Fc Receptor Signaling to the Nucleus

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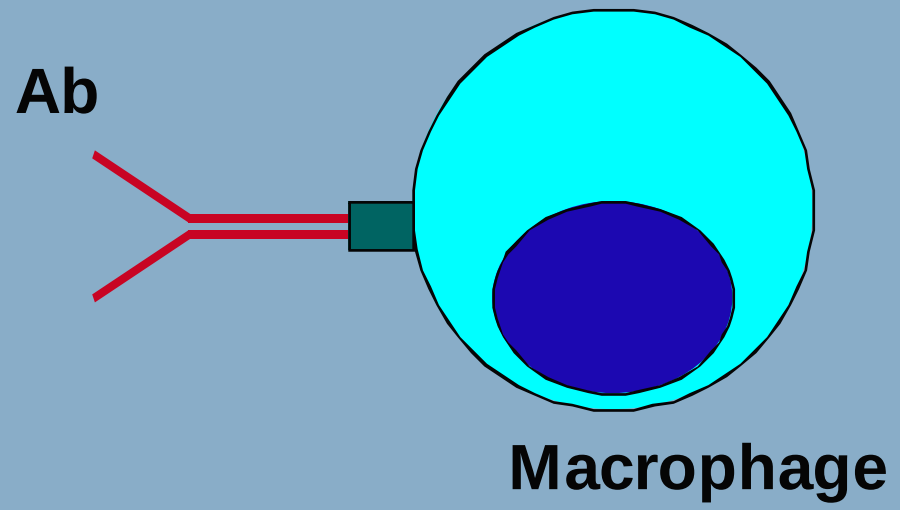
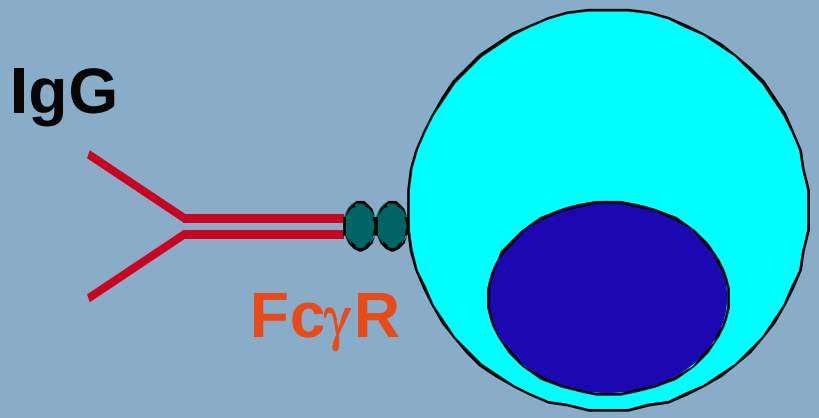
Universidad Nacional Autónoma de México

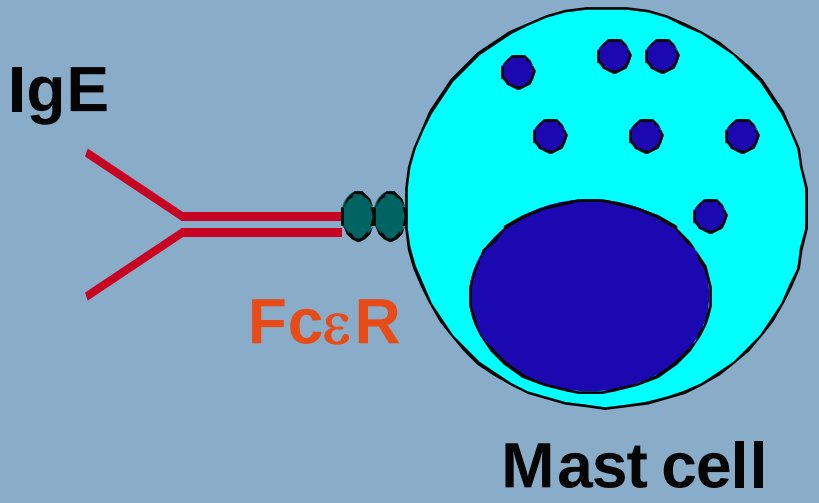
Receptors for Fc part of IgG



Berken & Benacerraf
*J. Exp. Med.*1966; 123:119

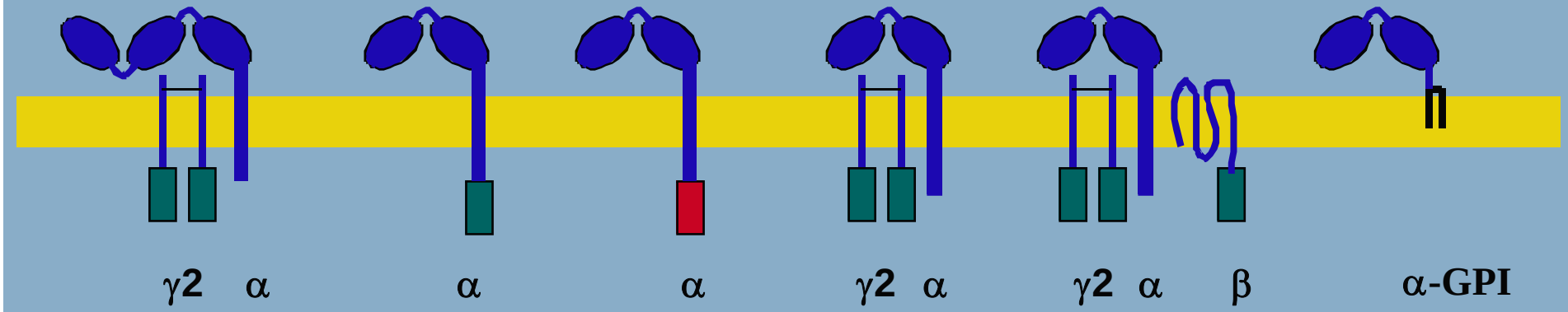
Fc Receptor Functions





Phagocytosis
ADCC
Respiratory Burst
Degranulation
Inflammatory Mediators
Gene Activation
Cytokine Production

Human IgG Fc Receptors

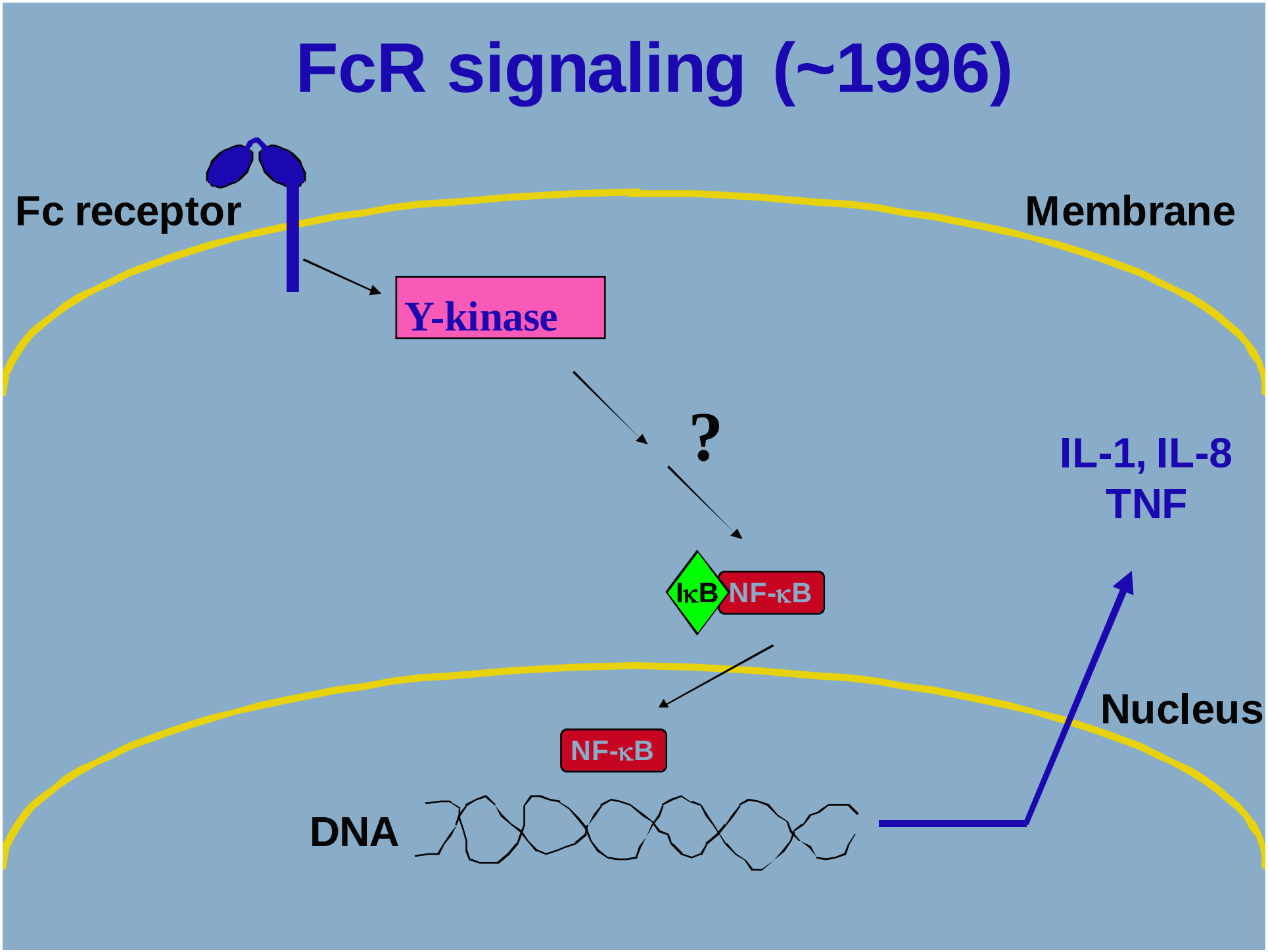


FcγRI	FcγRIIA	FcγRIIB	FcγRIIIA		FcγRIIIB
Macrophage	Macrophage	Macrophage	Macrophage	Mast Cell	Neutrophil
Neutrophil	Neutrophil	Neutrophil	Mast Cell	Basophil	
Eosinophil	Mast Cell	Mast Cell	Basophils		
Dendritic Cell	Eosinophil	Eosinophil	NK Cell		
	Platelet	Dendritic Cell	Dendritic Cell		
	Dendritic Cell	B Cell			

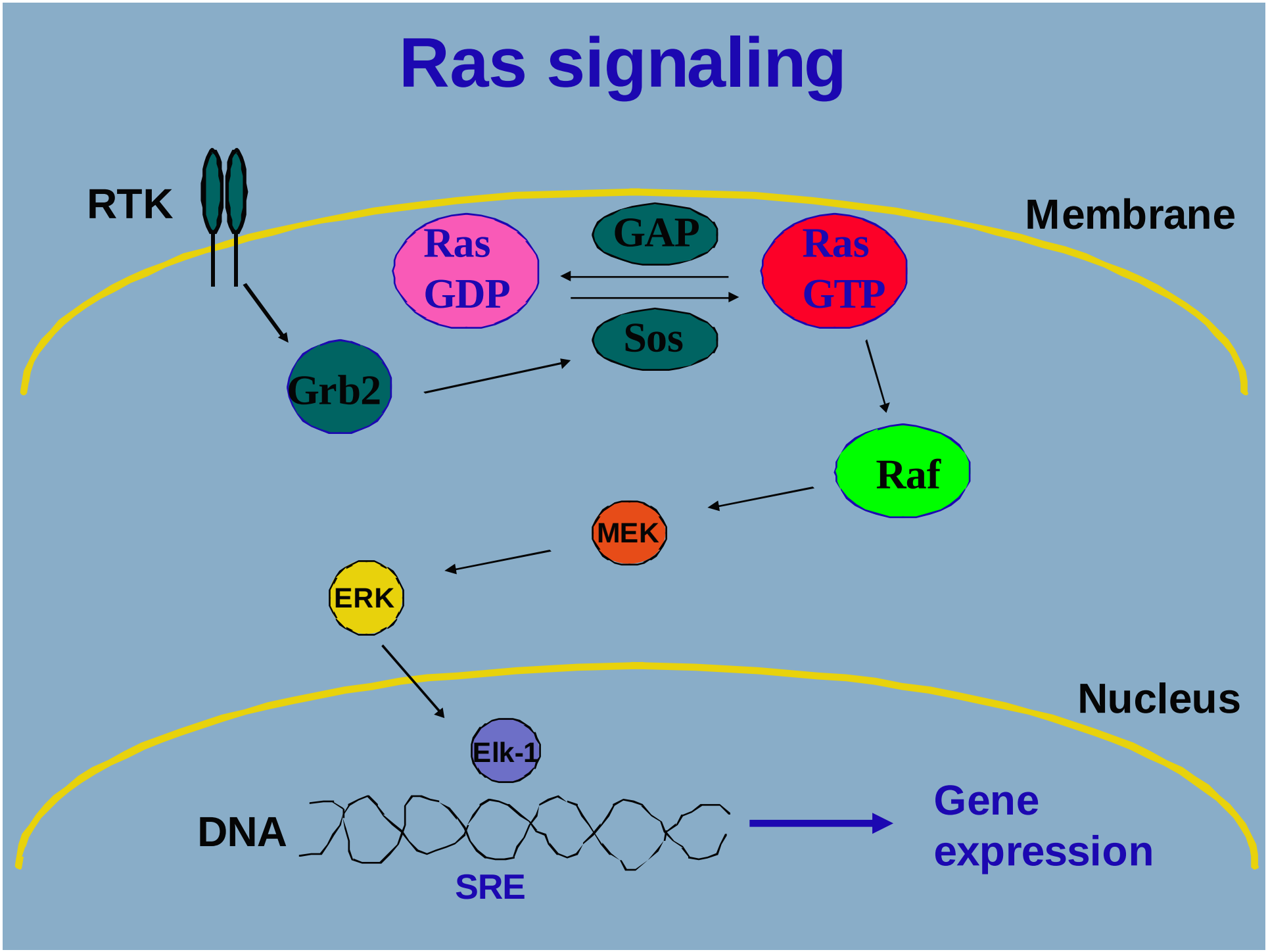
ITAM

ITIM

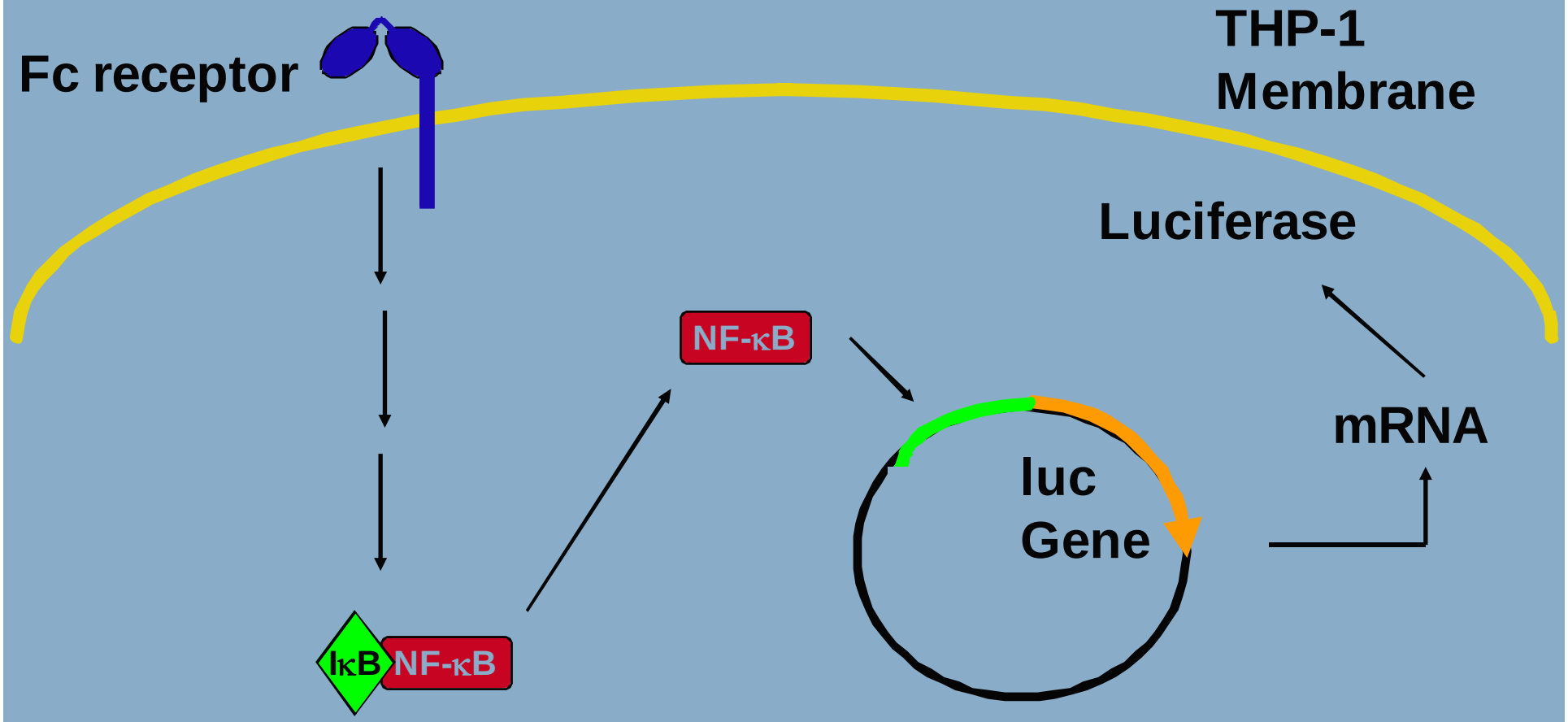
Annu. Rev. Immunol. 1991; 9:457
Annu. Rev. Immunol. 1997; 15:203


FcR signaling (~1996)
Fc receptor
Membrane
Y-kinase
?
IL-1, IL-8
TNF
IκB
NF-κB
Nucleus
NF-κB
DNA

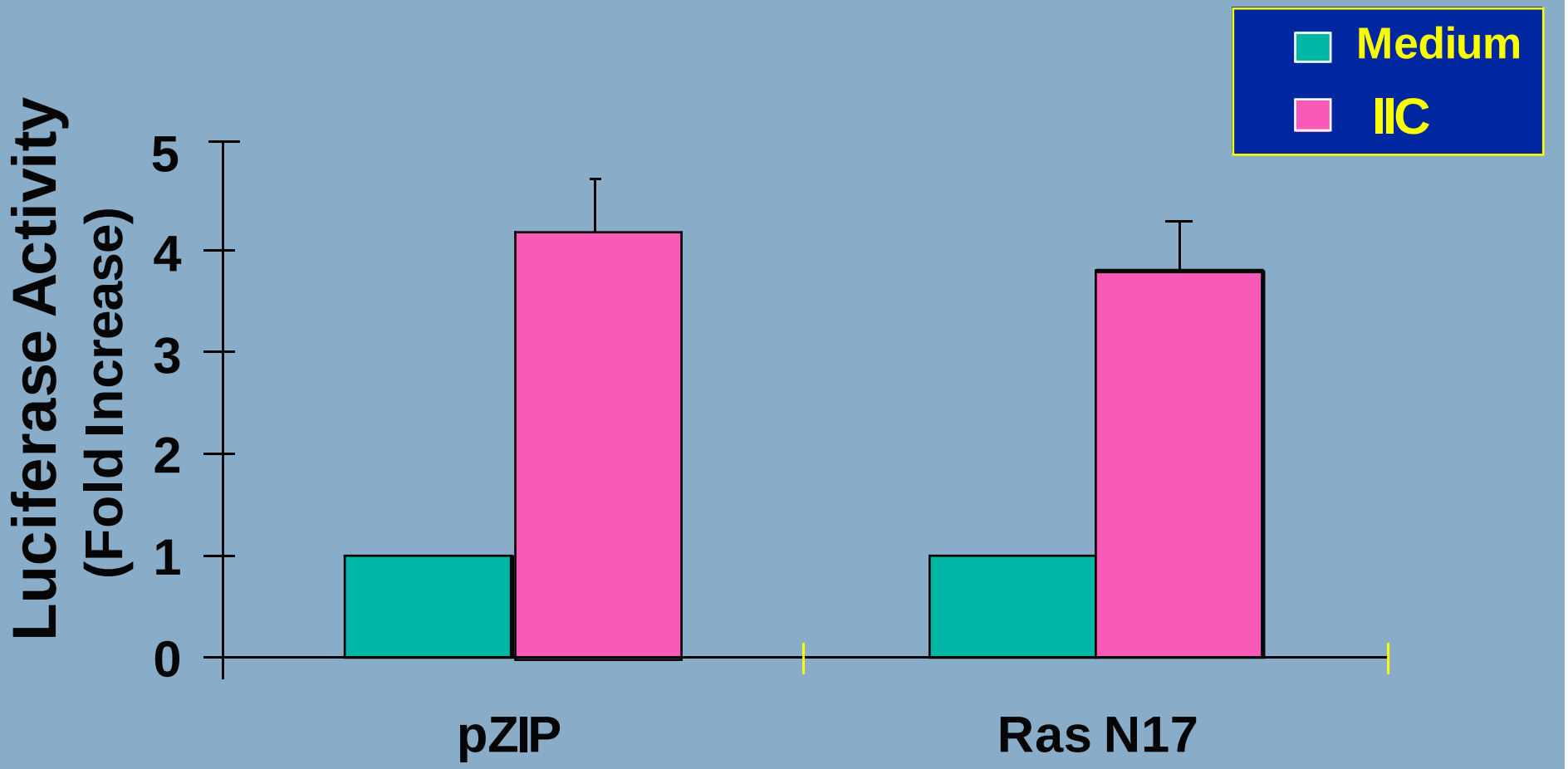
Ras signaling



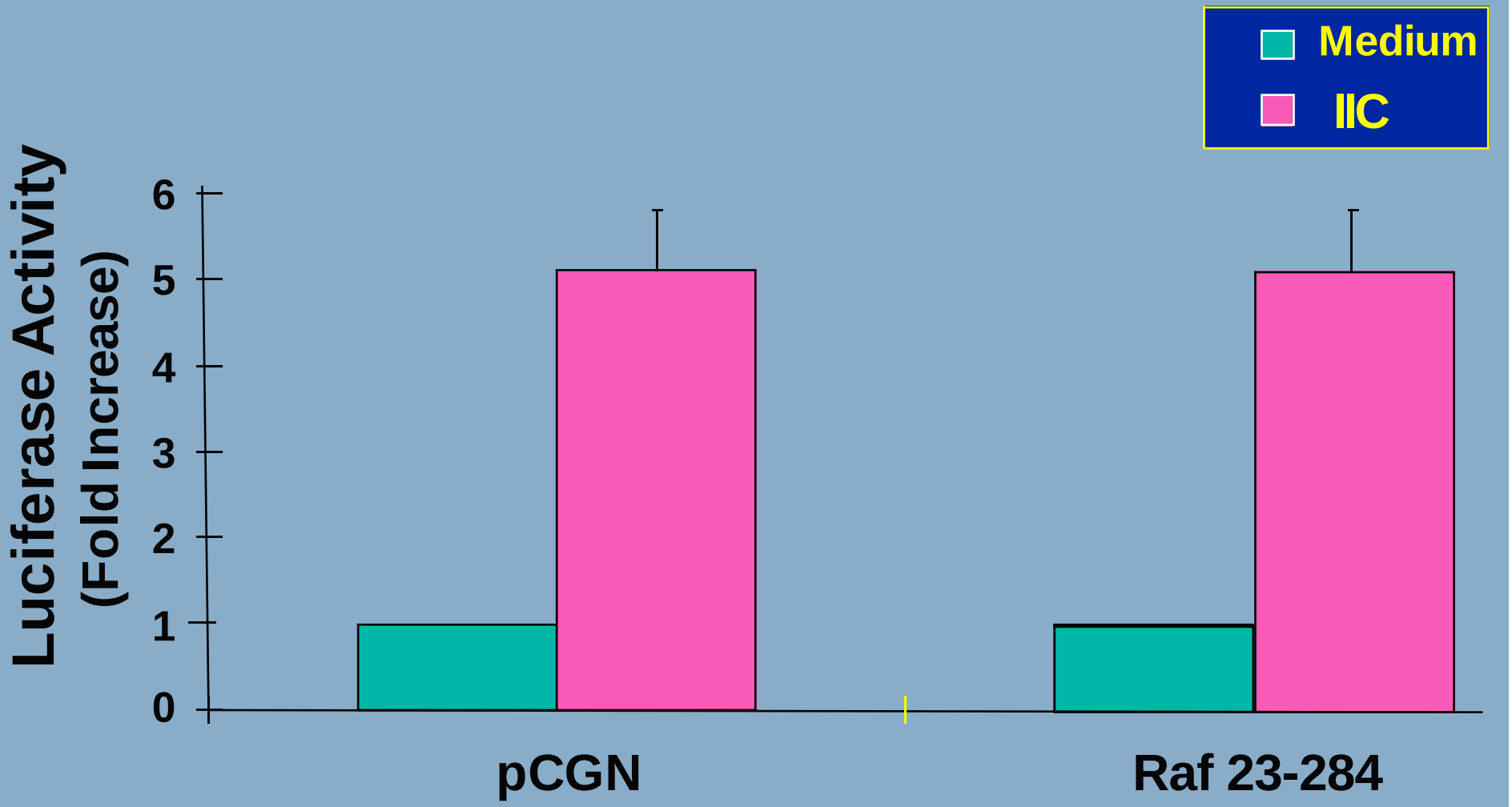
Assay for NF-κB activation



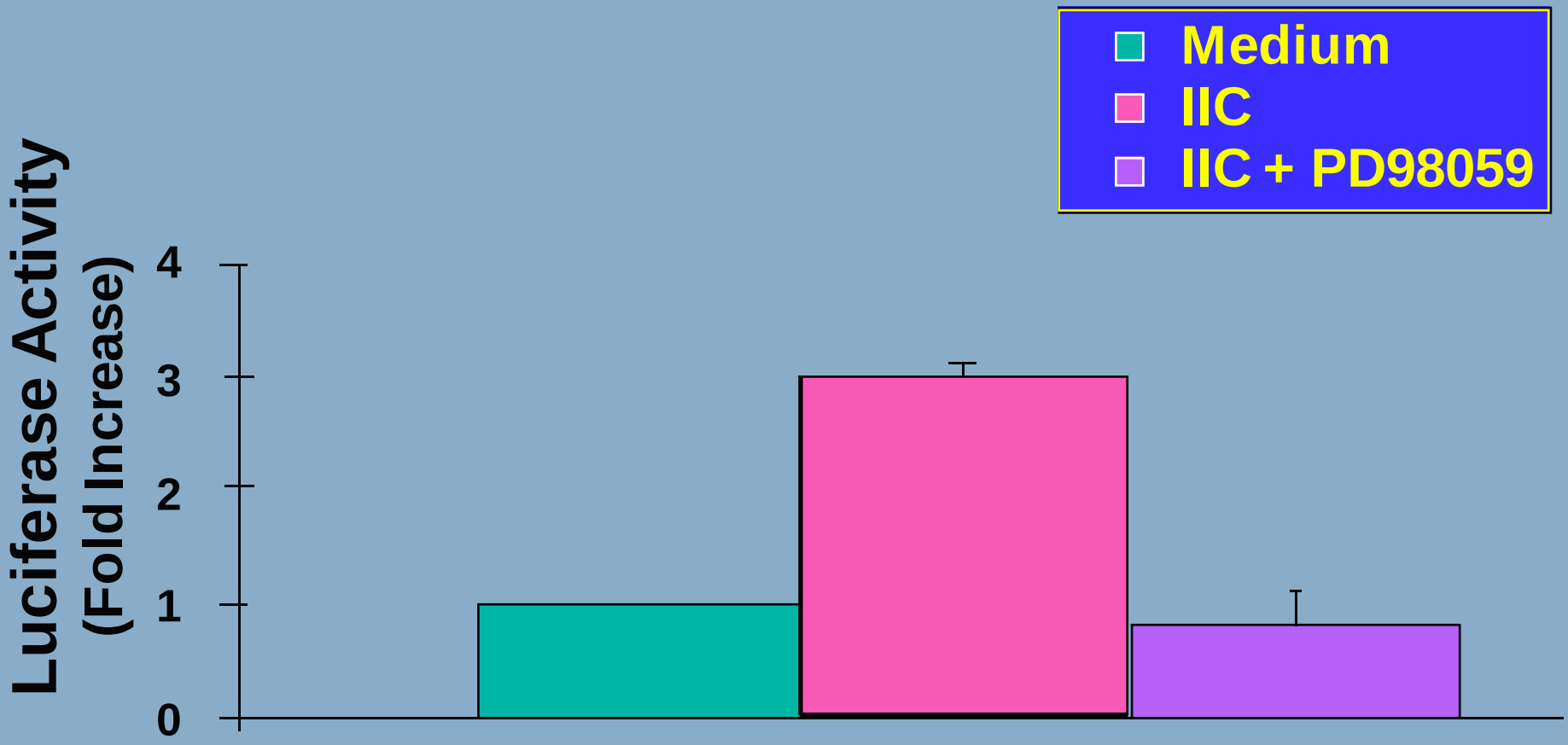
Dominant negative Ras does not inhibit NF-κB activation



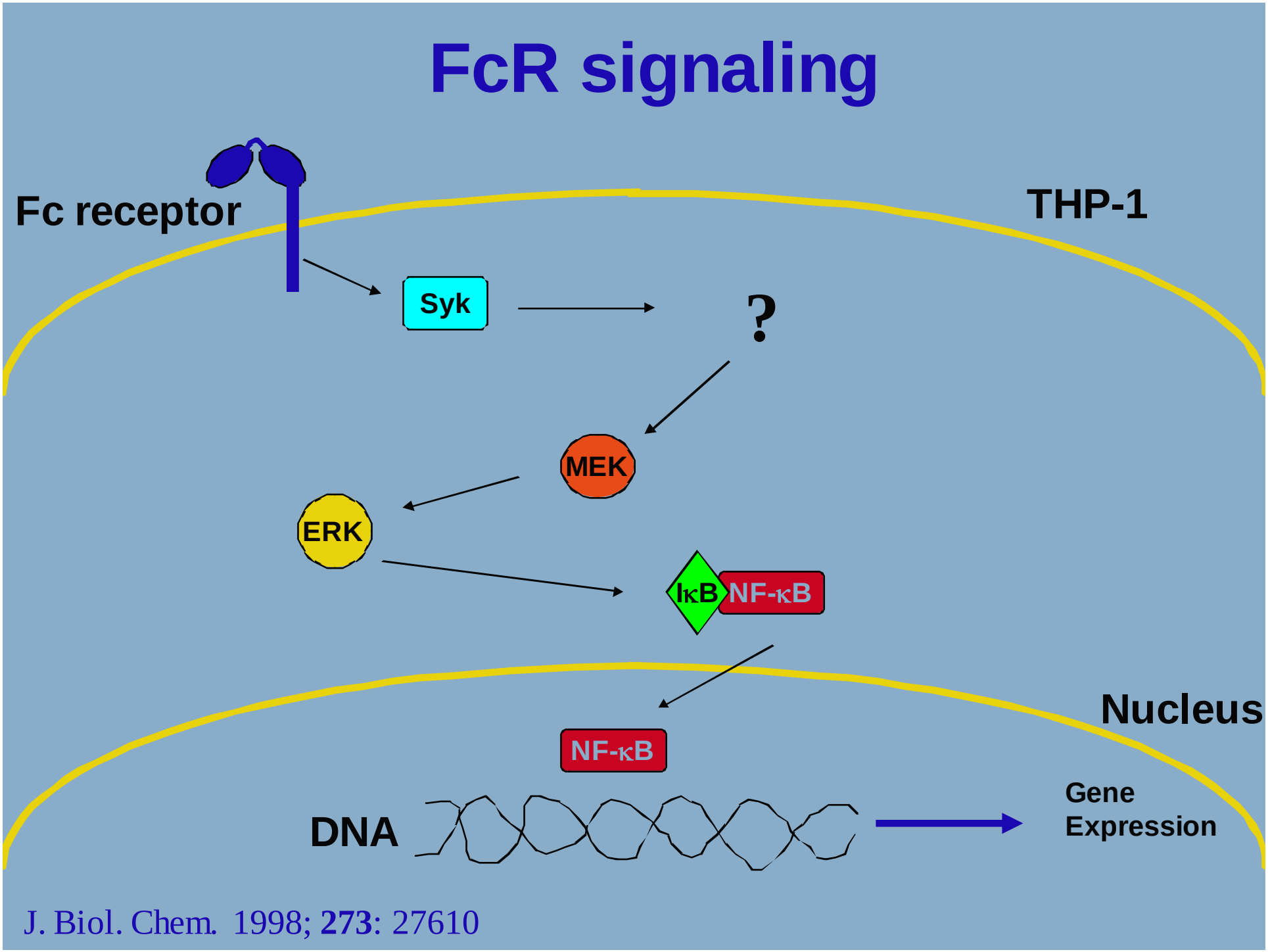
Dominant negative Raf does not inhibit NF-κB activation



MEK is required for immune complex-mediated NF-κB activation

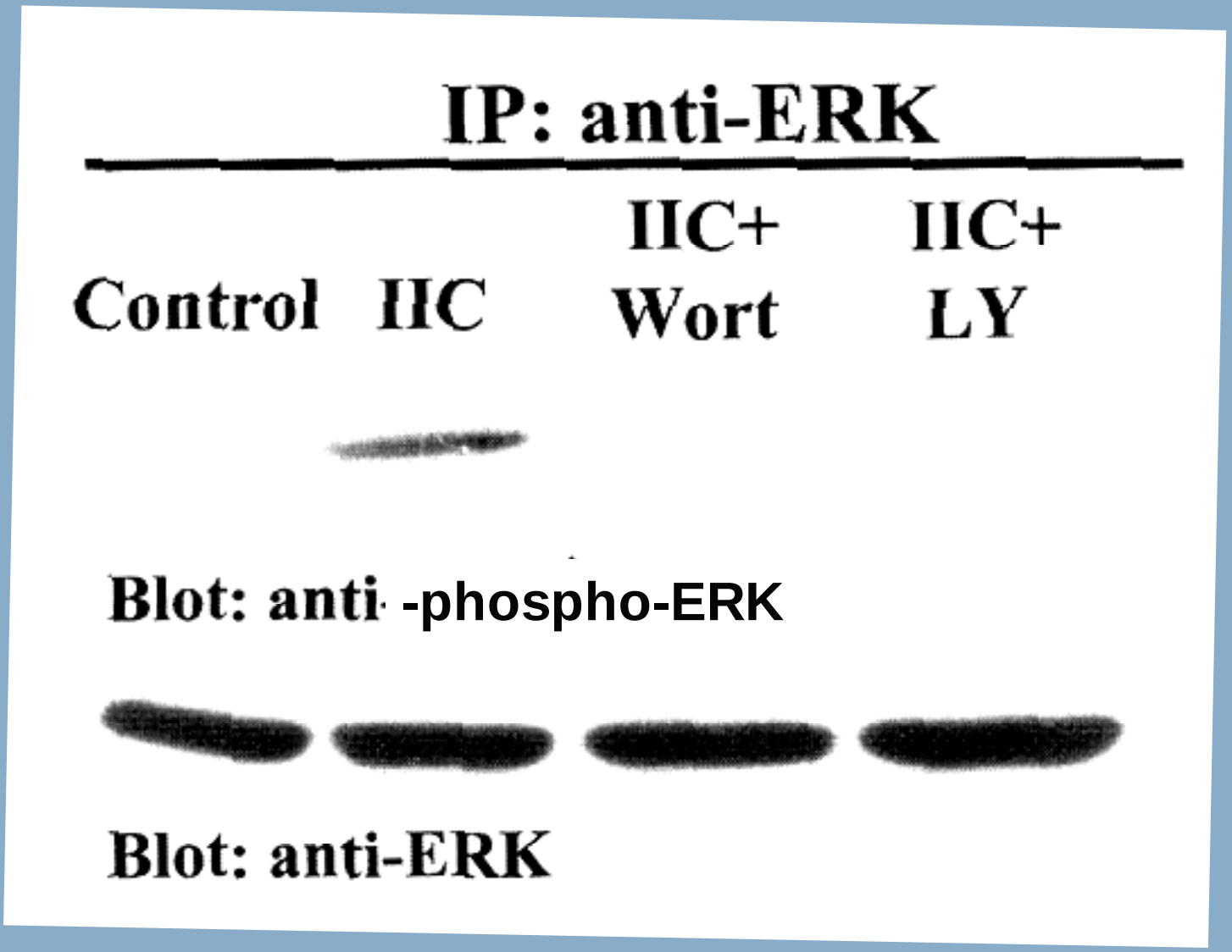


FcR signaling

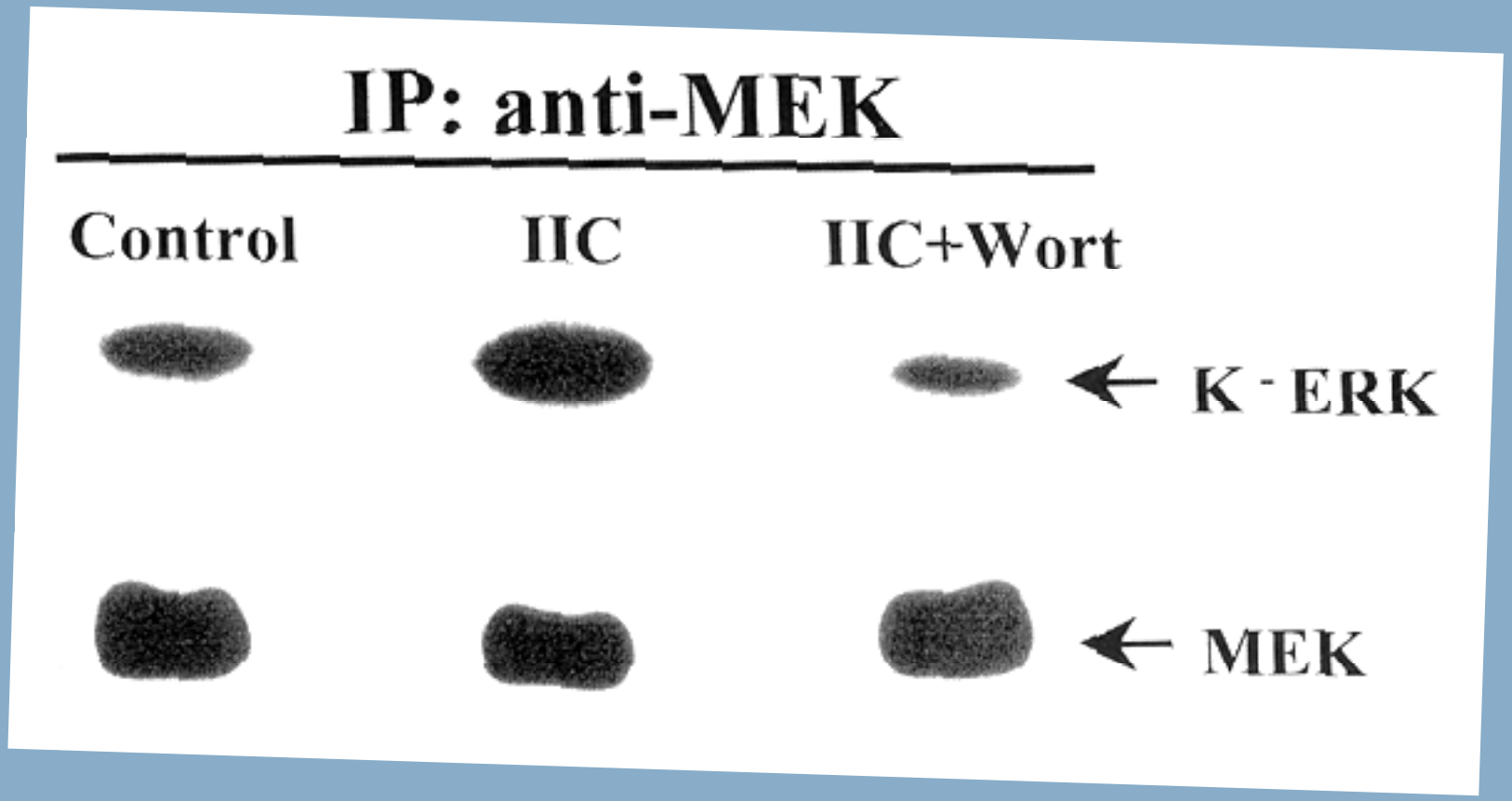


J. Biol. Chem. 1998; **273**: 27610

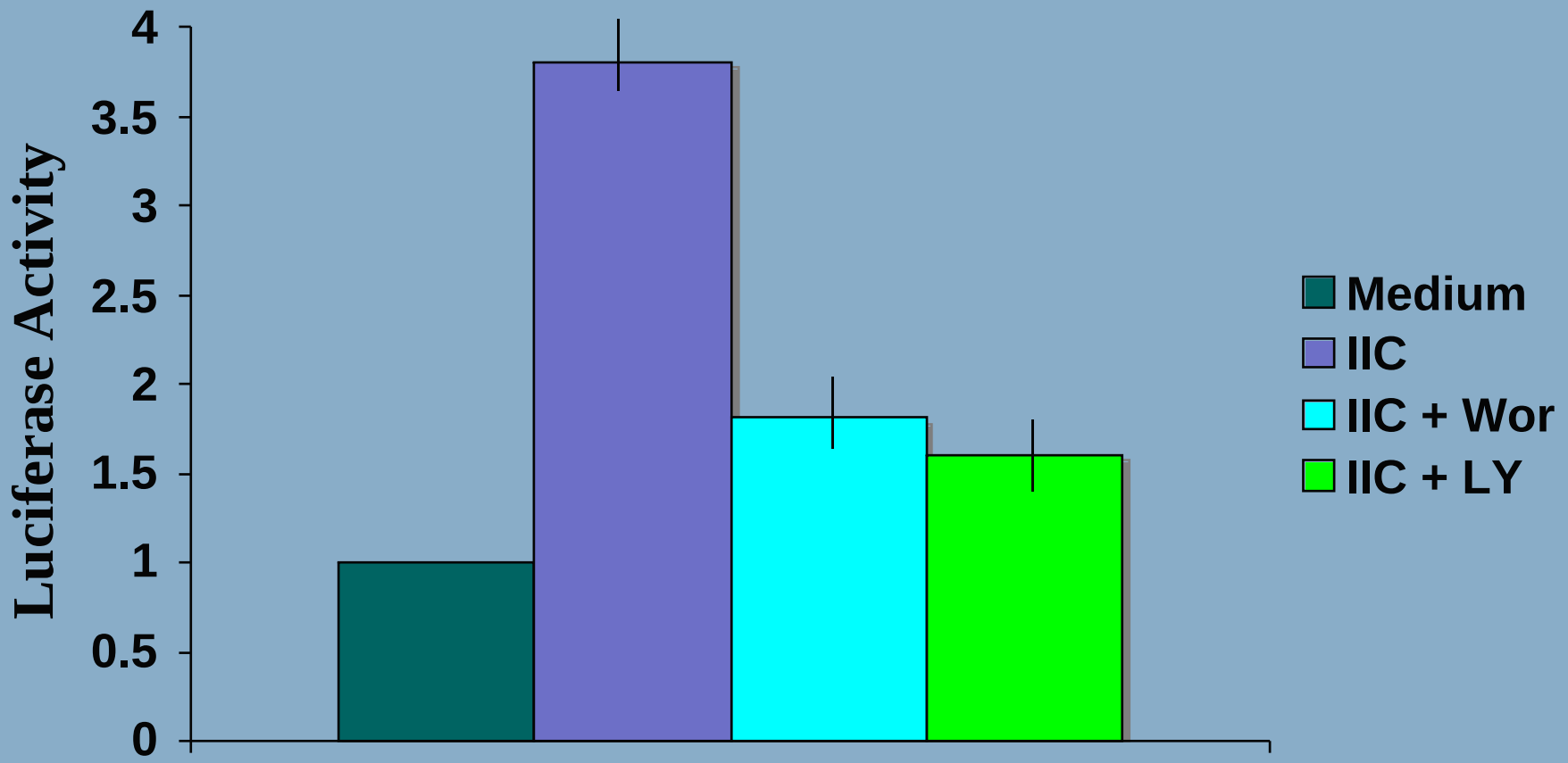
ERK activation requires PI 3-K



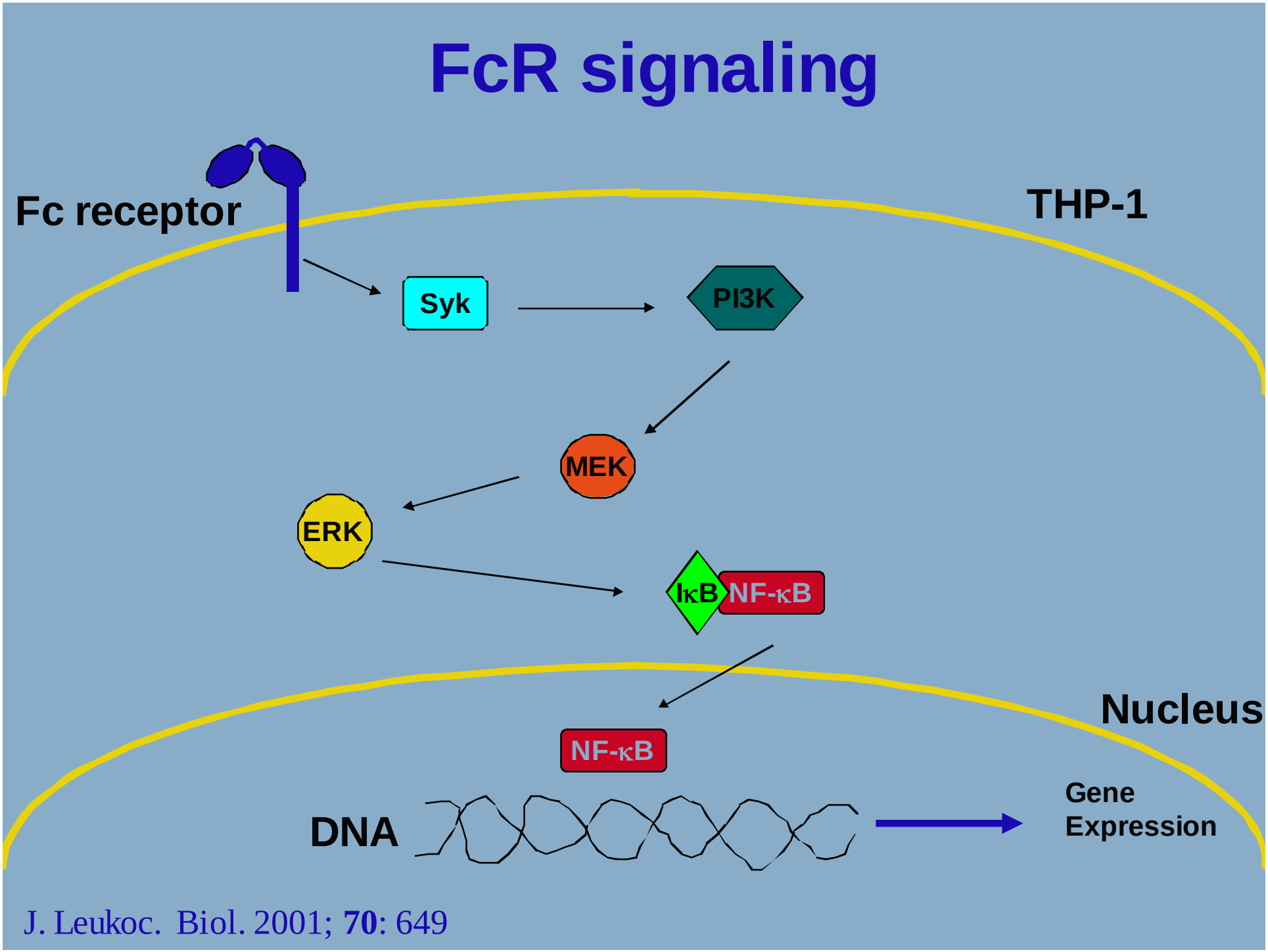
MEK activation depends on PI 3-K



PI 3-K is required for NF-κB activation



FcR signaling

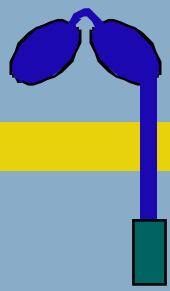


J. Leukoc. Biol. 2001; **70**: 649

Neutrophil Fc Receptors

FcγRIIA

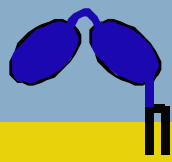
CD32



α

FcγRIIIB

CD16



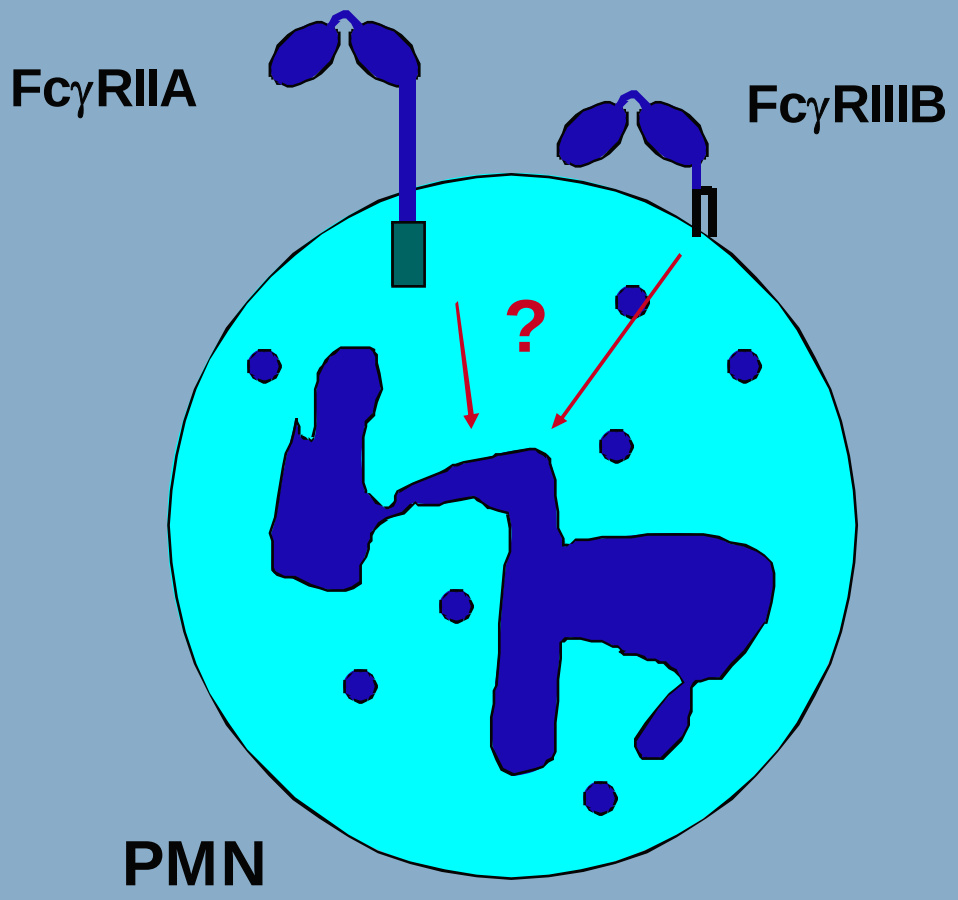
α-GPI

Phagocytosis
Calcium Rise
Degranulation
Respiratory Burst

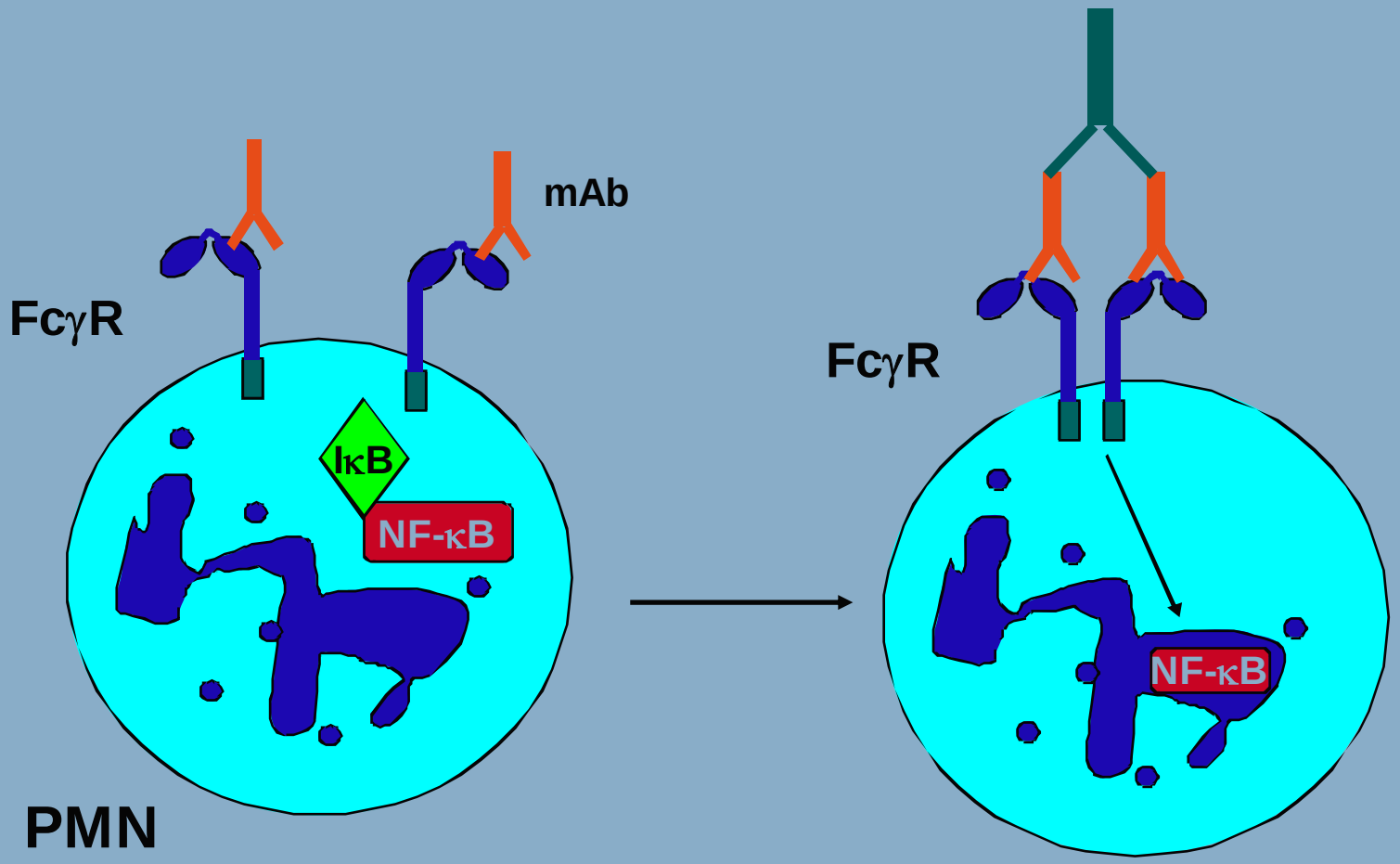
Calcium Rise
Respiratory Burst
Actin assembly
Integrin activation

J. Biol. Chem. 1992; 267: 5265
Biochem. Biophys. Acta 1999; 1452: 46
J. Leukoc. Biol. 2005; 15: 203

Are FcRIIA and FcRIIIB Signaling Different?

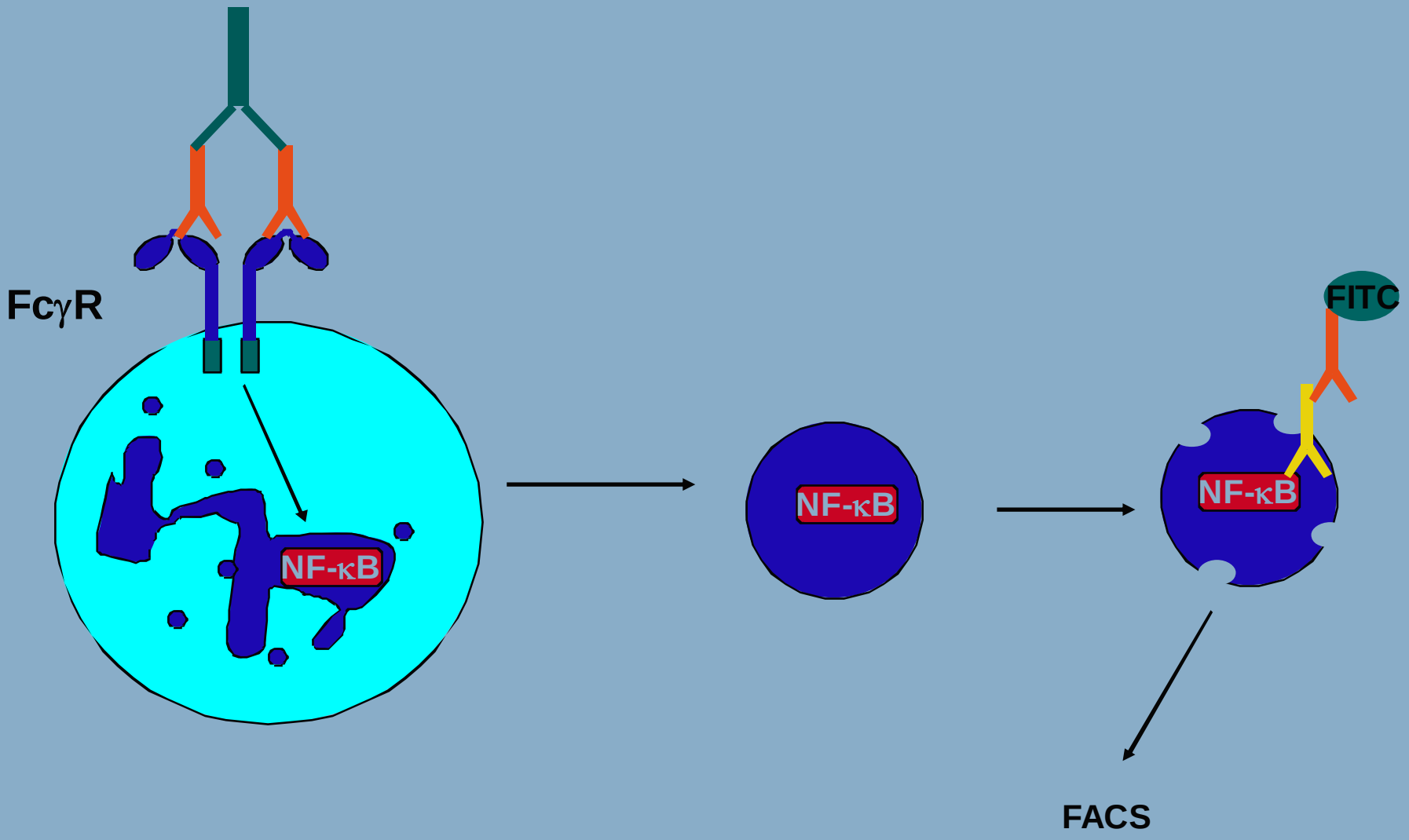


Nuclear Factor Activation



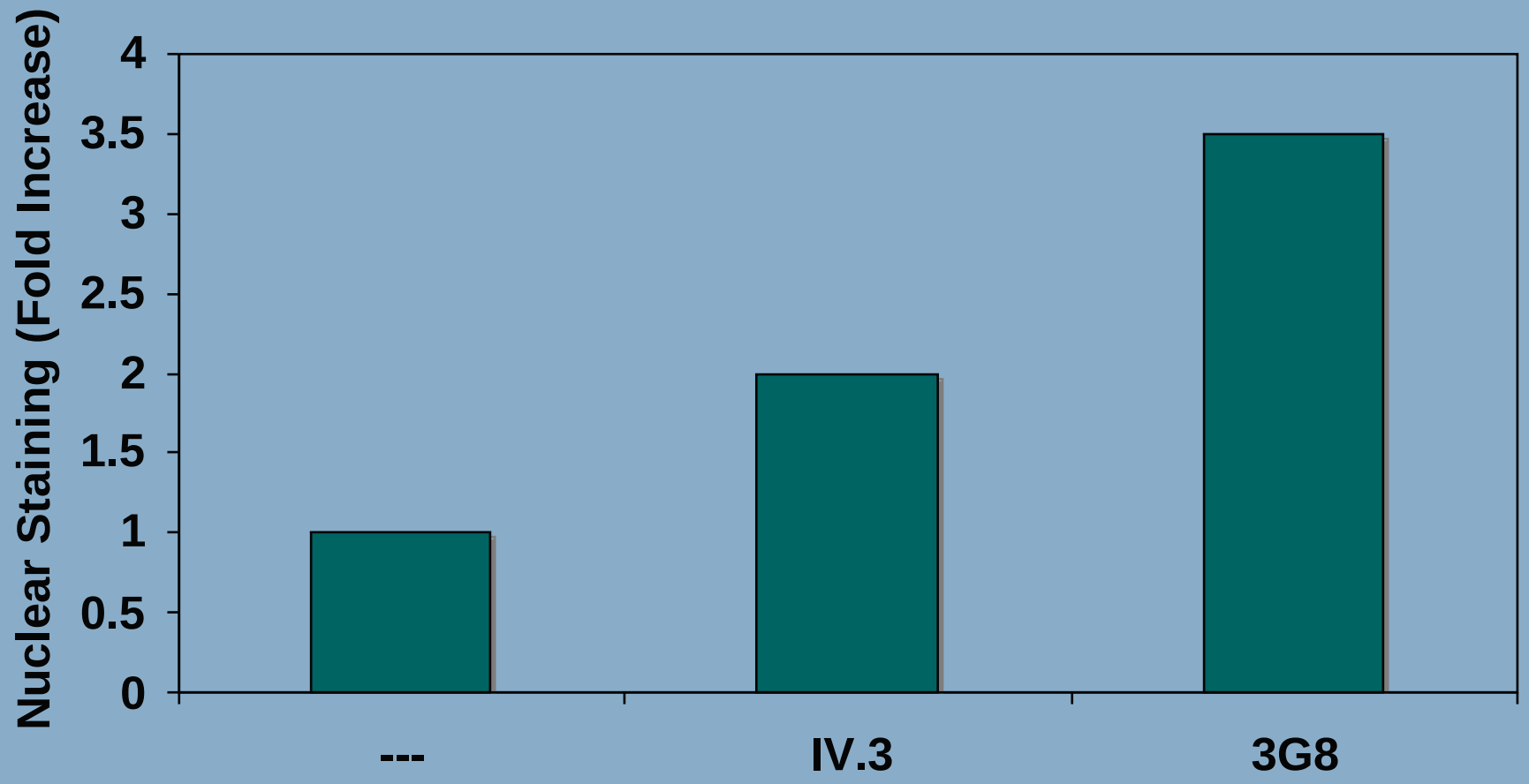
J. Immunol. Meth. 2007; 320: 104

Nuclear Factor Activation

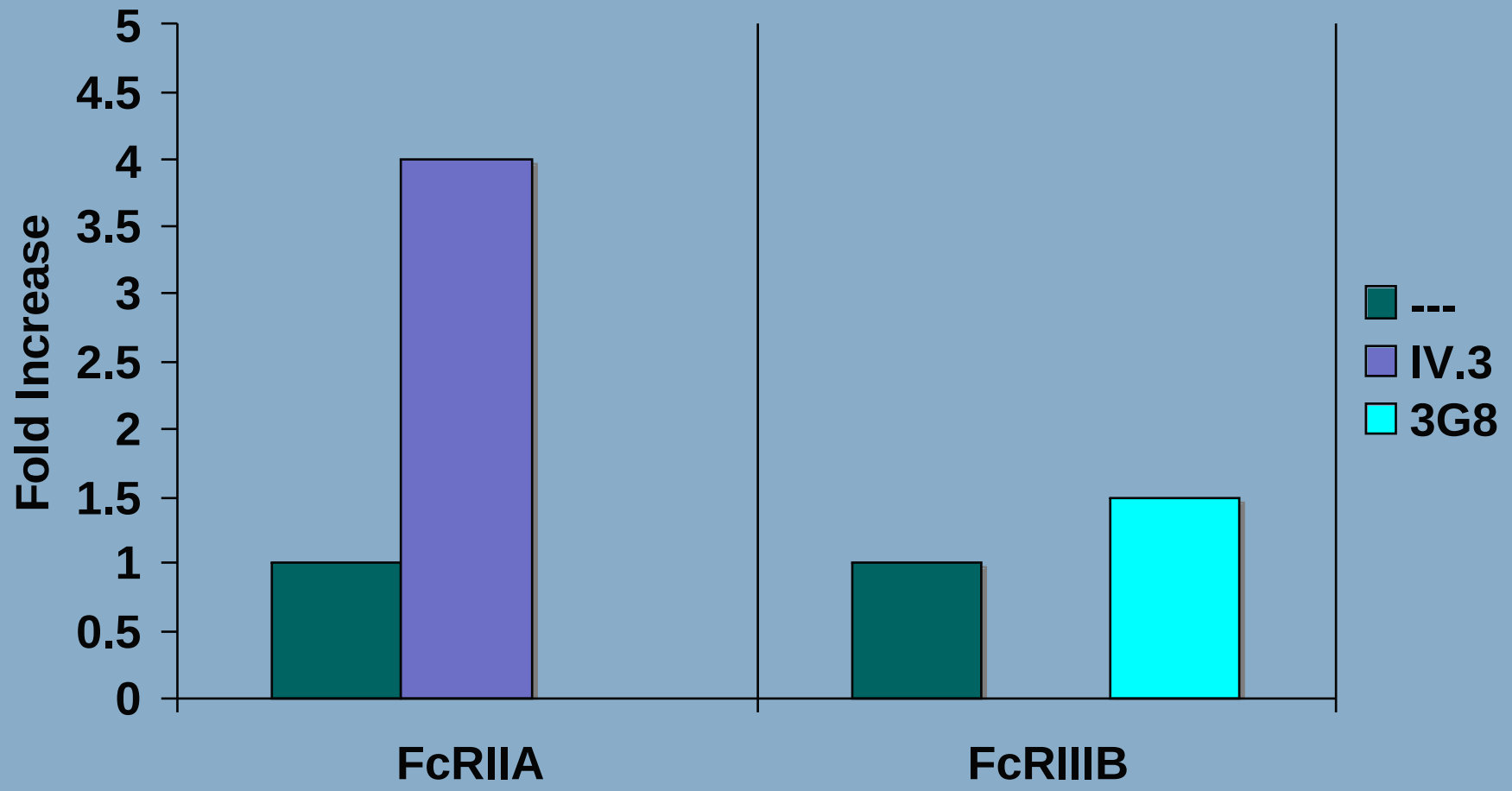


J. Immunol. Meth. 2007; 320: 104

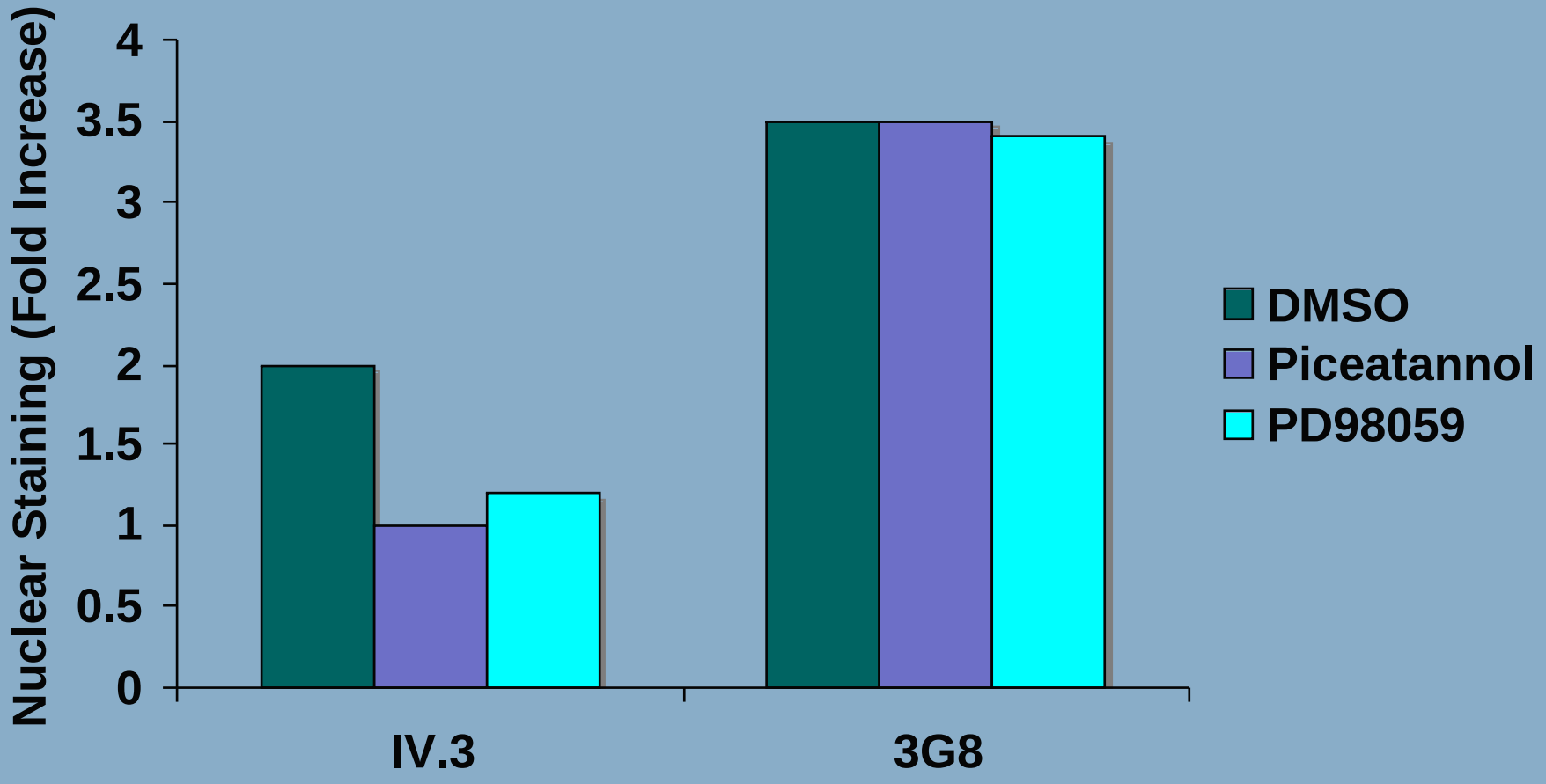
NF-κB Activation



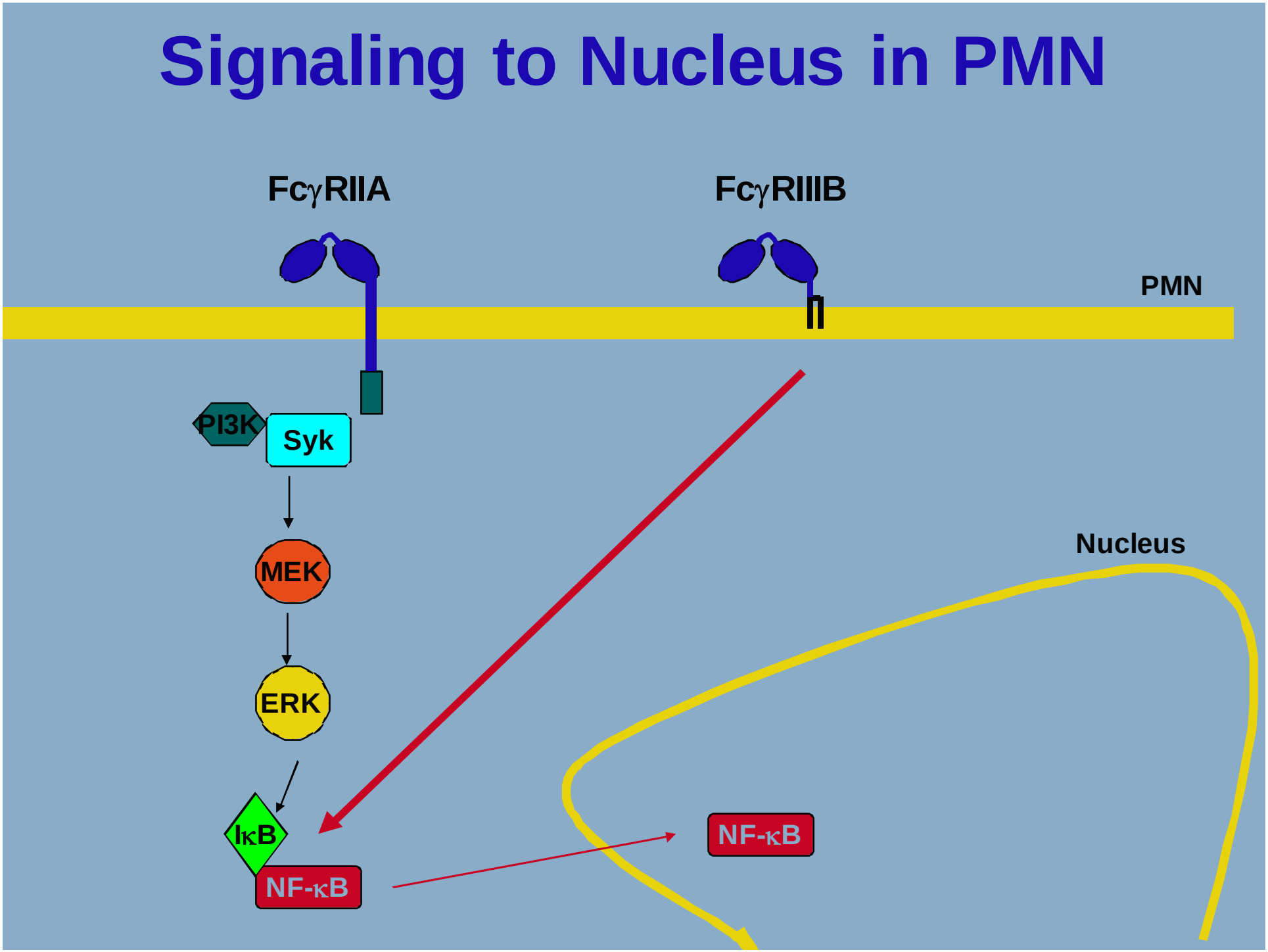
Phagocytosis



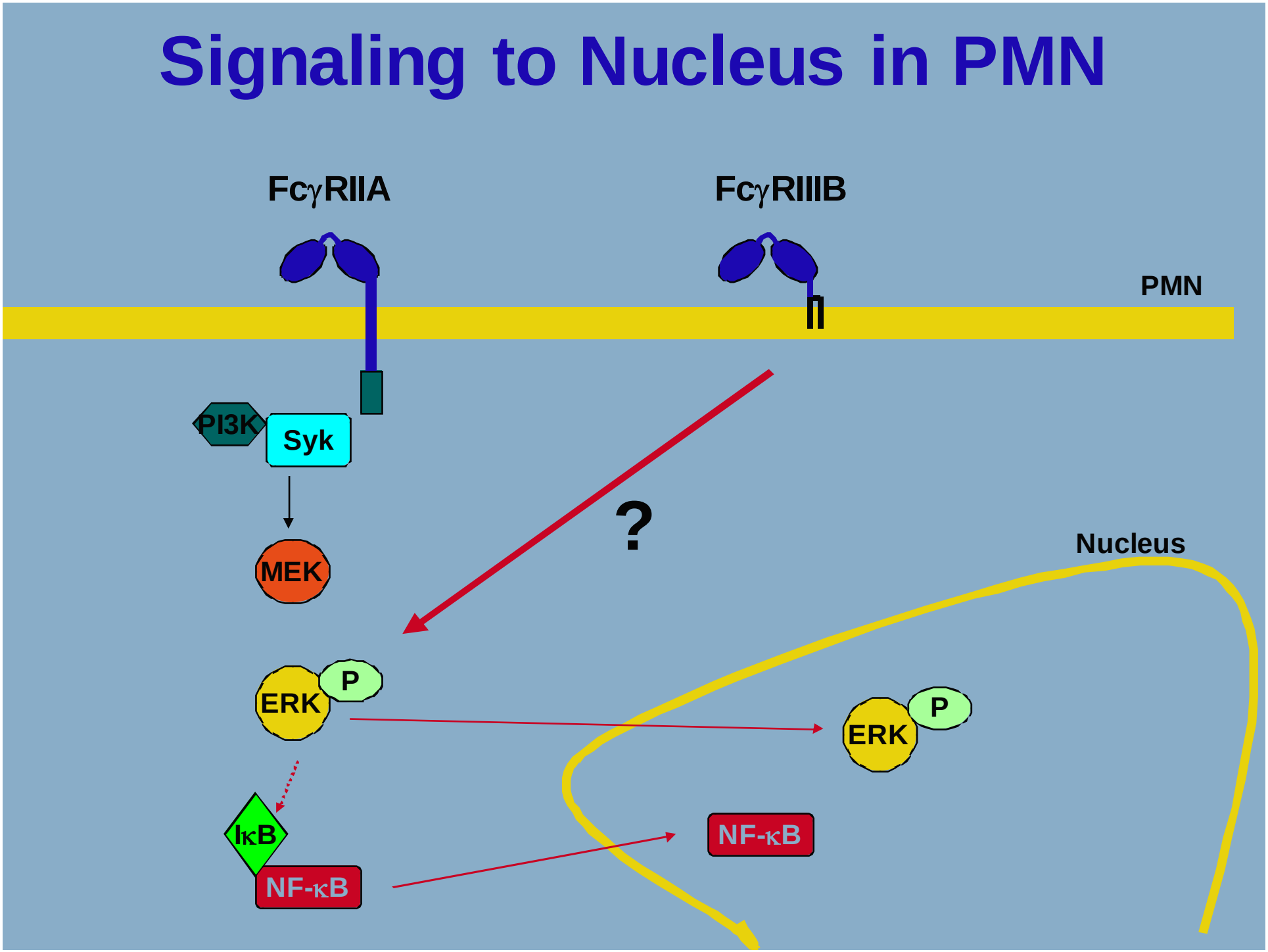
FcRIIIB signal to NF-κB is independent of Syk and MEK



Signaling to Nucleus in PMN

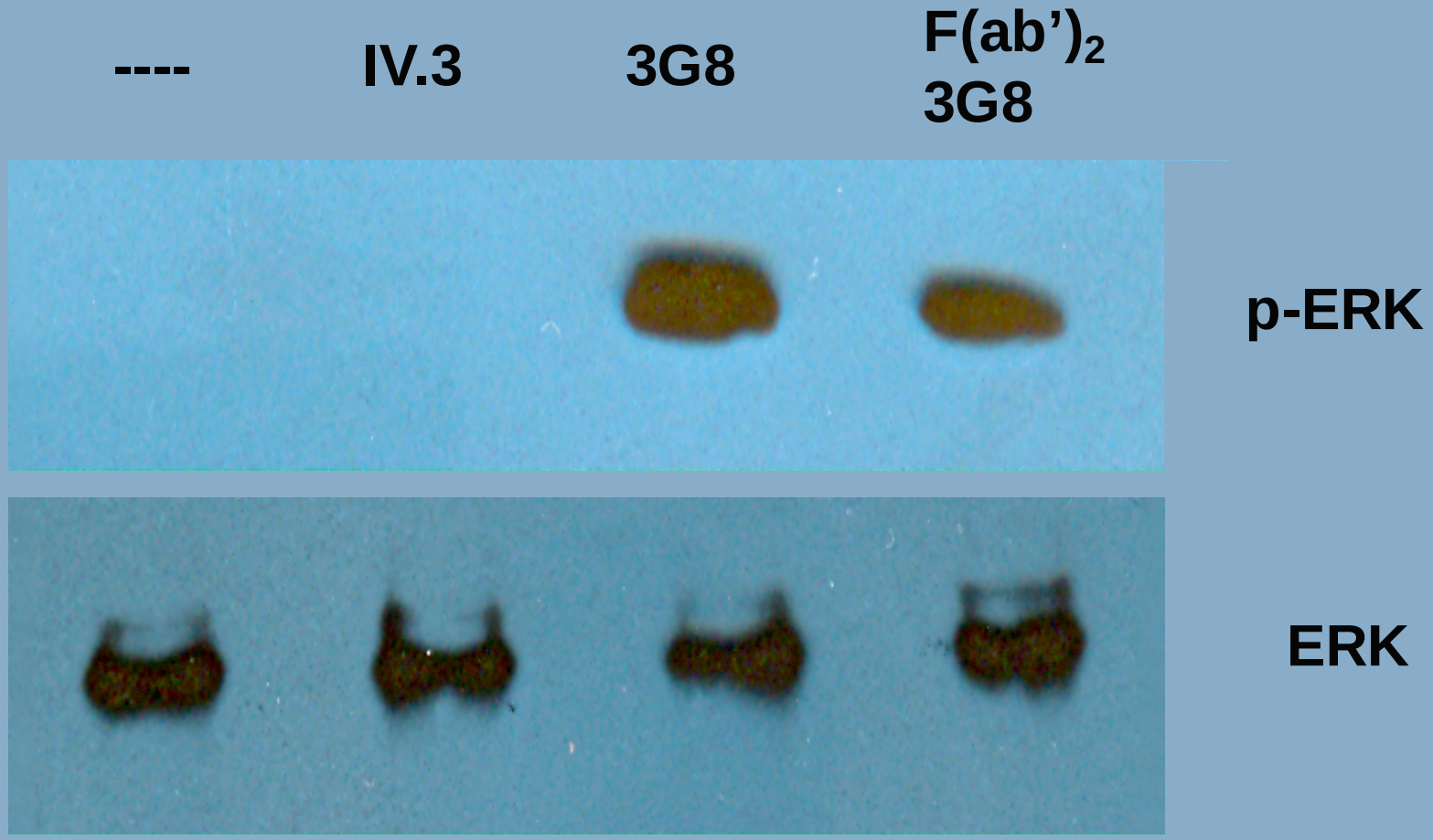


Signaling to Nucleus in PMN

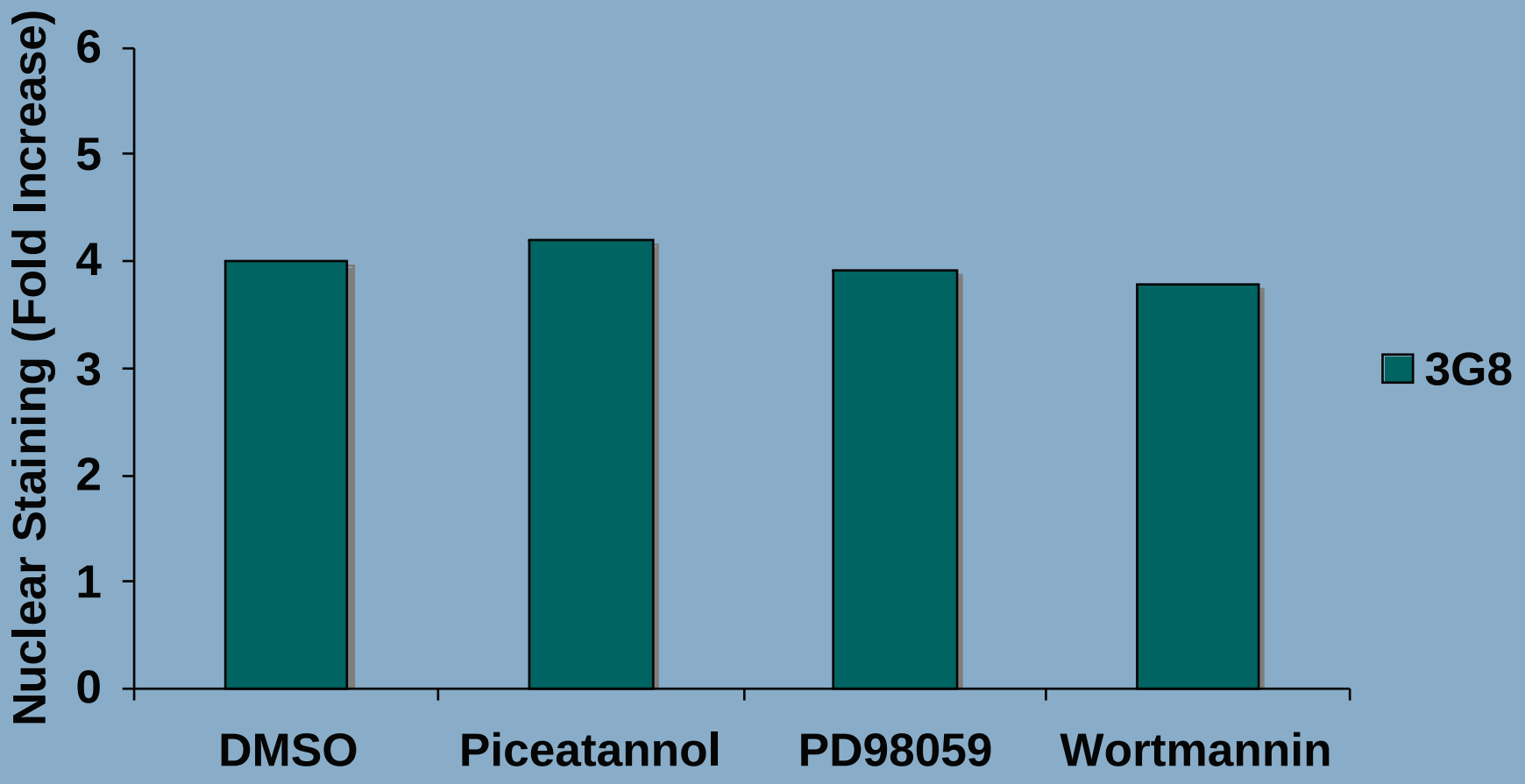


Nuclear phospho-ERK

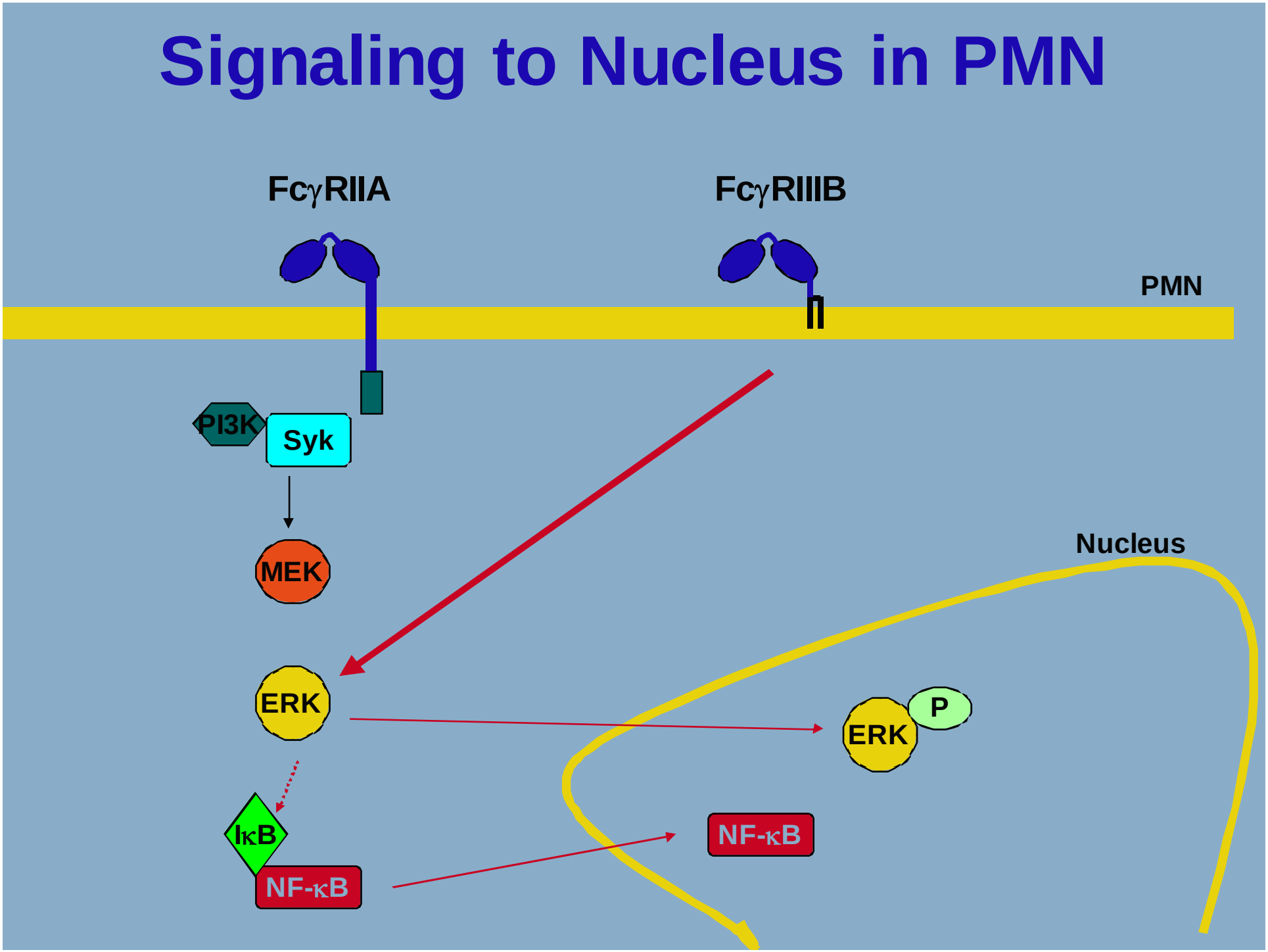
Nuclear phospho-ERK



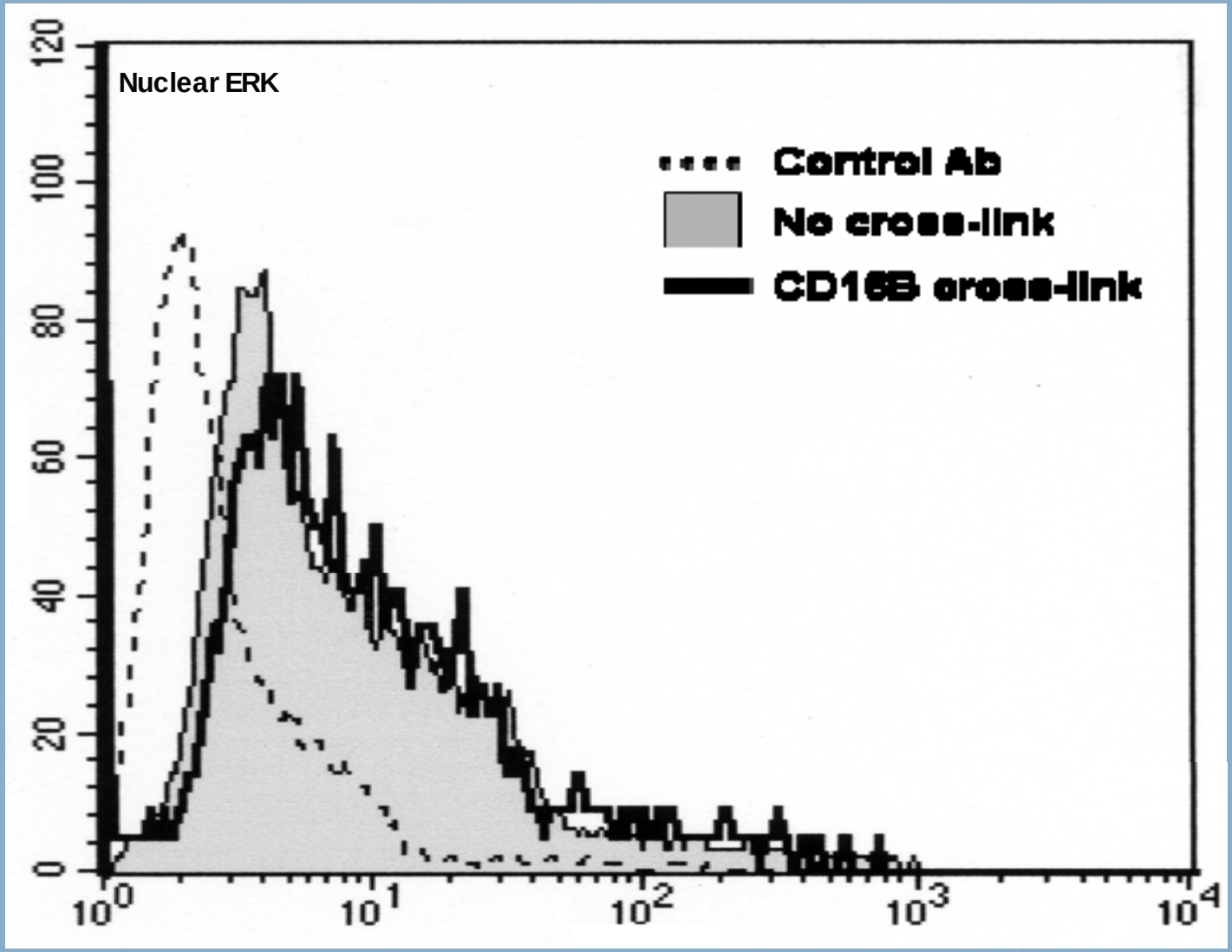
Nuclear phopho-ERK is independent Syk, MEK, and PI 3-K



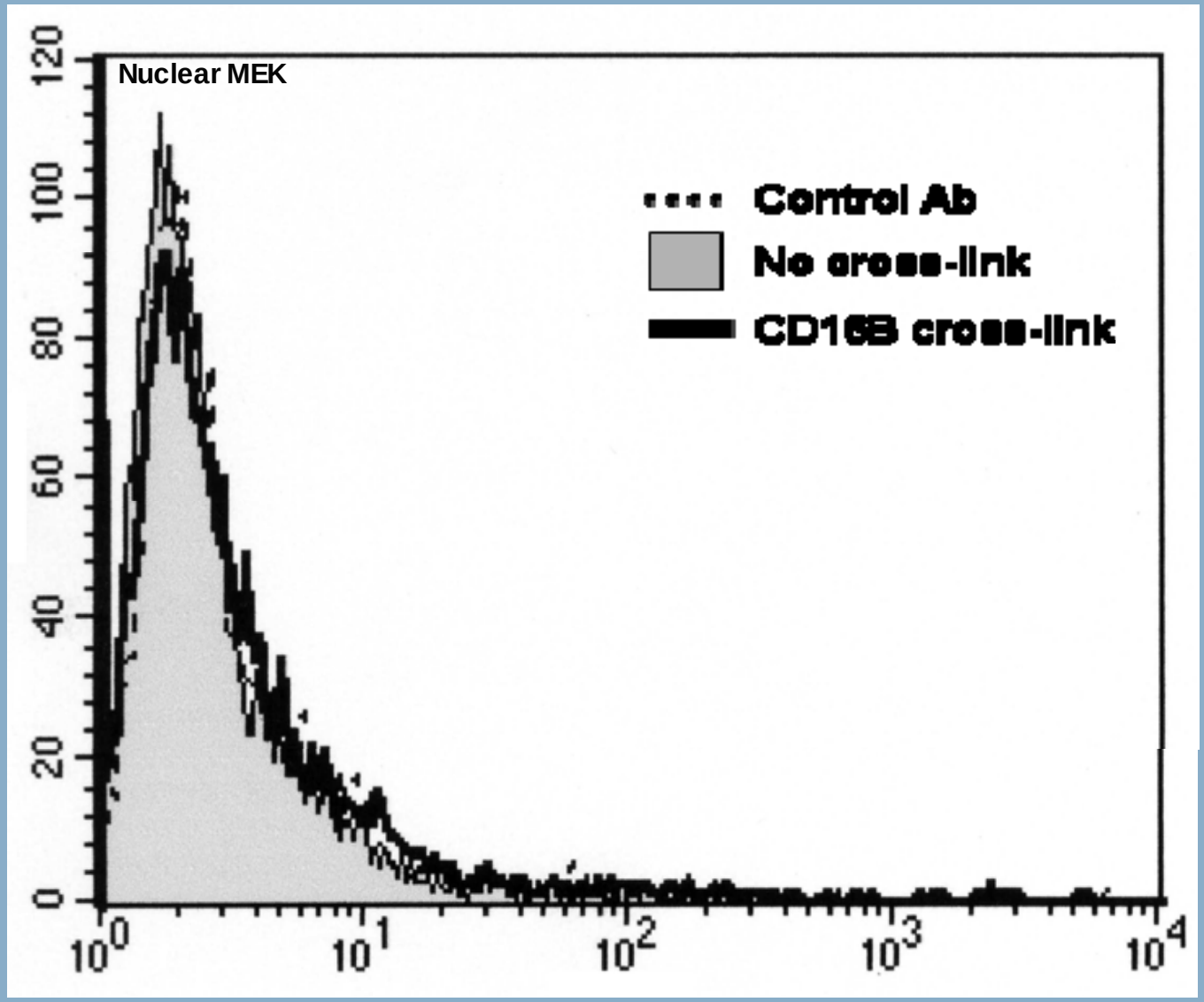
Signaling to Nucleus in PMN



Nuclear ERK does not change after FcγRIIIB crosslinking

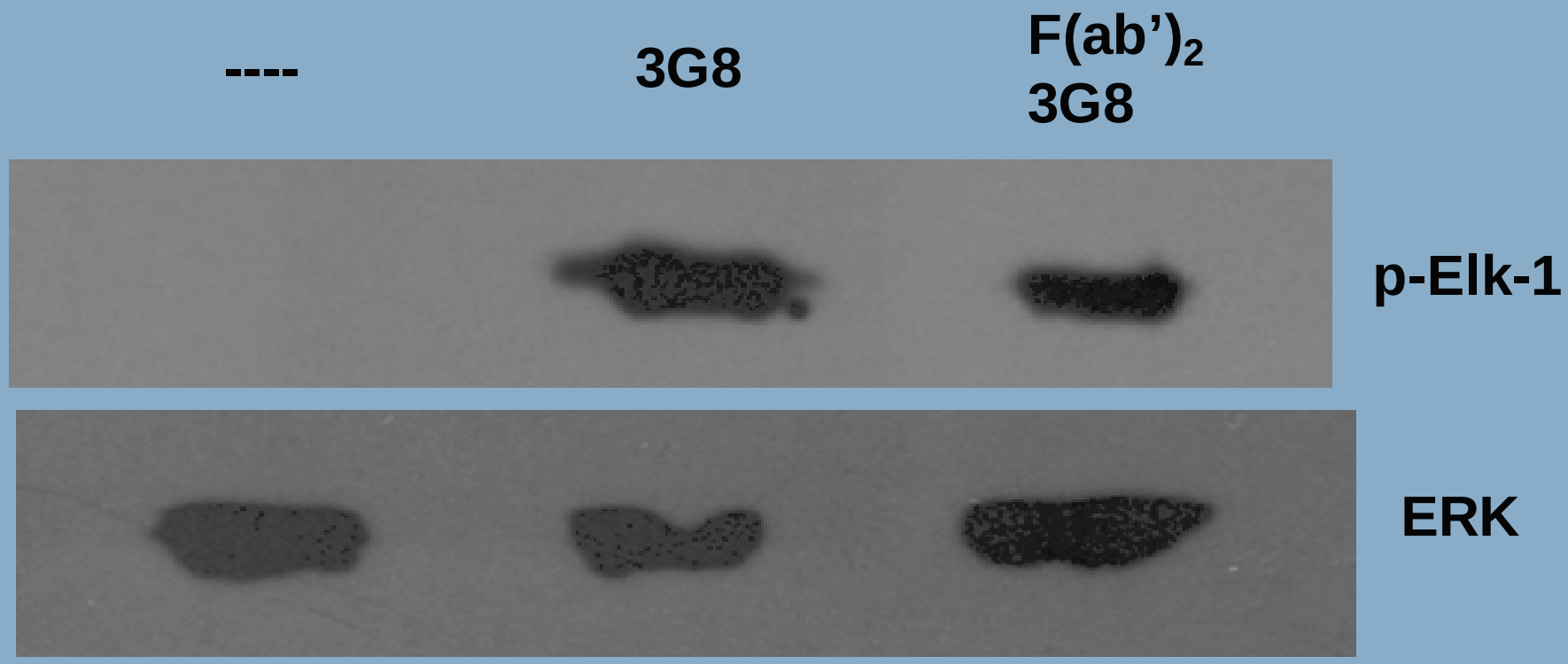


MEK is not present in PMN nucleus

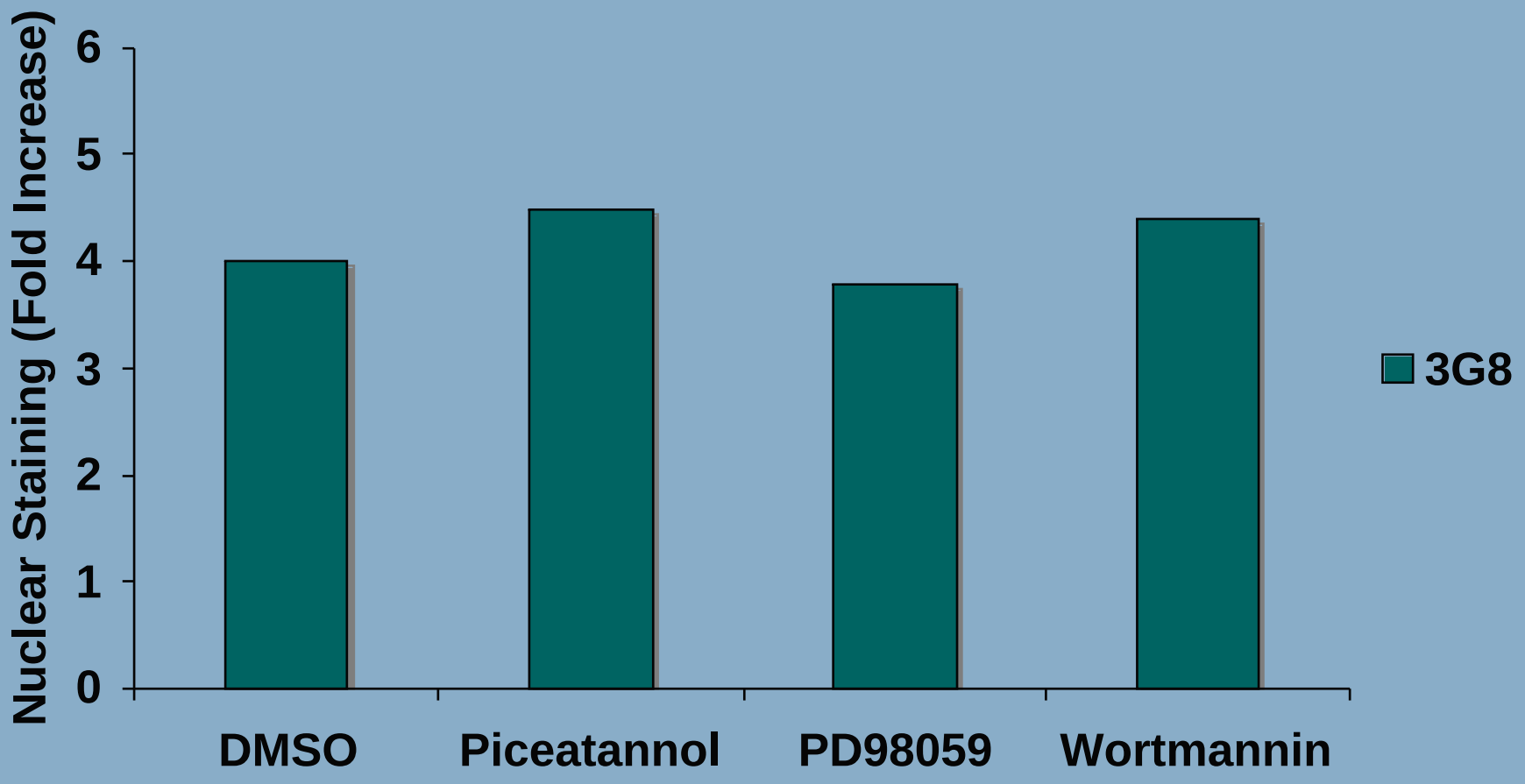


Nuclear phospho-Elk-1

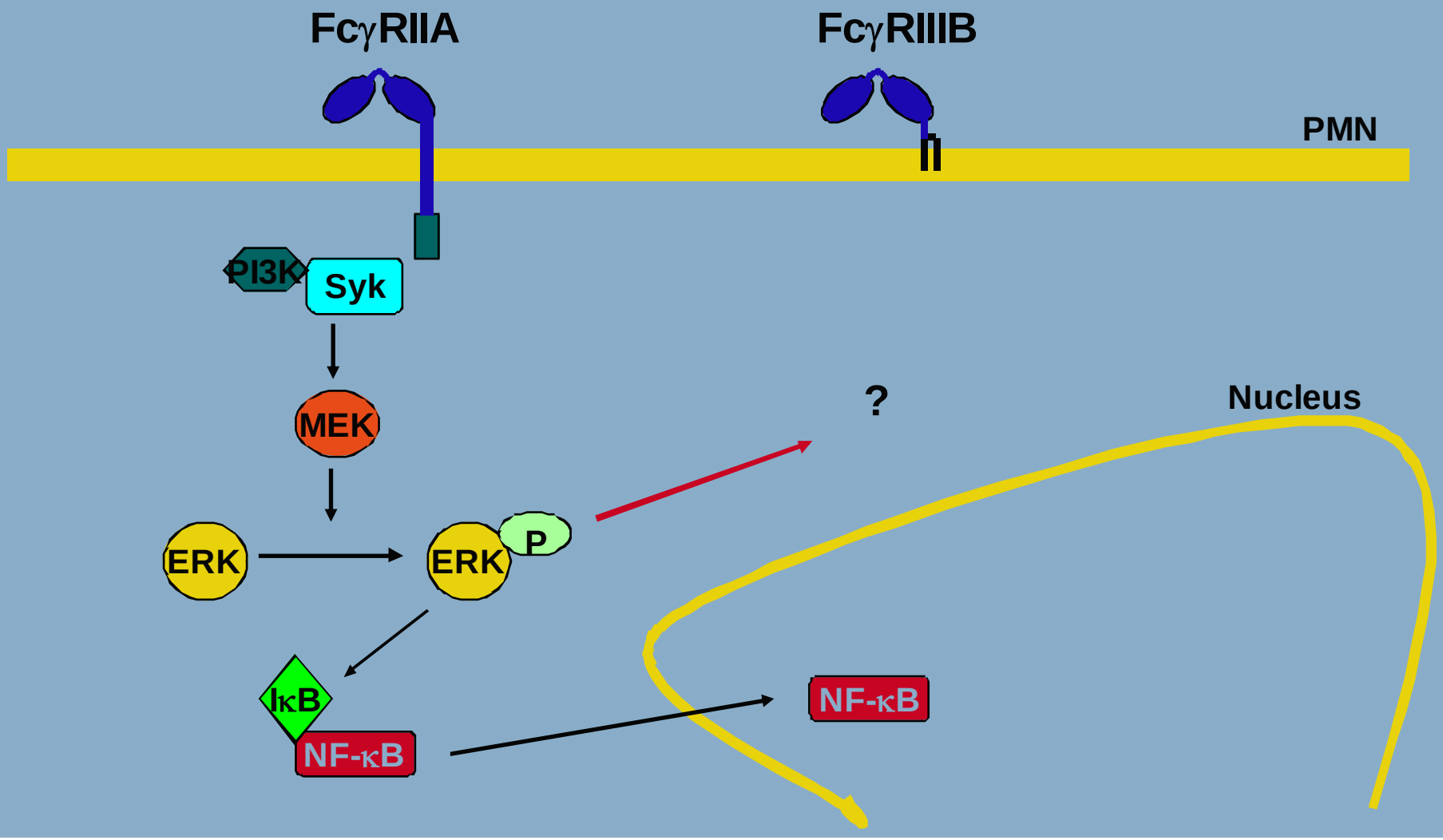
Nuclear phospho-Elk-1



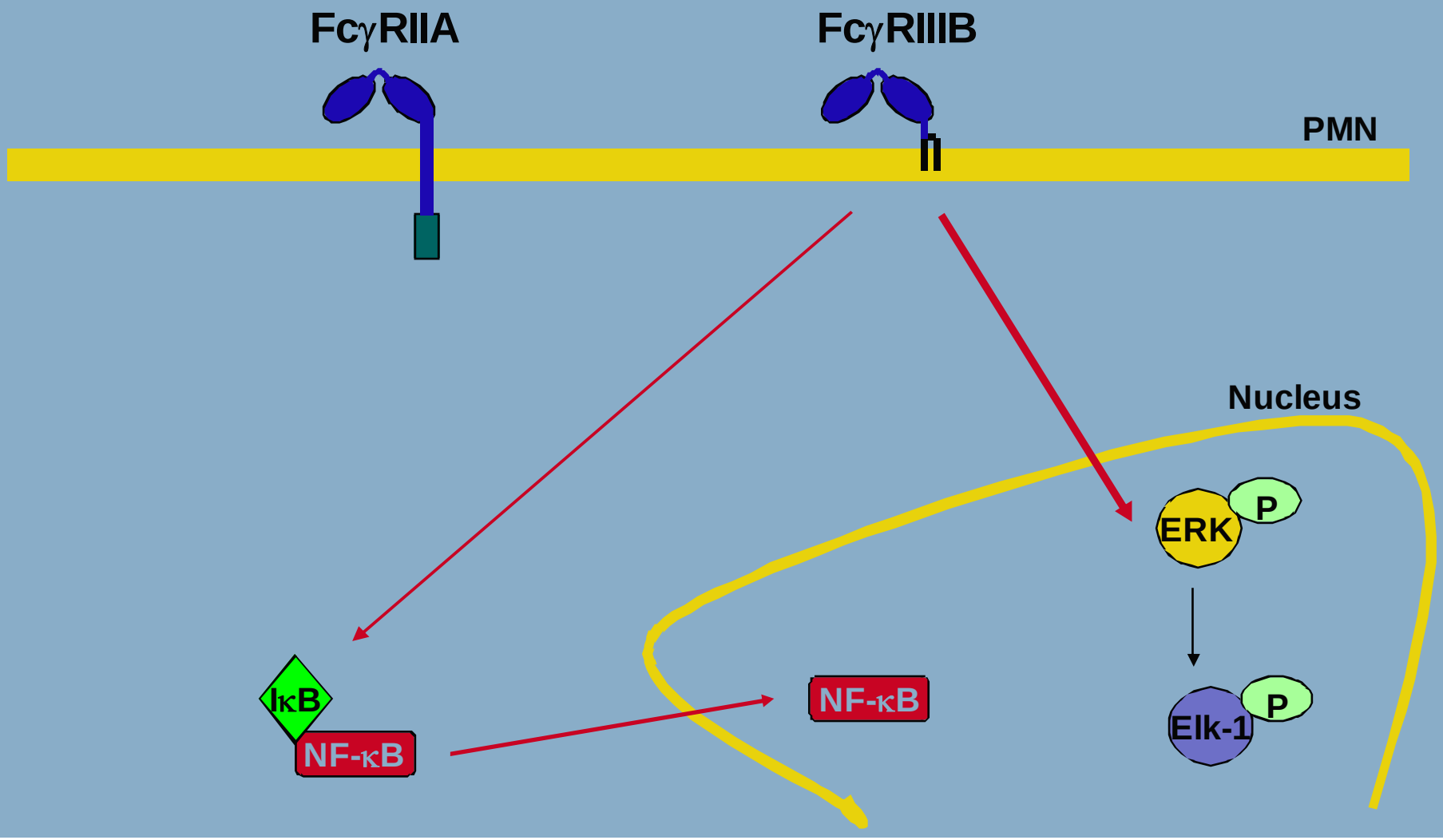
Nuclear phopho-Elk-1 is independent Syk, MEK, and PI 3-K



FcγR activation of ERK in PMN cytoplasm



FcγRIIIB activates nuclear factors in PMN



Conclusions

- **FcγRIIA and FcγRIIIB signal differently in the PMN**
- **FcγRIIA induces efficient phagocytosis**
- **FcγRIIIB induces efficient ERK and Elk-1 activation**
- **FcγRIIIB signal transduction does not involve Syk, MEK, PI 3-K, Src family kinases, or Tec family kinases**

Acknowledgments

- Gabriela Sánchez-Mejorada
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