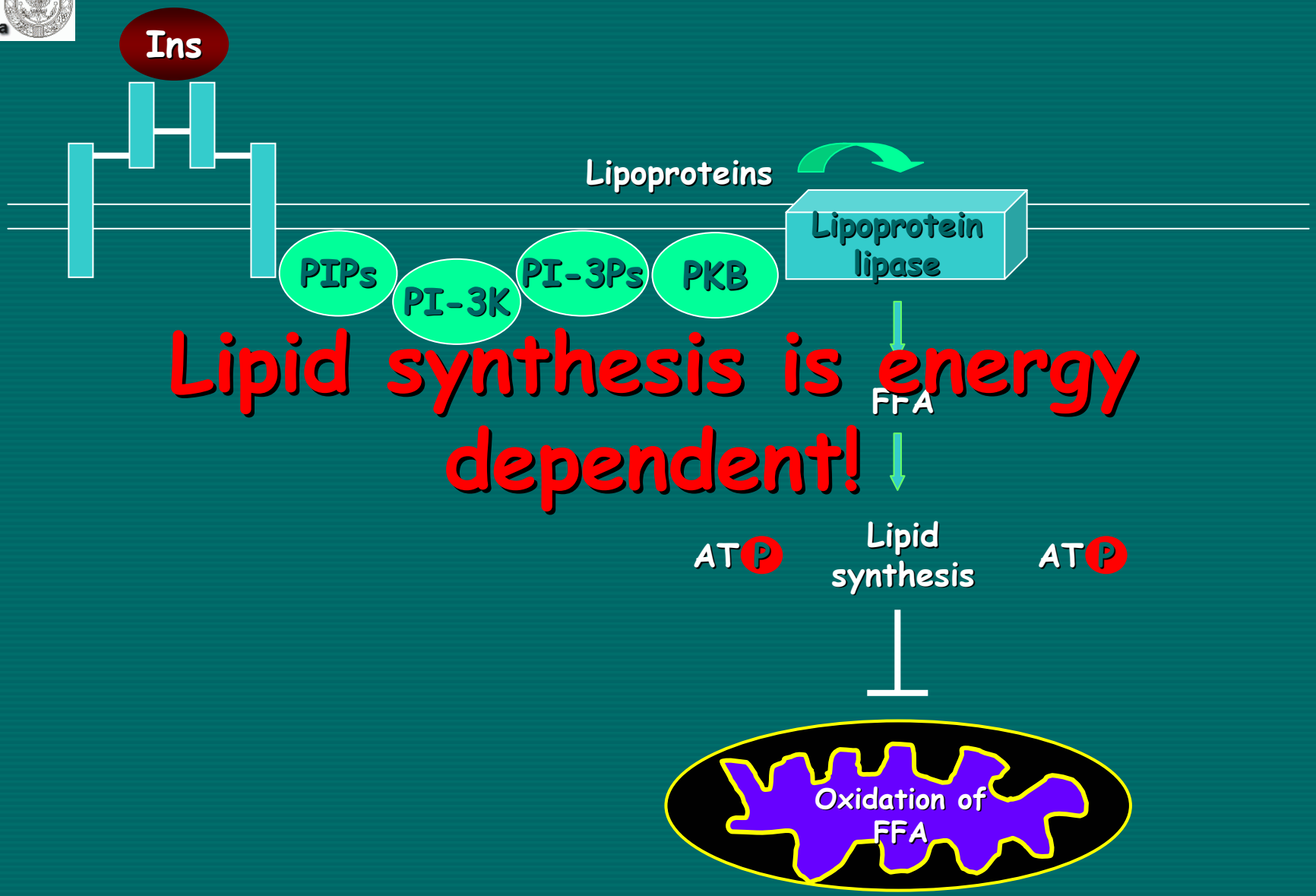
Evidence that supports amino-acid regulation of protein synthesis

- „Effect of immune system stimulation and dietary methionine plus cysteine intake on protein deposition and digestability in growing pigs" by Rakhshadeh et al.
- „Amino acid signalling: methionine regulates the S6K1 pathway and protein synthesis in avian QM7 myoblasts" by Custard et al.
- „Leucine suppresses myofibrillar proteolysis by down-regulating ubiquitin-proteasome pathway in chick skeletal muscles" by Nakashima et al.
- „Protein deposition in the body, content of nucleic acids in the *mld* muscle of pigs as affected by limitation of protein during growing period" by Skiba et al.

Insulin pleiotropic effects

- Lipid synthesis

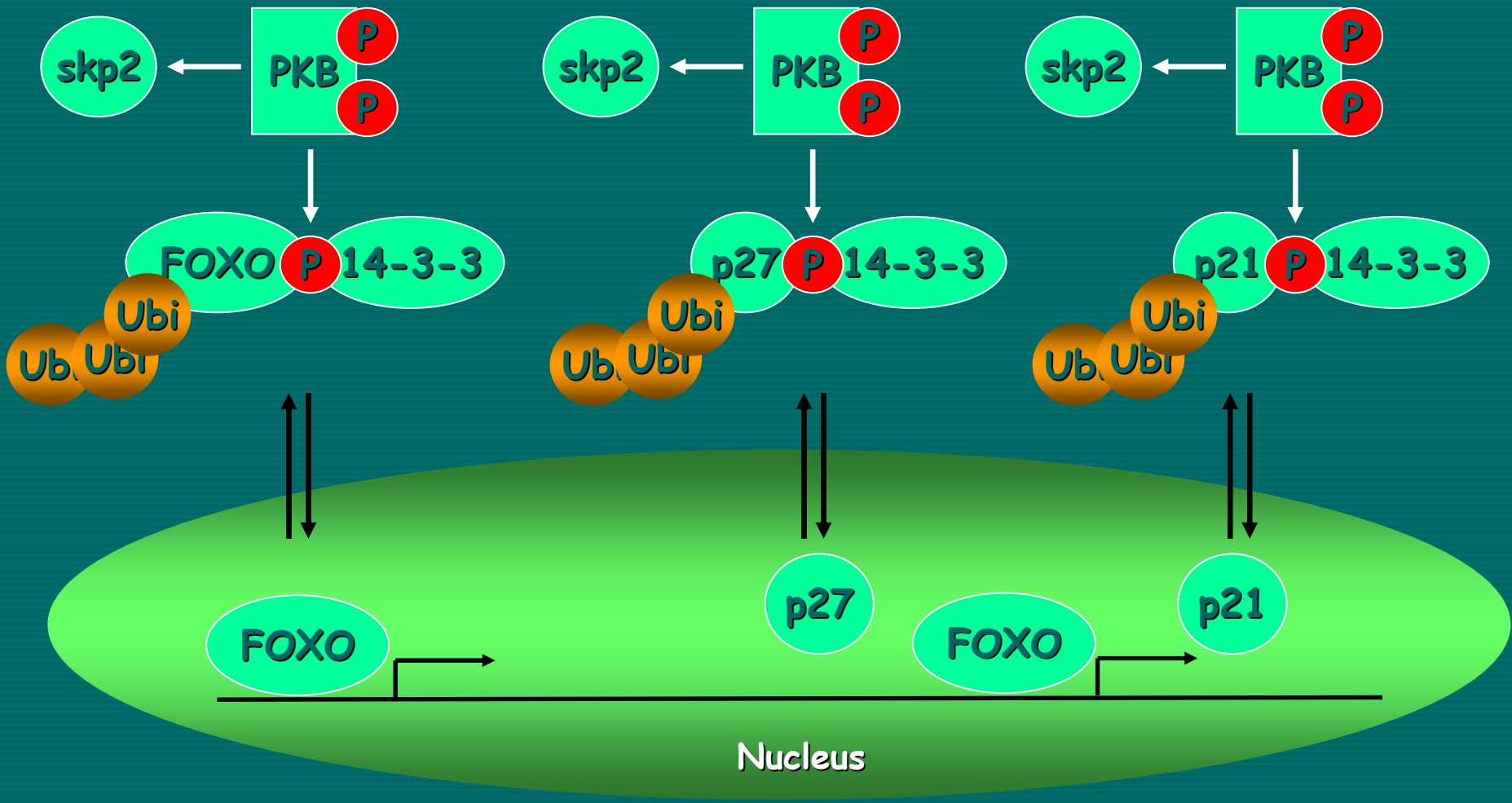
Insulin-mediated synthesis of muscle lipids



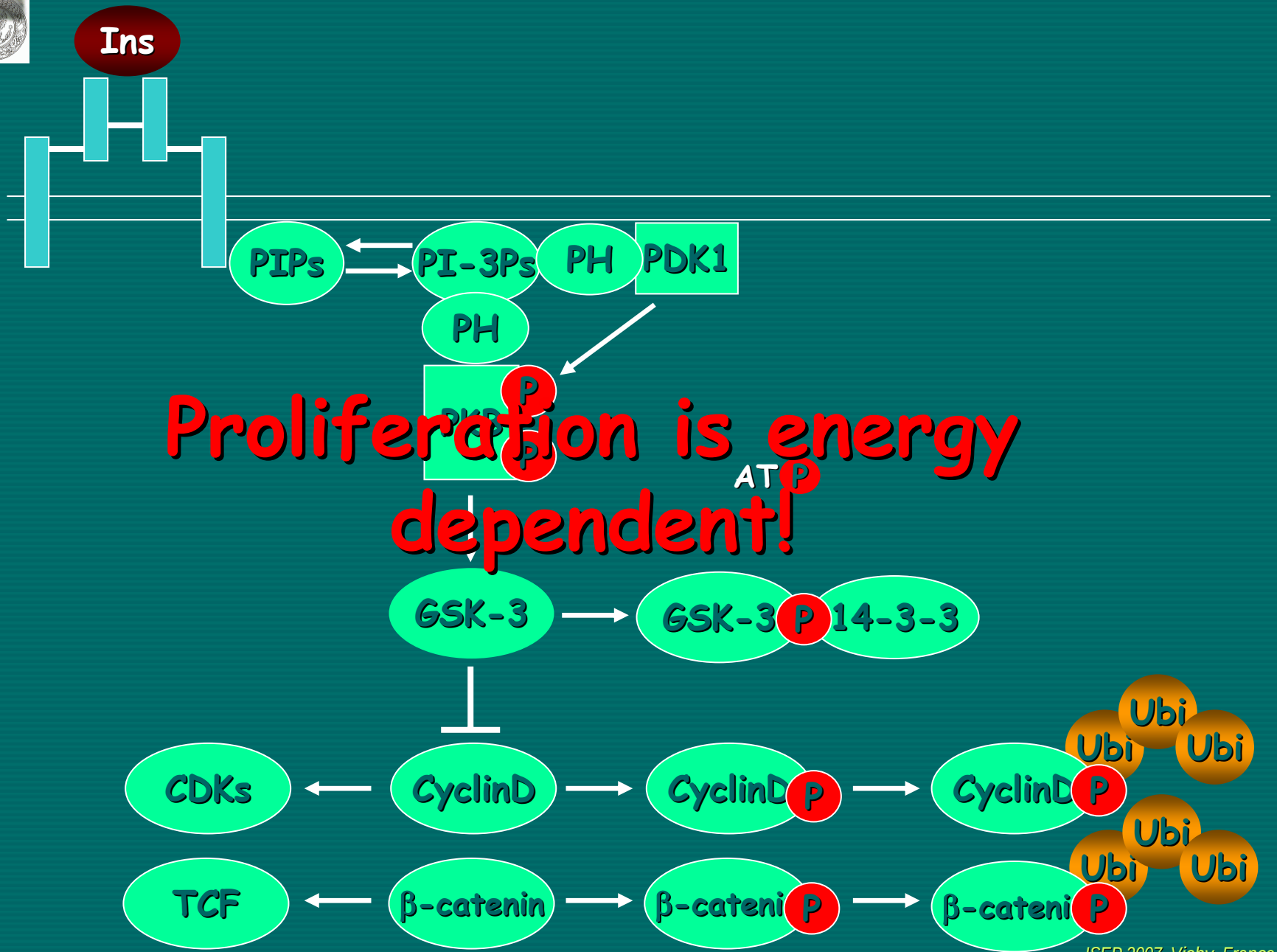
Insulin pleiotropic effects

- Proliferation

Insulin-dependent proliferation



Insulin-dependent proliferation



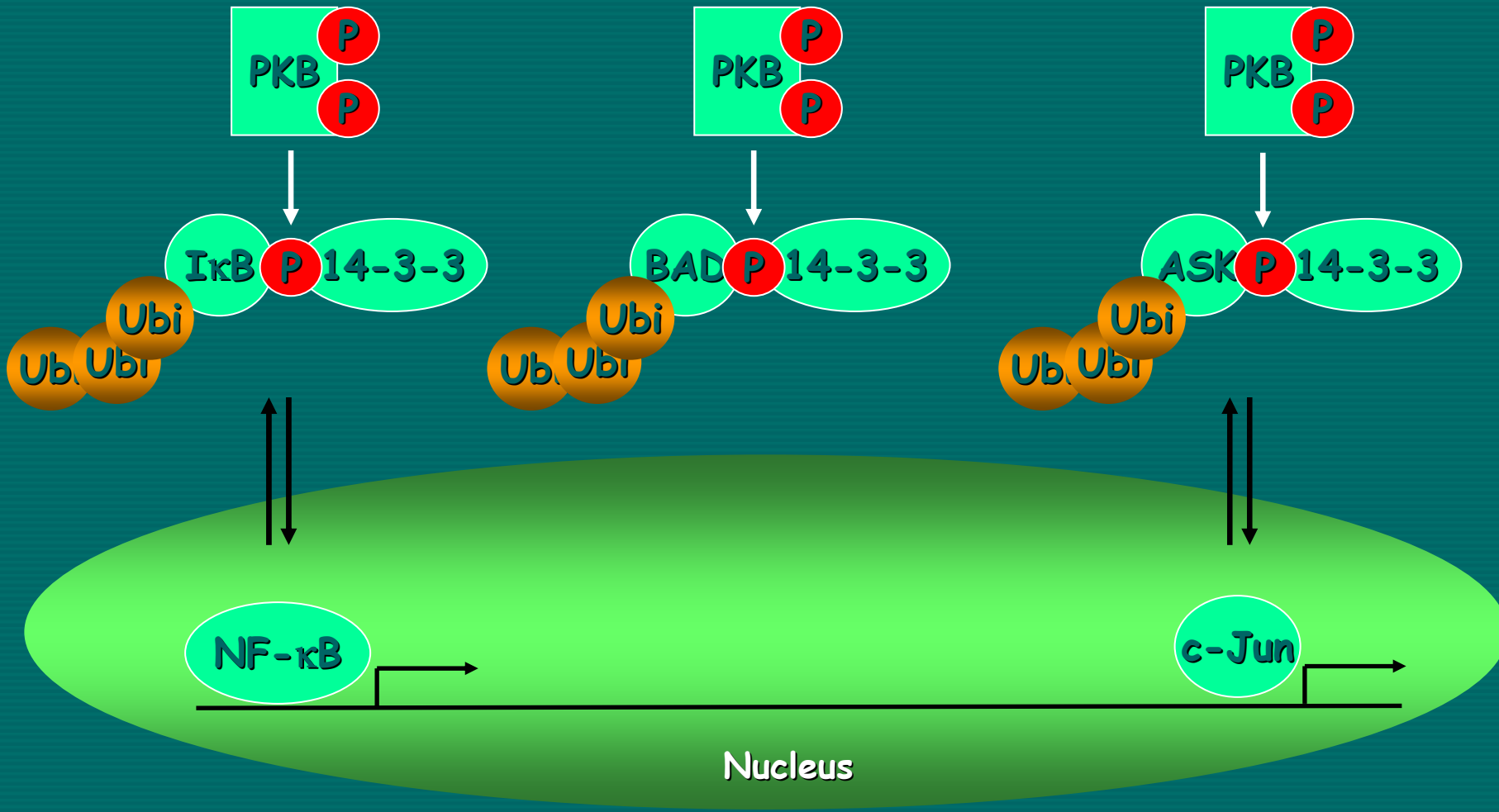
Evidence that supports impaired cell proliferation in catabolic states

- „Estrogenic and isoflavonic actions on differentiation and protein metabolism in porcine muscle satellite cell cultures" by Mau and Rehfeldt

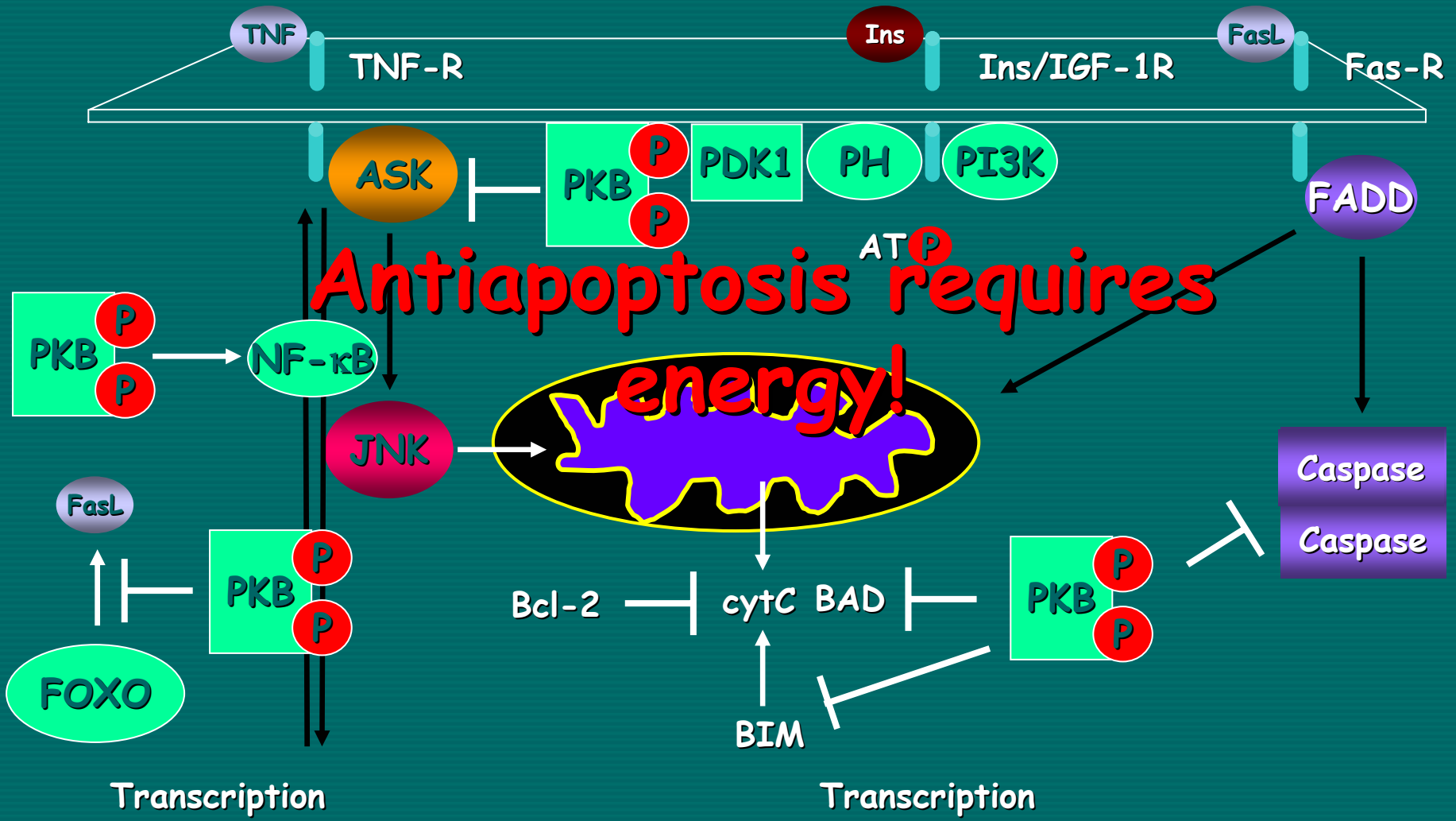
Insulin pleiotropic effects

- Viability/Antiapoptosis

Insulin-dependent antiapoptosis



Insulin-dependent antiapoptosis



Evidence that supports impaired antiapoptosis in catabolic states

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Evidence for energy requirements in insulin-dependent effects